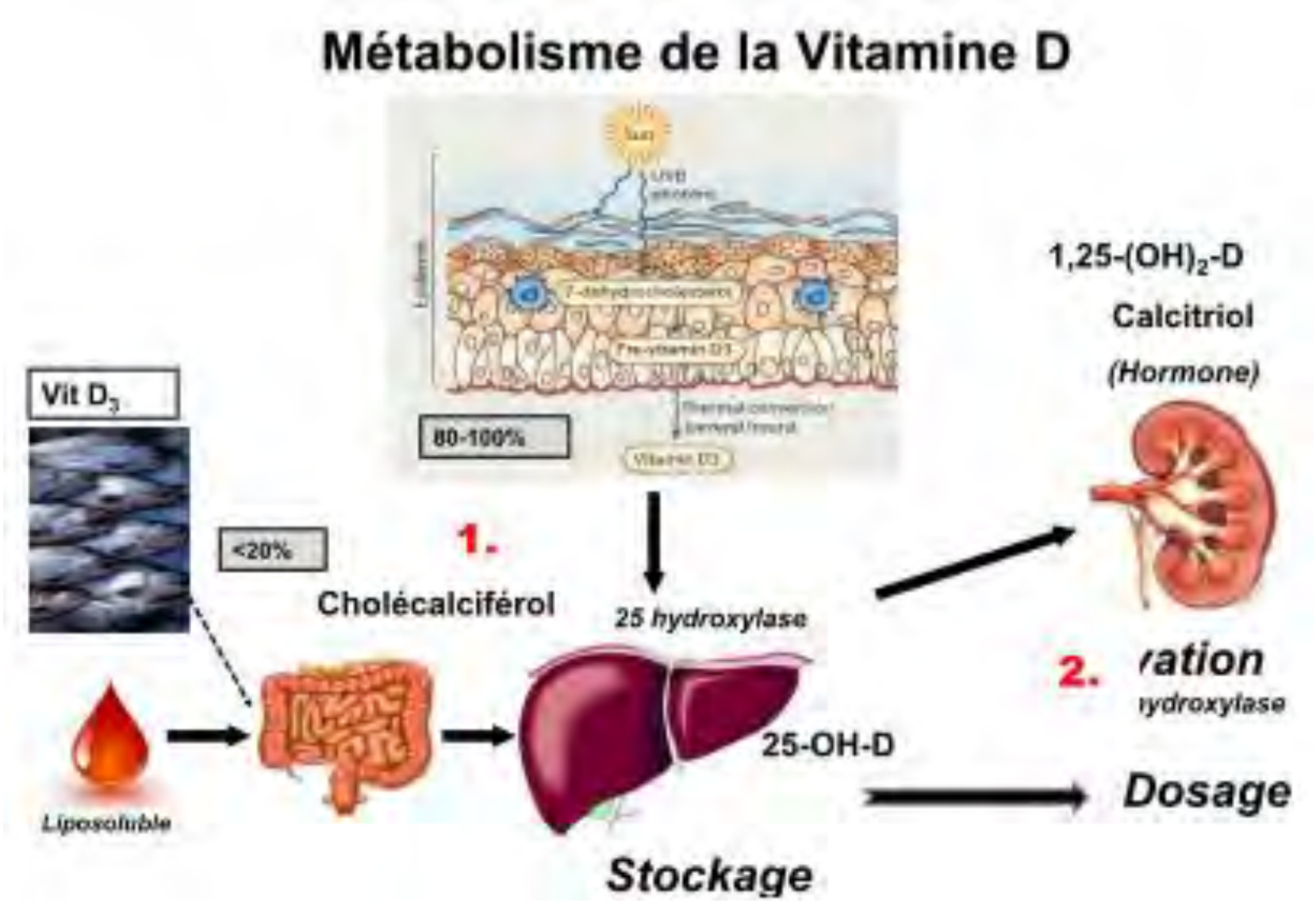
Utilité du dosage de la vitamine D

Physiologie



Définition

- Carence < 25 nmol/L
- Insuffisance 25-50 nmol/L

Apports

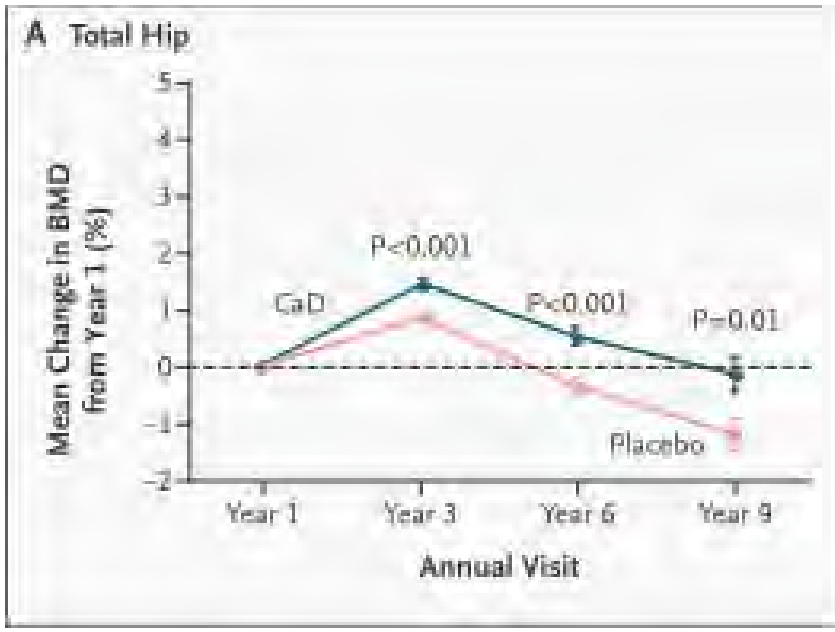
- UV-B

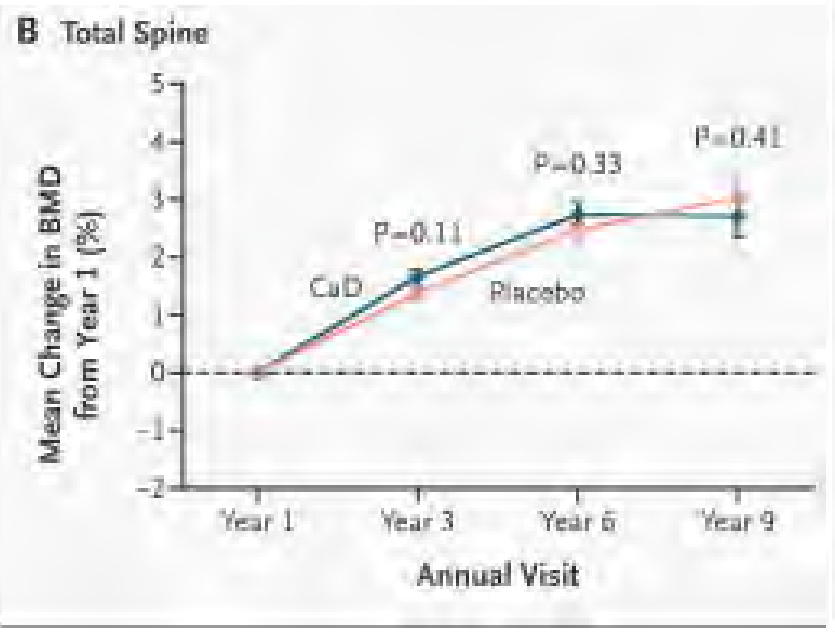
- Alimentaires

Aliments	Portion	Vitamine D (UI)
Saumon sauvage	100 g	600-1000
Saumon d'élevage	100 g	100-250
Sardine en conserve	100 g	300-600
Maquereaux en conserve	100 g	250
Thon en conserve	100 g	236
Huile de foie de morue	1 cuillère à soupe	400-1000
Champignons shiitake frais	100 g	100
Champignons shiitake séchés	100 g	1600
Jaune d'oeuf	par jaune	20
Champignons frais (Suisse)	100 g	76
Beurre	100 g	52
Fromage Emmental	100 g	44

- Augmentation importante du dosage de la vitamine D
- Augmentation de 250% entre 2007 et 2009 en France
- Coût: 92 M d’euros en France en 2011
- Dosage en Suisse coûte 50 CHF
- Substitution sur un an: 20 CHF

Dosage chez le sujet sain?


A Total Hip
Mean Change in BMD from Year 1 (%)
5
4
3
2
1
0
−1
−2
P<0.001
CaD
P<0.001
P=0.01
Placebo
Year 1
Year 3
Year 6
Year 9
Annual Visit


B Total Spine
Mean Change in BMD from Year 1 (%)
5
4
3
2
1
0
−1
−2
P=0.11
P=0.33
P=0.41
CaD
Placebo
Year 1
Year 3
Year 6
Year 9
Annual Visit

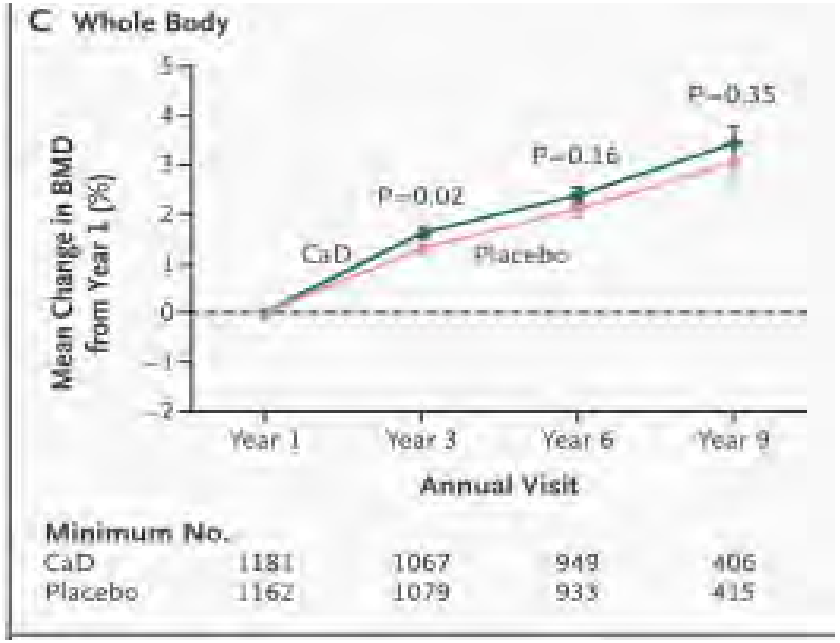
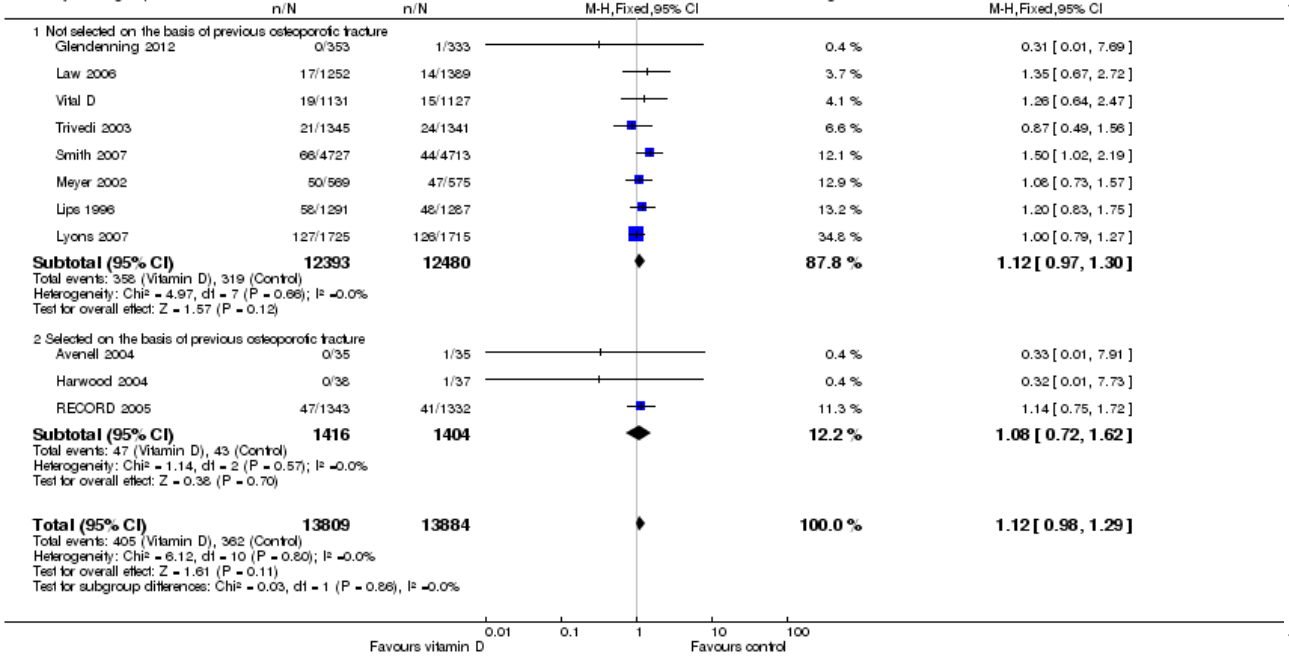

C Whole Body
Mean Change in BMD from Year 1 (%)
5
4
3
2
1
0
−1
−2
P=0.02
P=0.16
P=0.35
CaD
Placebo
Year 1
Year 3
Year 6
Year 9
Annual Visit
Minimum No.
CaD 1181 1067 949 406
Placebo 1162 1079 933 415

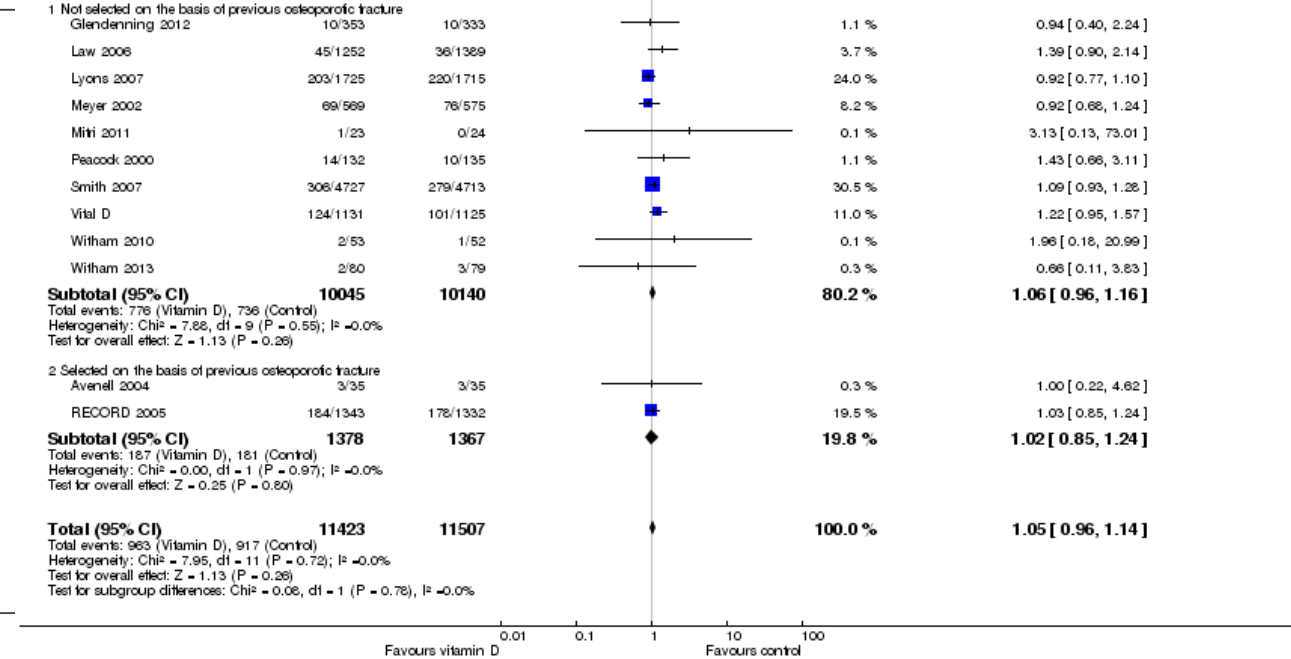
Table 4. Odds Ratios for Hip Fracture and Total Fractures According to Quartiles of Serum 25-Hydroxyvitamin D Level and Study Group, as Determined in a Nested Case–Control Study.*

Fracture Category and 25-Hydroxyvitamin D Level†	Main-Effect Odds Ratio (95% CI)‡	Calcium + Vitamin D	Placebo	Intervention Odds Ratio (95% CI)§	P Value for Interaction¶
		no. of case participants/ no. of controls			
Hip fracture					0.64
≥60.2 nmol/liter	1.00	32/49	42/40	0.61 (0.32–1.15)	
43.7–60.1 nmol/liter	1.51 (0.96–2.37)	44/40	52/39	0.86 (0.48–1.53)	
32.2–43.6 nmol/liter	1.17 (0.73–1.89)	43/48	48/49	0.92 (0.53–1.62)	
<32.2 nmol/liter	1.32 (0.82–2.13)	47/44	49/48	1.06 (0.60–1.86)	
Total fractures					0.15
≥60.2 nmol/liter	1.00	178/185	177/201	1.09 (0.81–1.47)	
43.7–60.1 nmol/liter	1.12 (0.91–1.38)	170/179	205/191	0.89 (0.66–1.18)	
32.2–43.6 nmol/liter	1.18 (0.94–1.47)	179/183	204/181	0.87 (0.66–1.16)	
<32.2 nmol/liter	1.14 (0.91–1.44)	196/167	182/204	1.32 (0.99–1.76)	

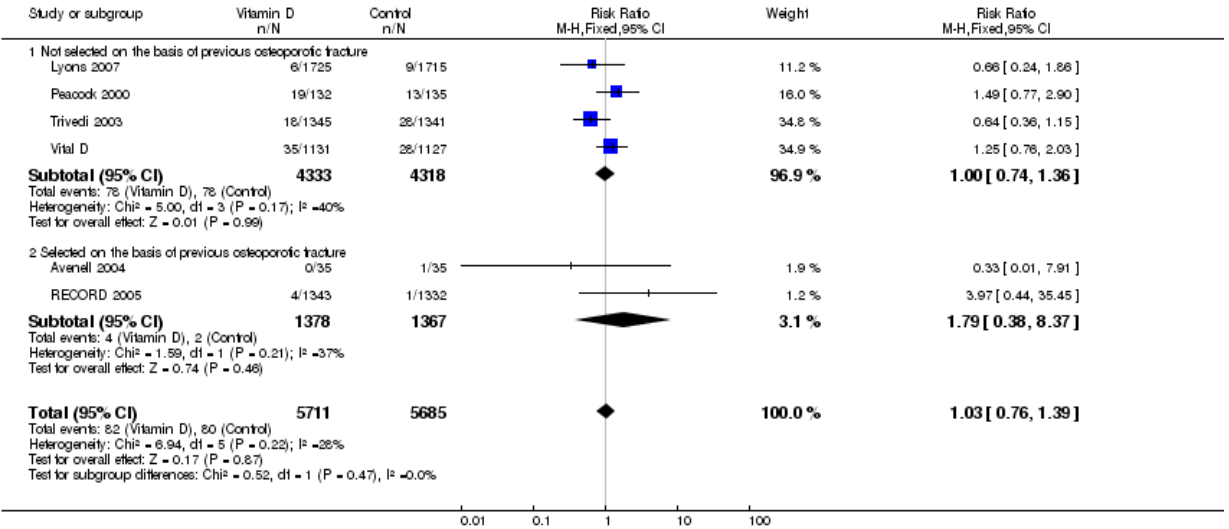
Review: Vitamin D and vitamin D analogues for preventing fractures in postmenopausal women and older men
Comparison: 1 Vitamin D [D2, D3 or 25(OH)D] versus control or placebo
Outcome: 1 Persons sustaining new hip fracture



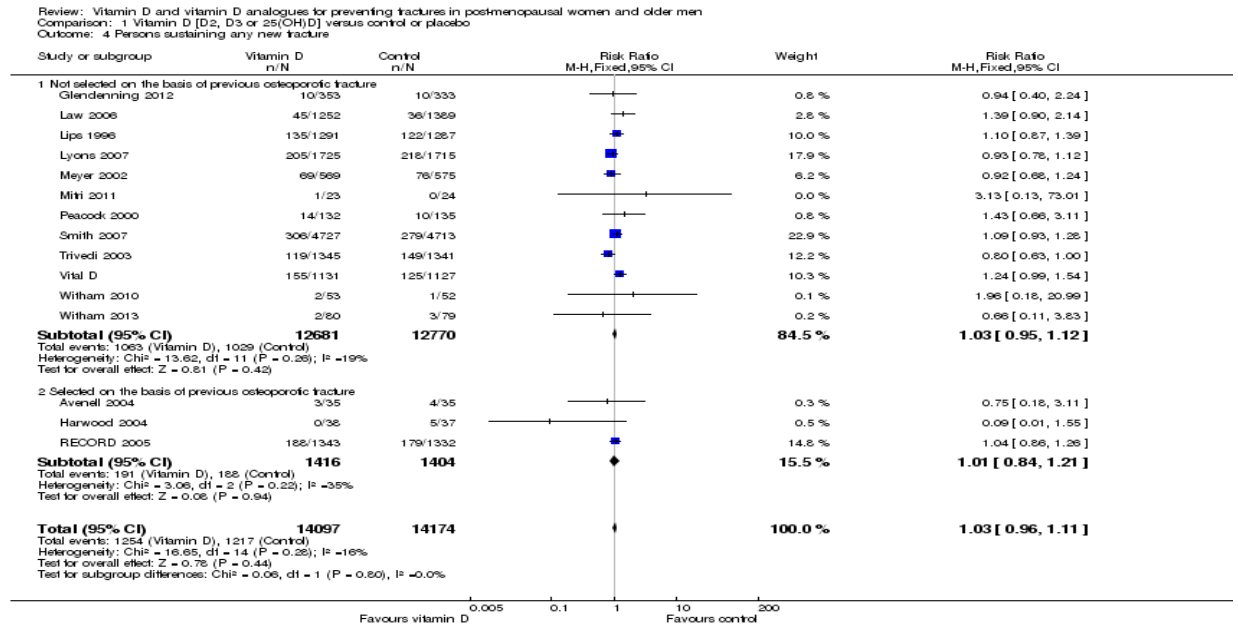
Review: Vitamin D and vitamin D analogues for preventing fractures in postmenopausal women and older men
Comparison: 1 Vitamin D [D2, D3 or 25(OH)D] versus control or placebo
Outcome: 2 Persons sustaining new non-vertebral fracture

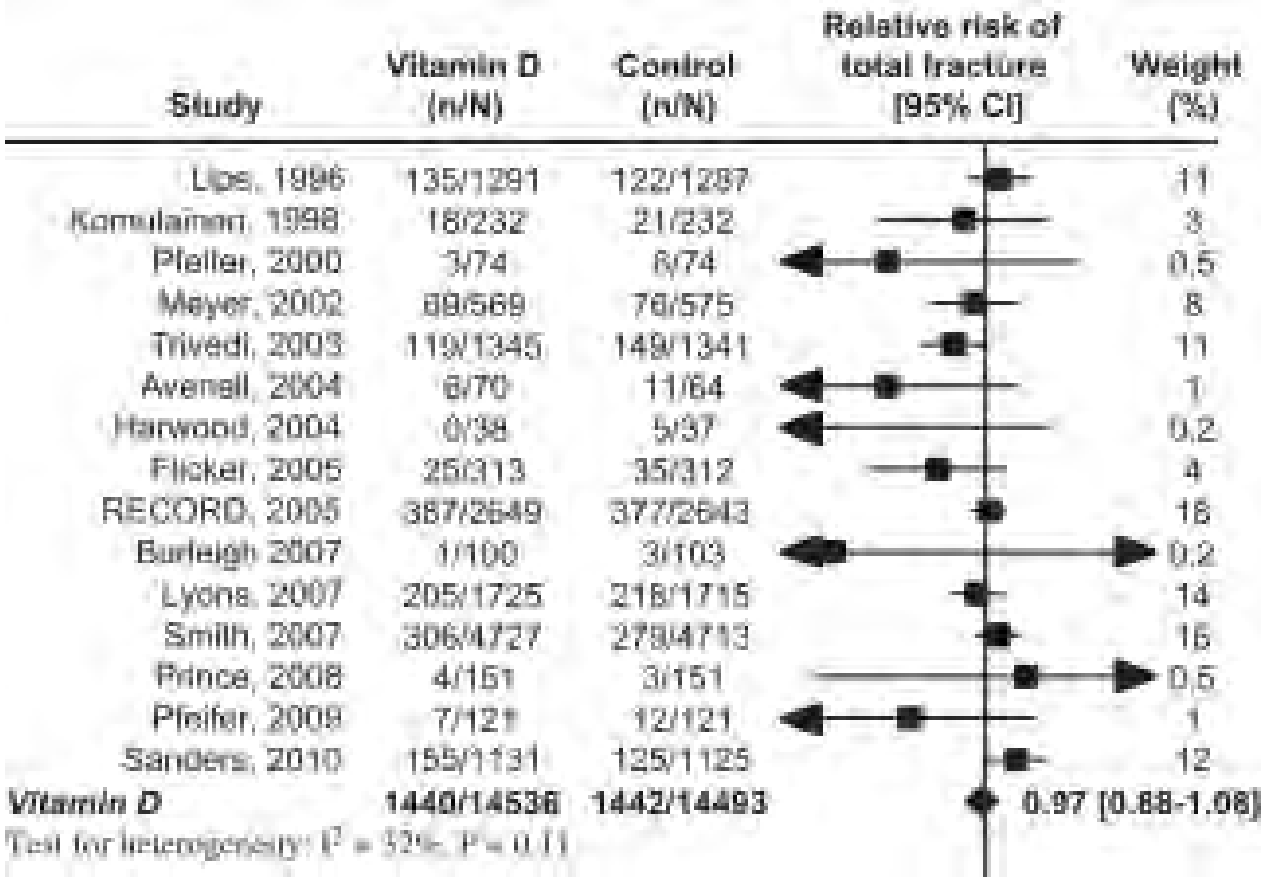


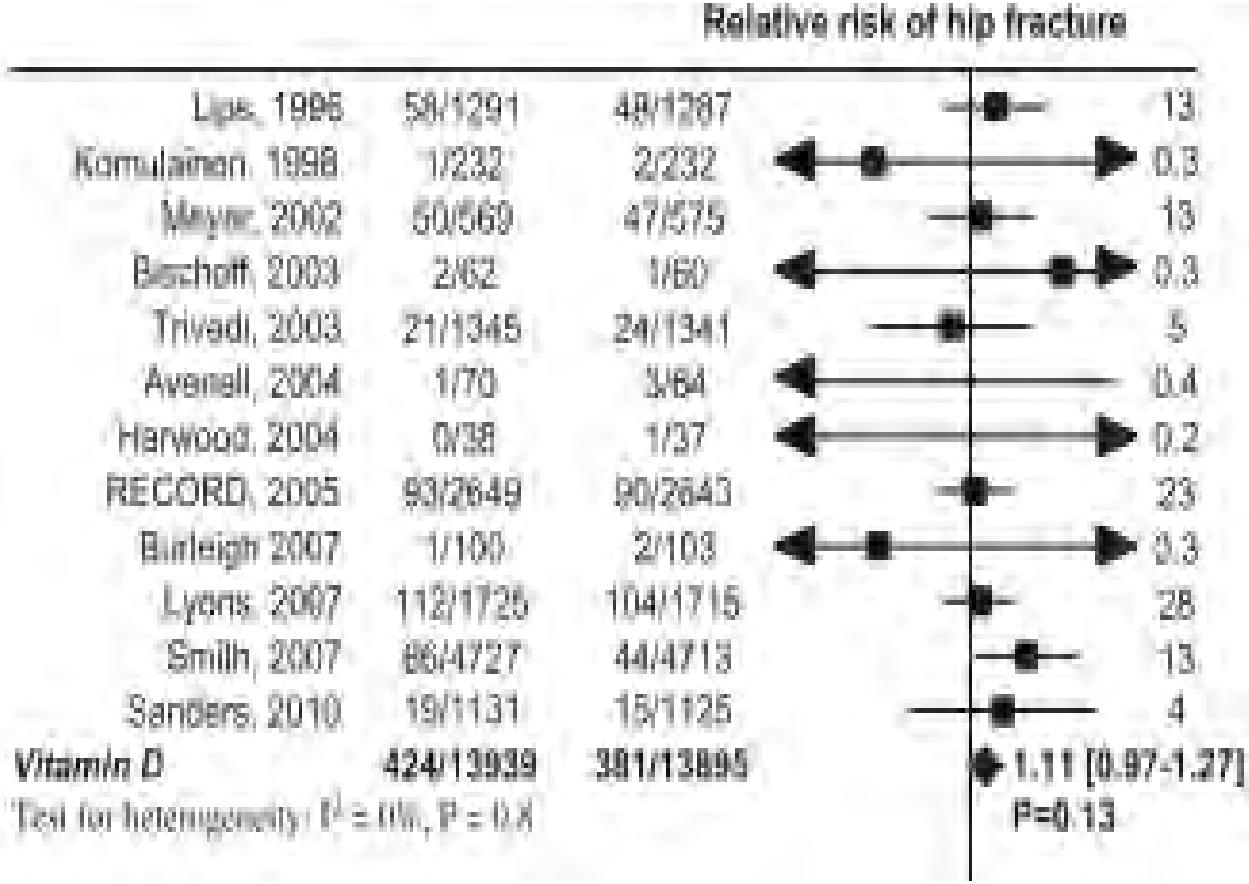
Review: Vitamin D and vitamin D analogues for preventing fractures in postmenopausal women and older men
Comparison: 1 Vitamin D [D2, D3 or 25(OH)D] versus control or placebo
Outcome: 3 Persons sustaining new vertebral fracture or deformity



Review: Vitamin D and vitamin D analogues for preventing fractures in postmenopausal women and older men
Comparison: 1 Vitamin D [D2, D3 or 25(OH)D] versus control or placebo
Outcome: 4 Persons sustaining any new fracture




Study
Vitamin D (n/N)
Control (n/N)
Relative risk of total fracture [95% CI]
Weight (%)
Lips, 1996 135/1291 122/1287 11
Komulainen, 1998 18/232 21/232 3
Pfeifer, 2000 3/74 6/74 0.5
Meyer, 2002 69/569 76/575 8
Trivedi, 2003 119/1345 149/1341 11
Avenell, 2004 6/70 11/64 1
Harwood, 2004 0/38 5/37 0.2
Flicker, 2005 25/313 35/312 4
RECORD, 2005 387/2649 377/2643 16
Burleigh 2007 1/100 3/103 0.2
Lyons, 2007 205/1725 218/1715 14
Smith, 2007 306/4727 279/4713 16
Prince, 2008 4/151 3/151 0.5
Pfeifer, 2009 7/121 12/121 1
Sanders, 2010 155/1131 125/1125 12
Vitamin D 1440/14536 1442/14493 0.97 [0.88-1.08]
Test for heterogeneity: I² = 32%, P = 0.11


Relative risk of hip fracture
Lips, 1996 58/1291 48/1287 13
Komulainen, 1998 1/232 2/232 0.3
Meyer, 2002 50/569 47/575 13
Bischoff, 2003 2/62 1/60 0.3
Trivedi, 2003 21/1345 24/1341 5
Avenell, 2004 1/70 3/64 0.4
Harwood, 2004 0/38 1/37 0.2
RECORD, 2005 93/2649 90/2643 23
Burleigh 2007 1/100 2/103 0.3
Lyons, 2007 112/1725 104/1715 28
Smith, 2007 66/4727 44/4713 13
Sanders, 2010 19/1131 15/1125 4
Vitamin D 424/13939 381/13895 1.11 [0.97-1.27]
Test for heterogeneity: I² = 0%, P = 0.8
P=0.13

- Un rapport Français, de la Haute Autorité de santé en 2013, ne retient pas d'indication de dosage de la vitamine D dans la population générale et celle de plus de 65 ans en bonne santé habituelle

- JCEM (Journal of Clinical Endocrinology and Metabolism) :

« There is no evidence demonstrating benefits of screening for vitamin D deficiency at a population level »

- CMAJ (Canadian Medical Association Journal) :

« Monitoring of routine supplement use and routine testing of otherwise healthy individuals as a screening procedure are not indicated »

Les facteurs associés à un risque accru de carence en VitD et en présence desquels un dosage de la VitD pourrait être proposé.

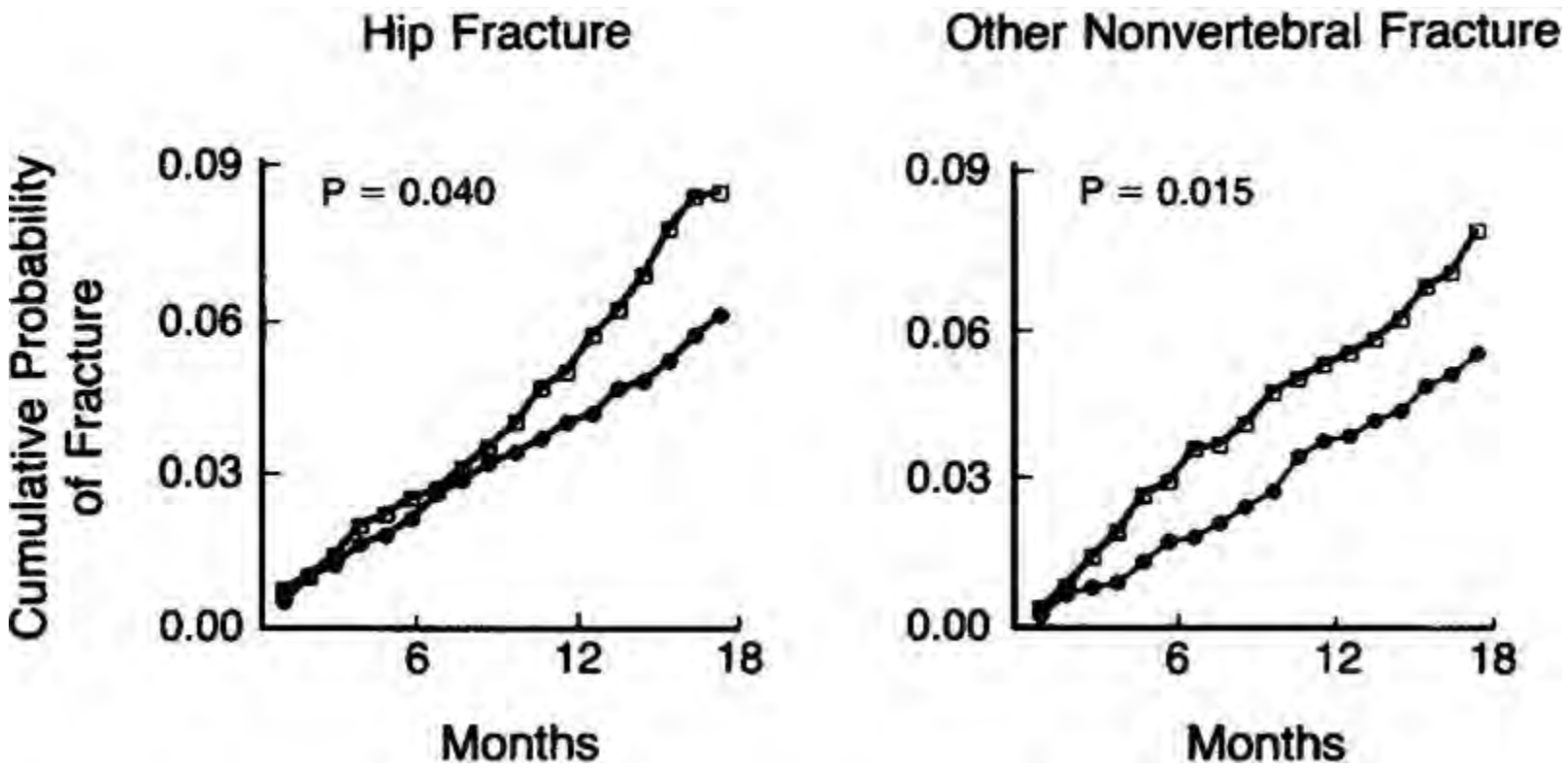
GROUPES DE PERSONNES	CONDITIONS SPÉCIFIQUES
Personnes à peau foncée	Africains Indiens Autres personnes à peau foncée
Sportifs	Sports surtout d'intérieur
Exposition faible au soleil	Personnes à mobilité réduite Personnes hospitalisées Personnes vivant en institution Utilisateurs de crèmes solaires Protection vestimentaire systématique
Personnes obèses	BMI > 30 kg/m2
Personnes très âgées	Anamnèse de chute Fracture sur traumatisme mineur
Personnes souffrant de maladies osseuses	Ostéomalacie Ostéoporose Fracture sur traumatisme mineur Hyperparathyroïdie
Syndrome de malabsorption	Chirurgie bariatrique Maladie coeliaque Maladies inflammatoires intestinales Maladie de Crohn
Insuffisance rénale chronique	
Insuffisance hépatique	
Granulomatoses	Sarcoïdose Tuberculose Histoplasmose Coccidioidomycose
Médicaments	Antiépileptiques Glucocorticoïdes Antirétroviraux (VIH) Antifongiques Colestyramine

Dosage de la vitamine D chez le sujet sain?

- Pas d’utilité clinique

Patients institutionalisés

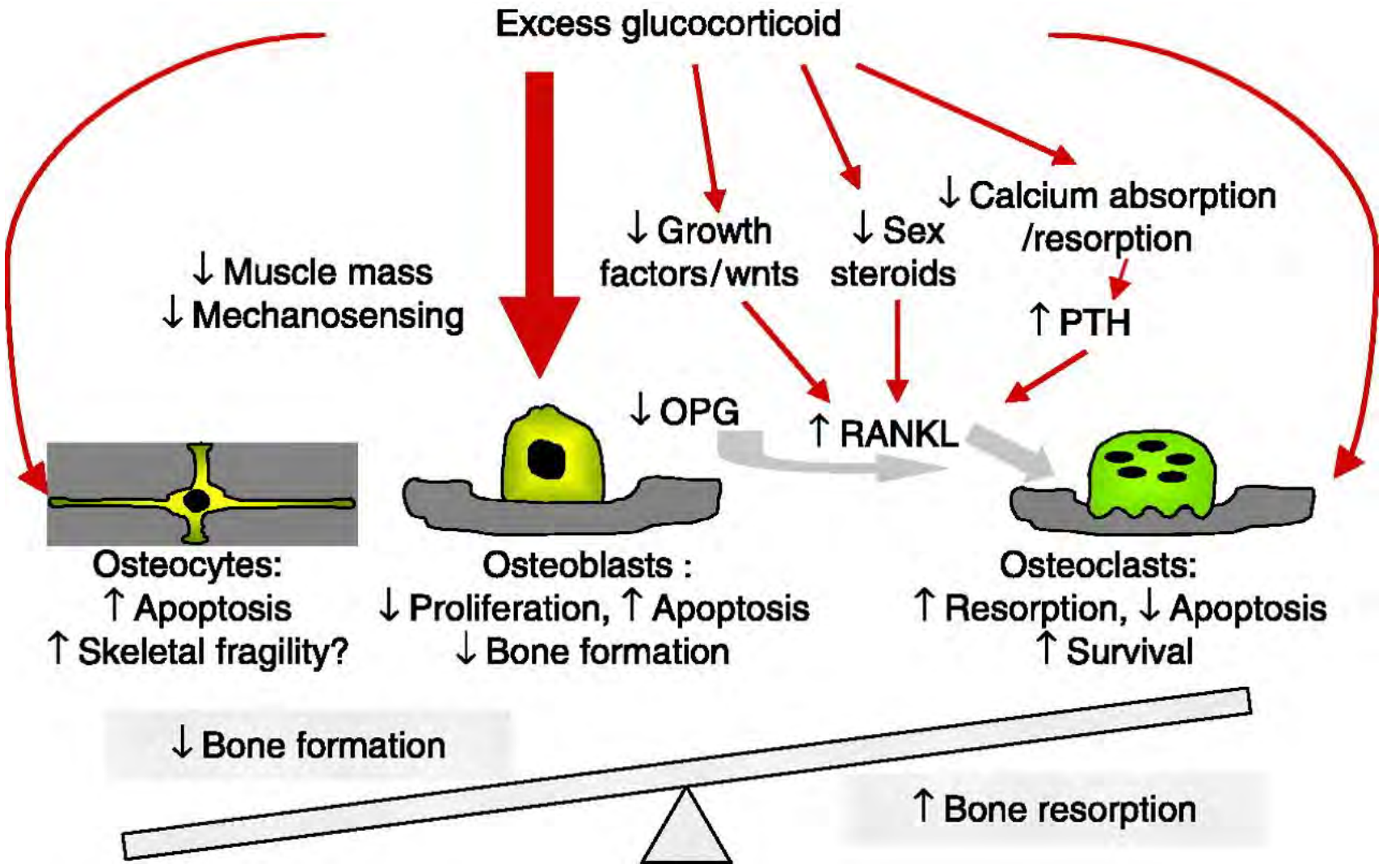
- Diminution du risque de fracture lors de la substitution
- Substitution pragmatique sans dosage de la vitamine D



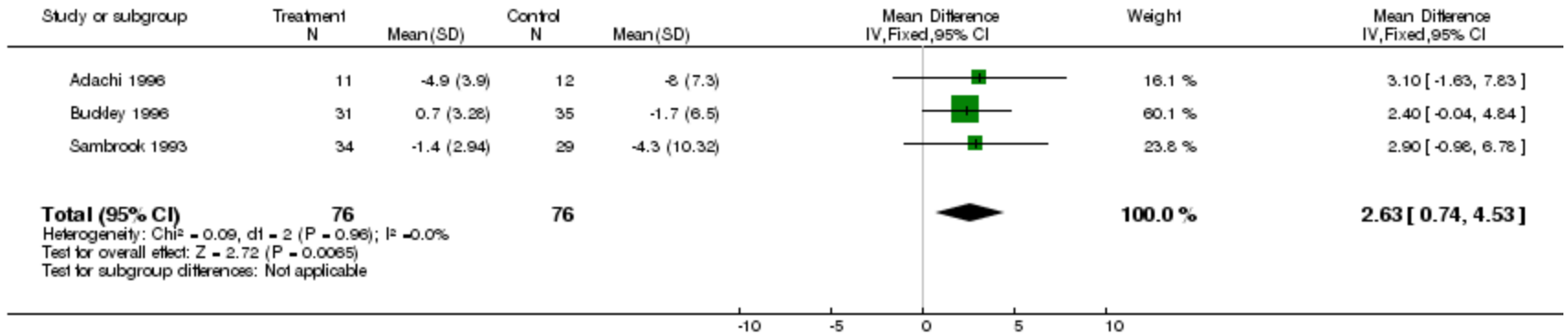
Dosage avant traitement d'ostéoporose?

- Risque d'hypocalcémie chez les patients avec un faible taux de vitamine D
- Correction par la substitution
- Utilité du dosage de la vitamine D

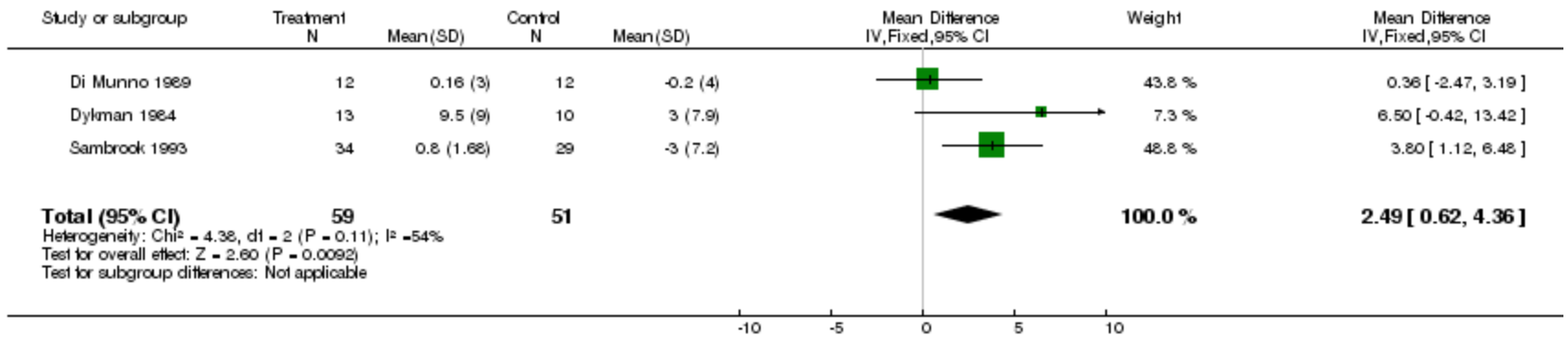
Dosage lors de corticothérapie au long cours?



Review: Calcium and vitamin D for corticosteroid-induced osteoporosis
Comparison: 1 Calcium and Vitamin D vs Calcium or Placebo
Outcome: 1 Bone mineral density, lumbar spine at one year



Review: Calcium and vitamin D for corticosteroid-induced osteoporosis
Comparison: 1 Calcium and Vitamin D vs Calcium or Placebo
Outcome: 2 Bone mineral density, distal radius at one year



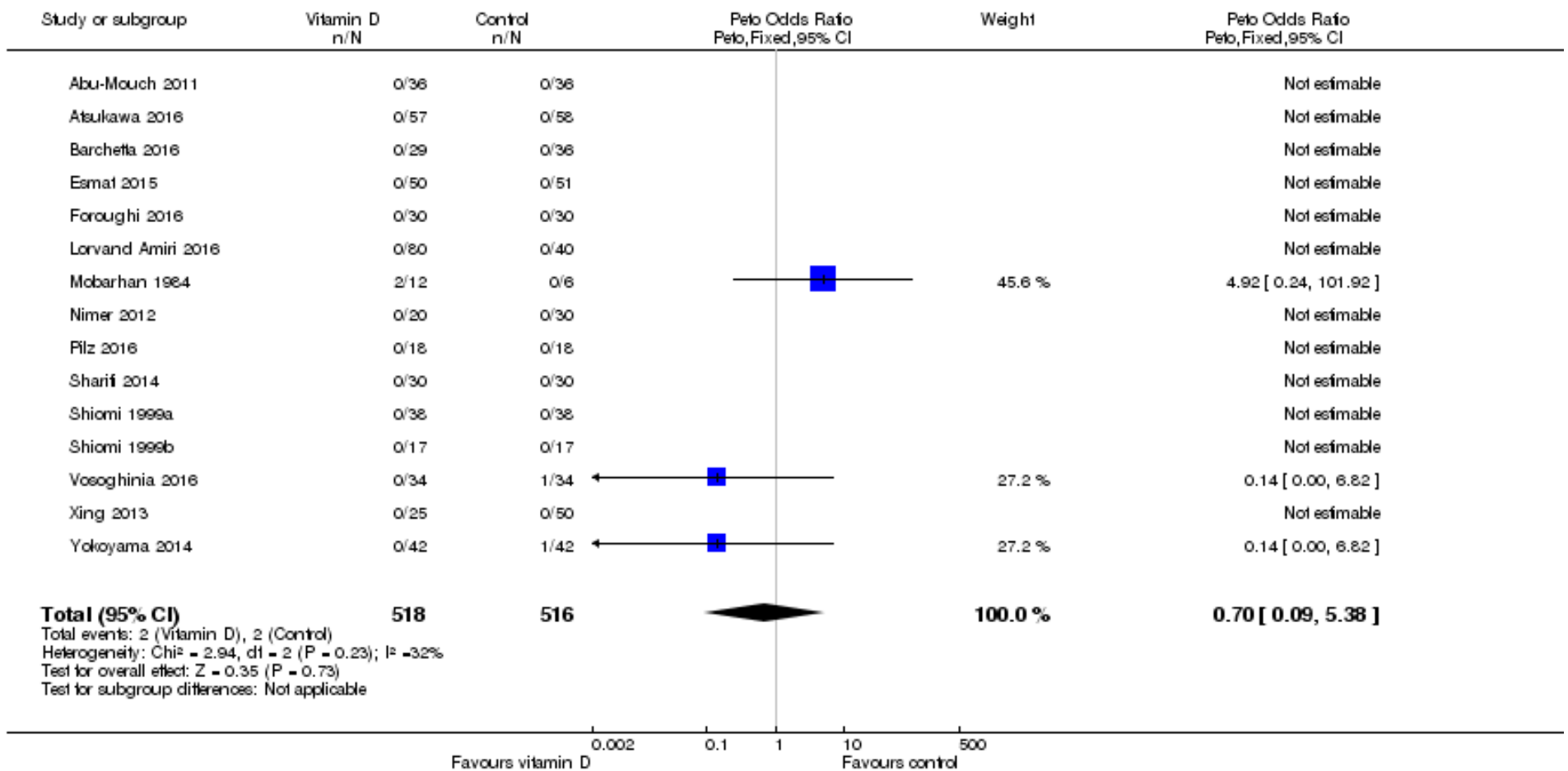
- American College of Rheumatology (ACR) Task Force osteoporosis guidelines: substitution par vitamine D chez les patients sous corticostéroïdes >3 mois

- Substitution par vitamine D sans dosage au préalable

Dosage lors de maladies hépatiques chroniques?

- Foie permet hydroxylation de la vitamine D
- 64-92% ont un déficit en vitamine D

Review: Vitamin D supplementation for chronic liver diseases in adults
Comparison: 1 Vitamin D versus placebo or no intervention
Outcome: 1 All-cause mortality



- Pas de preuves du bénéfice de la substitution de la vitamine D
- Peu d’études. Nombre de patients limité
- La littérature ne permet pas de conclure à l’utilité ou non du dosage de la vitamine D

Insuffisance rénale chronique

- Permet la 2ème hydroxylation de la vitamine D
- Déficit en vitamine D chez 75% des patients en IRC
- Associé à une mortalité plus importante

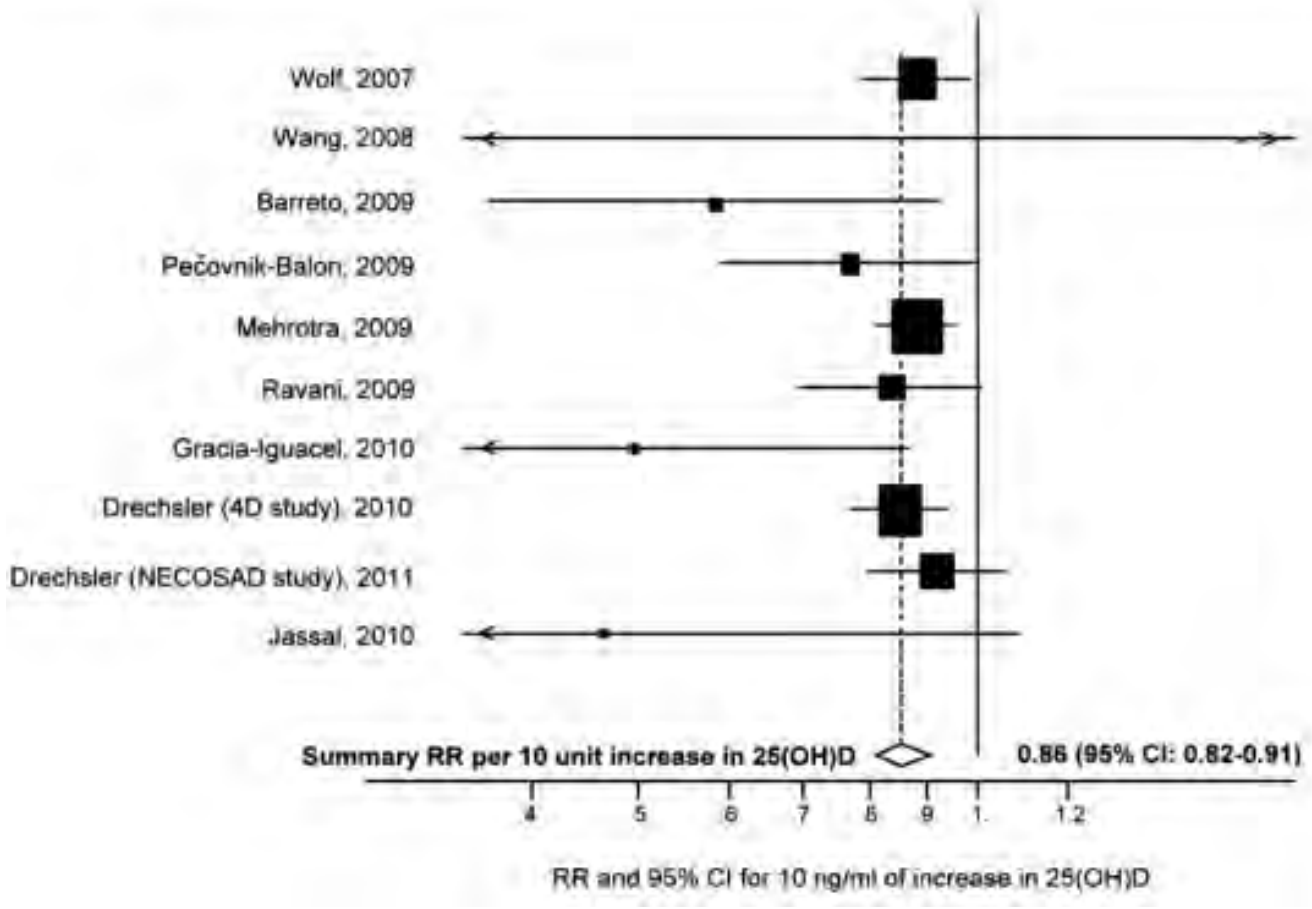


Figure 2. Forest plot and summary relative risk (RR) for the association of 25-hydroxyvitamin D (25[OH]D) level and mortality in patients with chronic kidney disease. The size of the box is proportional to the weight of the study (1/variance of the estimate). Abbreviations: 4D, Die Deutsche Diabetes Dialyse Studie; NECOSAD, Netherlands Cooperative Study on the Adequacy of Dialysis.

Taux de vitamine D plus élevé associé à une meilleure survie chez les IRC

Substitution diminue la mortalité?

CKD stage	Study	Risk ratio	Lower limit	Upper limit	p value	Adjusted risk ratio	Relative weight, %
HD	Taniguchi, 2010 [36]	0.54	0.51	0.57	<0.001	Yes	11.8
HD	Naves-Díaz, 2008 [32]	0.55	0.49	0.62	<0.001	Yes	11.0
HD	Wolf, 2008 [40]	0.66	0.50	0.86	0.002	Yes	8.0
HD	Shoji, 2004 [34]	0.70	0.44	1.14	0.15	No	4.7
HD	Melamed, 2006 [31]	0.74	0.56	0.98	0.03	Yes	7.9
HD	Kalantar-Zadeh, 2006 [27, 28]	0.75	0.71	0.79	<0.001	Yes	11.8
HD	Teng, 2005 [37]	0.80	0.76	0.84	<0.001	Yes	11.8
HD	Tentori, 2006 [38]	0.83	0.76	0.91	<0.001	Yes	11.4
HD	Jean, 2011 [26]	0.89	0.74	1.07	0.22	Yes	9.8
HD	Tentori, 2009 [39]	0.89	0.84	0.94	<0.001	Yes	11.8
HD	**Overall** (I^2 = 94%)	**0.73**	**0.64**	**0.83**	**<0.001**		
preHD	Kovesdy, 2008 [29]	0.69	0.55	0.86	0.001	No	43.8
preHD	Shoben, 2008 [33]	0.76	0.58	1.00	0.05	Yes	39.4
preHD	Sugiura, 2010 [35]	0.80	0.44	1.46	0.46	Yes	16.8
preHD	**Overall** (I^2 = 0%)	**0.73**	**0.55**	**0.98**	**0.04**		
Overall (I^2 = 97%)		**0.73**	**0.65**	**0.82**	**<0.001**		

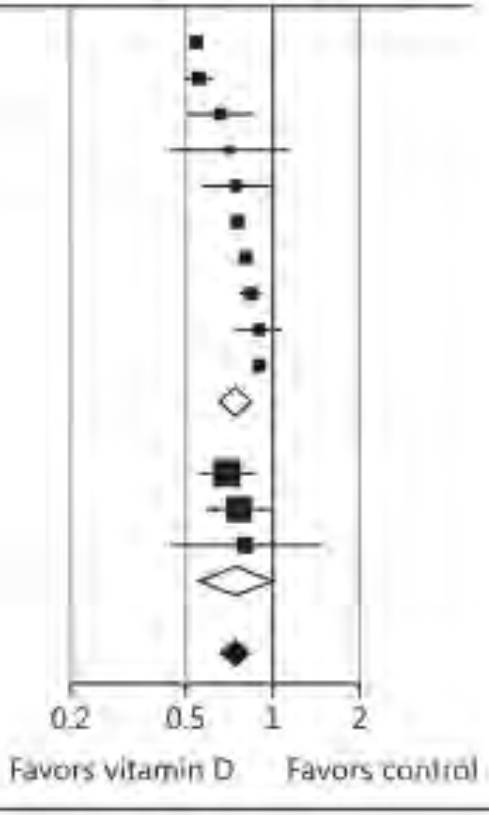


Fig. 2. Forest plots and summary estimates of all-cause mortality RRs depending on vitamin D treatment in hemodialysis patients (HD) or patients at CKD stages not requiring dialysis (preHD). RRs <1 indicate a greater chance of survival in the vitamin D therapy group as compared with the control group.

Study	Risk ratio	Lower limit	Upper limit	p value	Adjusted risk ratio	Relative weight, %
Shoji, 2004 [34]	0.38	0.25	0.58	<0.001	Yes	17.0
Sugiura, 2010 [35]	0.45	0.14	1.50	0.19	Yes	6.6
Naves-Díaz, 2008 [32]	0.55	0.45	0.67	<0.001	Yes	20.8
Marco, 2003 [30]	0.64	0.35	1.18	0.15	No	13.8
Taniguchi, 2011 [36]	0.75	0.58	0.97	0.03	Yes	19.9
Kalantar-Zadeh, 2006 [27, 28]	1.02	0.97	1.07	0.47	No	22.0
Overall (I^2 = 92%)	**0.63**	**0.44**	**0.92**	**0.02**		

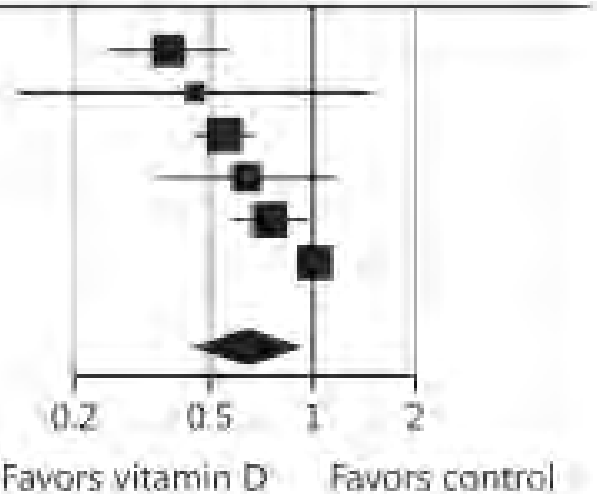


Fig. 4. Forest plot and summary estimate of cardiovascular mortality RRs depending on vitamin D treatment.

Substitution a permis de diminuer la mortalité cardiovasculaire

- Plus marqué chez les patients avec un hyperparathyroïdisme secondaire à l’IRC

Dosage de la vitamine D chez les IRC?

- Utilité clinique

- Recommandations 2017 de la société internationale de néphrologie:

  « In patients with CKD G3a – G5D, we suggest that 25(OH)D (calcidiol) levels might be measured »

  « We suggest that vitamin D deficiency and insufficiency be corrected using treatment strategies recommended for the general population »

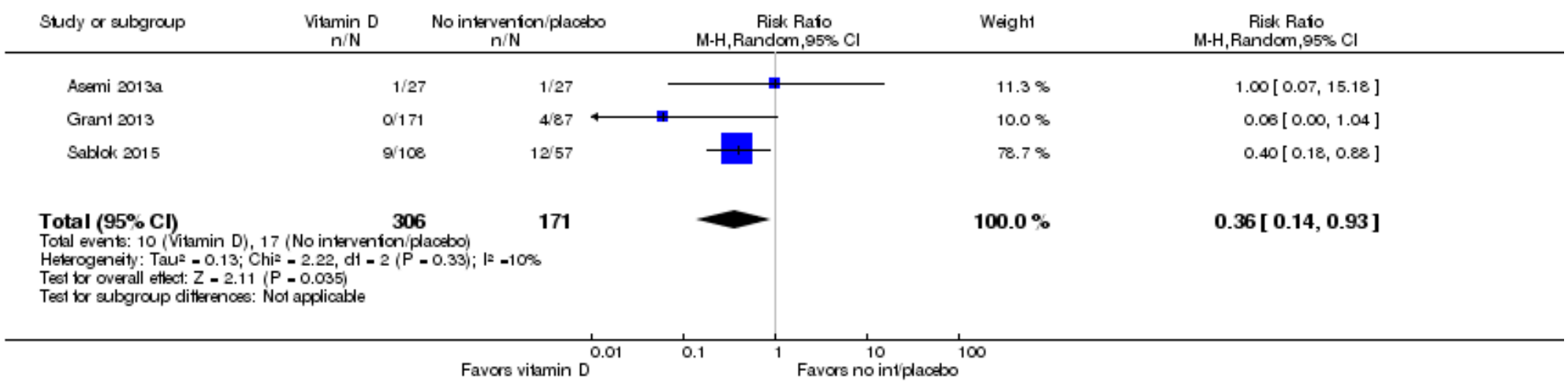
Utilité du dosage chez les femmes enceintes?

- Déficit en vitamine D de plus en plus fréquent

- Surtout chez les femmes végétariennes, voilées ou peau noire

Outcomes	No of studies	Pooled odds ratio (95% CI)	Pooled weighted mean difference (95% CI) (nmol/L)
Gestational diabetes			
Overall	10	1.49 (1.18 to 1.89)	—
Pre-eclampsia			
Overall	7	1.79 (1.25 to 2.58)	—
Small for gestational age			
Overall	6	1.85 (1.52 to 2.26)	—

Review: Vitamin D supplementation for women during pregnancy
Comparison: 1 Vitamin D alone versus no treatment/placebo (no vitamins or minerals)
Outcome: 10 Preterm birth (less than 37 weeks' gestation) (ALL)



Review: Vitamin D supplementation for women during pregnancy
Comparison: 1 Vitamin D alone versus no treatment/placebo (no vitamins or minerals)
Outcome: 11 Low birthweight (less than 2500 g) (ALL)

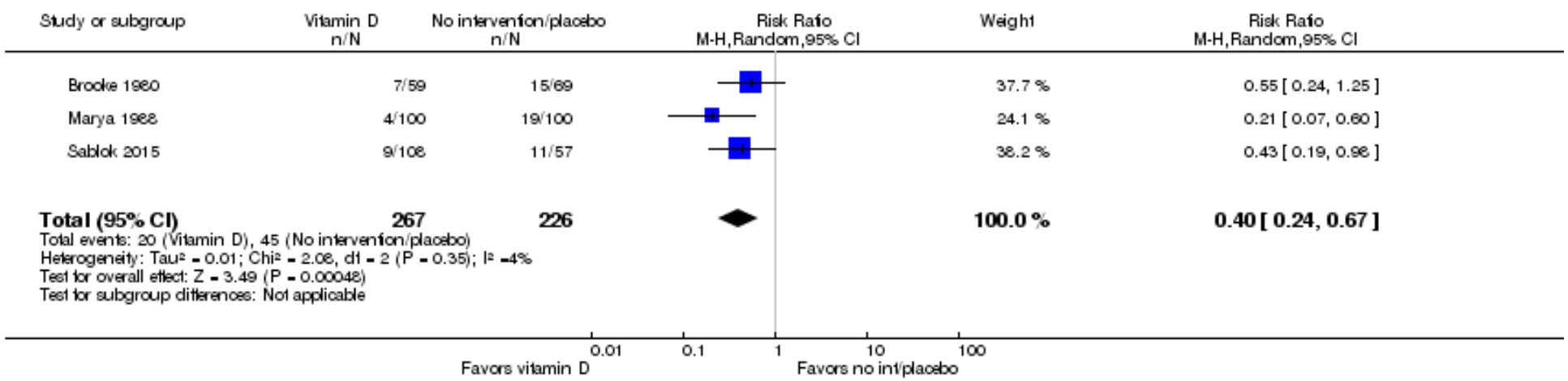


Table 2. Anthropometric Outcomes in Infants at 1 Year of Age.*

Outcome	Maternal Study-Group Assignment					
	Placebo (N=259)	Prenatal 4200 (N=260)	Prenatal 16,800 (N=259)	Prenatal 28,000 (N=260)	Prenatal and Postpartum 28,000 (N=260)	P Value†
Age at measurement — days						0.70
Median	364	365	365	365	365	
Range	364–419	365–415	364–418	364–419	364–416	
Length						
No. of children measured	229	237	237	230	231	
Length — cm	72.62±2.76	72.31±2.84	72.56±2.54	72.39±2.80	72.67±2.53	0.53
Length-for-age z score	−0.93±1.05	−1.11±1.12	−0.97±0.97	−1.06±1.07	−0.94±1.00	0.23
Stunted — no. (%)‡	36 (15.7)	46 (19.4)	36 (15.2)	39 (17.0)	31 (13.4)	0.49
Other anthropometric indexes						
Weight-for-age z score§	−0.81±1.12	−1.00±1.14	−0.86±1.09	−0.96±1.09	−0.89±1.04	0.34
Weight-for-length z score§	−0.47±1.07	−0.60±1.03	−0.52±1.08	−0.58±1.01	−0.59±1.01	0.62
BMI-for-age z score§	−0.36±1.05	−0.48±1.00	−0.40±1.07	−0.46±0.99	−0.48±1.00	0.66
Head-circumference-for-age z score¶	−1.11±0.99	−1.25±0.96	−1.21±1.05	−1.22±0.92	−1.22±0.89	0.61
Mid–upper-arm-circumference-for-age z score¶	−0.14±0.97	−0.27±0.92	−0.21±0.93	−0.29±0.88	−0.23±0.86	0.42
Wasted — no. (%)‖	14 (6.1)	22 (9.3)	18 (7.6)	18 (7.8)	21 (9.1)	0.72

Table 3. **Delivery Characteristics and Pregnancy Outcomes.**[a]

Characteristic or Outcome	Maternal Study-Group Assignment					
	Placebo (N=259)	Prenatal 4200 (N=260)	Prenatal 16,800 (N=259)	Prenatal 28,000 (N=260)	Prenatal and Postpartum 28,000 (N=260)	P Value†
Live birth — no. (%)	247 (95.4)	254 (97.7)	252 (97.3)	252 (96.9)	249 (95.8)	0.53
Gestational age at birth (wk)						0.62
Median	39.1	39.1	39.0	39.1	39.1	
Range	32–43	34–42	26–43	29–43	30–42	
Preterm (<37 wk) — no. (%)	24 (9.7)	21 (8.3)	31 (12.3)	26 (10.3)	22 (8.8)	0.60
Cesarean section — no. (%)	121 (49.0)	143 (56.3)	131 (52.0)	127 (50.4)	132 (53.0)	0.54
Facility (hospital or clinic) delivery — no. (%)‡	211 (85.4)	216 (85.0)	216 (85.7)	212 (84.1)	207 (83.1)	0.93
Female infant — no. (%)	129 (52.2)	117 (46.1)	132 (52.4)	124 (49.2)	121 (48.6)	0.58
Maternal serum 25-hydroxyvitamin D at or near delivery — nmol/liter§	23.8±13.9	69.7±19.5	100.9±23.6	110.7±28.0	113.6±25.7	<0.001¶
Newborn anthropometry‖						
Birth weight — kg**	2.72±0.36	2.70±0.39	2.72±0.35	2.67±0.34	2.76±0.35	0.25
Length at birth — cm††	47.4±2.1	47.5±1.9	47.4±1.9	47.2±2.1	47.5±2.0	0.74
Head circumference at birth — cm‡‡	33.0±1.3	33.0±1.3	33.0±1.1	32.9±1.2	33.0±1.1	0.73
Size for gestational age and sex according to standardized measures‖						
Weight-for-gestational-age z score at birth**	−1.12±0.83	−1.27±0.89	−1.15±0.90	−1.30±0.82	−1.12±0.85	0.16
Length-for-gestational-age z score at birth††	−0.83±1.04	−0.95±1.00	−0.90±1.05	−1.00±1.02	−0.88±0.95	0.61
Head-circumference-for-gestational-age z score at birth‡‡	−0.58±0.96	−0.66±1.04	−0.57±0.94	−0.72±0.98	−0.58±0.91	0.57
Low birth weight — no. (%)**§§	42 (25.1)	53 (31.0)	42 (25.0)	53 (32.9)	40 (23.7)	0.23
Small for gestational age — no. (%)**¶¶	72 (43.4)	88 (51.5)	77 (45.8)	84 (52.2)	76 (45.0)	0.38

OMS

- De 2012 à 2019 recommandation de doser et substituer les femmes enceintes

- Au vu des dernières études:
  - « La supplémentation en vitamine D n'est pas recommandée chez les femmes enceintes dans le but d'améliorer les issues maternelles et périnatales de la grossesse »

- The American College of Obstetricians and Gynecologists 2011:
  - « At this time, there is insufficient evidence to support a recommendation for screening all pregnant women for vitamin D deficiency. For pregnant women thought to be at increased risk of vitamin D deficiency, maternal serum 25-hydroxyvitamin D levels can be considered and should be interpreted in the context of the individual clinical circumstance »

Take Home Message

- Utilité dosage vitamine D:
  - Patients insuffisants rénaux stade 3a-5D
  - Avant un traitement de biphosphonates
  - Patients dans les catégories à risque

- Il est inutile de doser et de substituer avec de la vitamine D pour diminuer le risque de chute, de fracture ou pour améliorer la densité osseuse dans une population saine

- Substitution sans dosage chez les patients institutionnalisés et sous corticothérapie au long court

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