# Faut-il prescrire de la vitamine D dans les rhumatismes inflammatoires?

## Role of Confounding Factors in the Evaluation of Vitamin D Deficiency

Ensoleillement
Origine géographique
Exposition au soleil
Religion
Travail
Temps passé au domicile
Ethnie
Grossesse
Génétique
Age
Saisons
Pathologies rénales, foie …
Alimentation
Traitements
Poids
…

# Covid 19 : l'effet protecteur de la vitamine D se confirme

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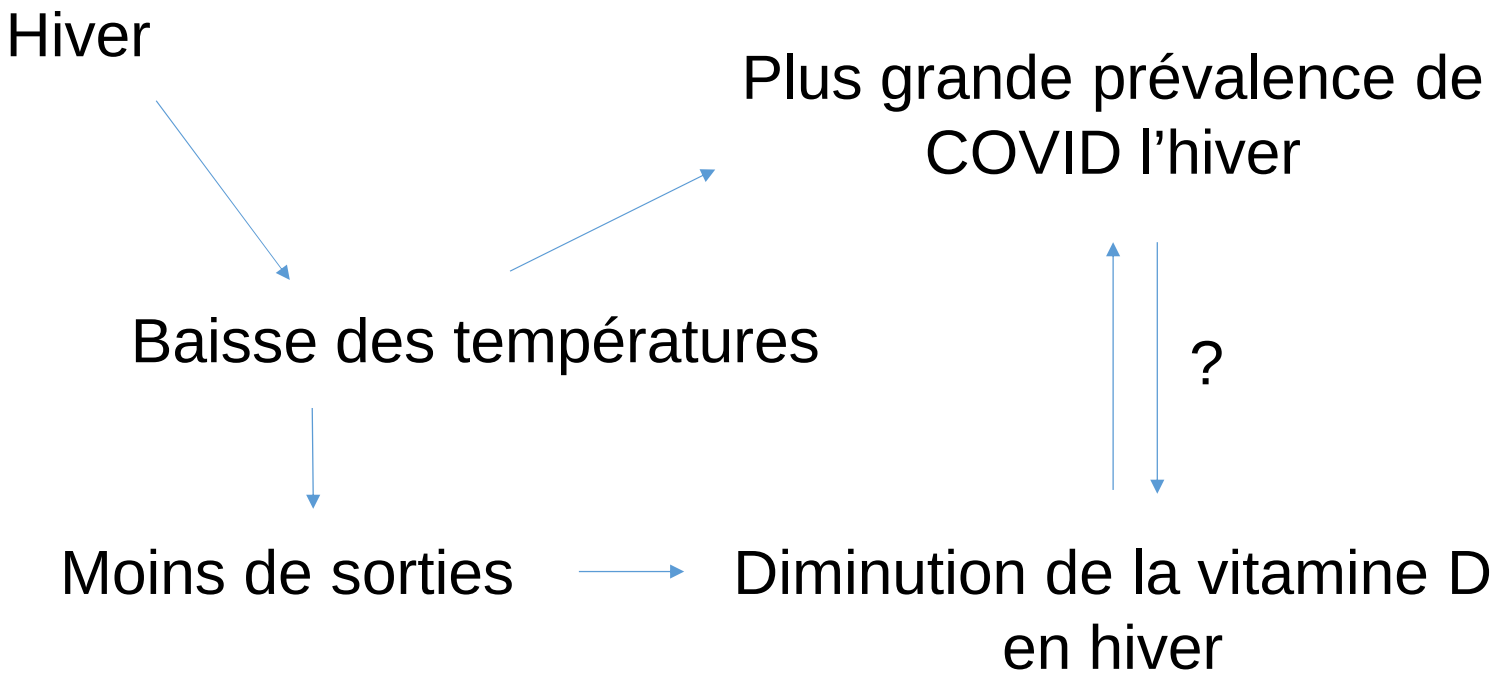
Auteur : Hugues TOLOU

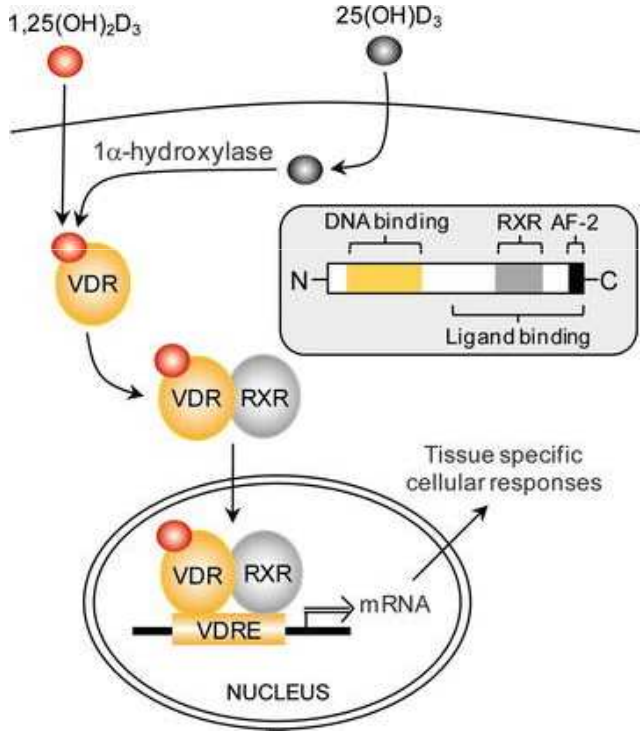
Le virus de la covid 19 est responsable d'une infection d'évolution très différente selon les individus. Elle peut être quasi inapparente (asymptomatique ou paucisymptomatique), ou se manifester au contraire par des atteintes graves, notamment de l'appareil respiratoire, pouvant entraîner le décès. Les recherches sur les facteurs responsables de ces différences ont été très actives, car elles peuvent déboucher sur des stratégies ou mesures de protection ciblées. Ainsi, l'association de l'âge avancé ou de certaines comorbidités avec une incidence élevée de formes graves a permis d'orienter et de prioriser la mise en œuvre de certaines mesures, dont la vaccination.

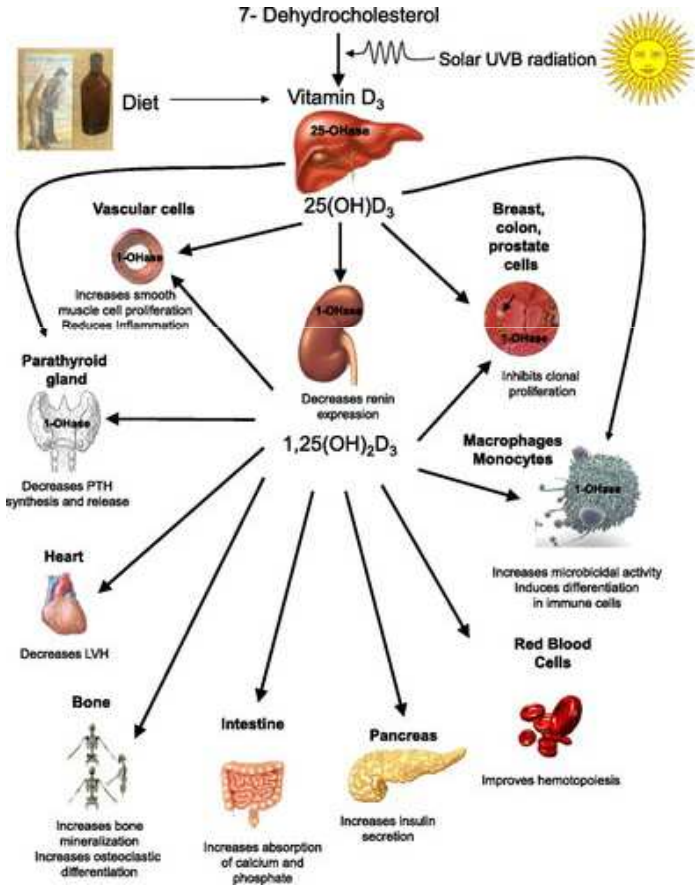
Très tôt, des observations ont indiqué qu'un déficit en vitamine D pouvait être une des circonstances associées à un risque accru de covid 19 et de forme grave (1). Ces observations ont été guidées par des travaux antérieurs ayant montré un effet protecteur de la vitamine D contre le syndrome de détresse respiratoire aigu (SDRA) qui peut être une complication, souvent mortelle, de certaines infections respiratoires (2). Une possible protection contre la grippe, la particulière sévérité de la covid 19 chez les personnes âgées ou obèses (deux conditions souvent associées à une hypovitaminose) et la prépondérance hivernale des infections (le manque d'exposition au soleil favorisant le déficit) avaient également orienté vers un possible rôle de la vitamine D dans la physiopathologie de la maladie.

# Pourquoi le raisonnement de Hugues est faux?



# Rôle ubiquitaire de la vitamine D



# Effet anticancéreux

Review

## Vitamin D: Its role in cancer prevention and treatment

Michael F. Holick*

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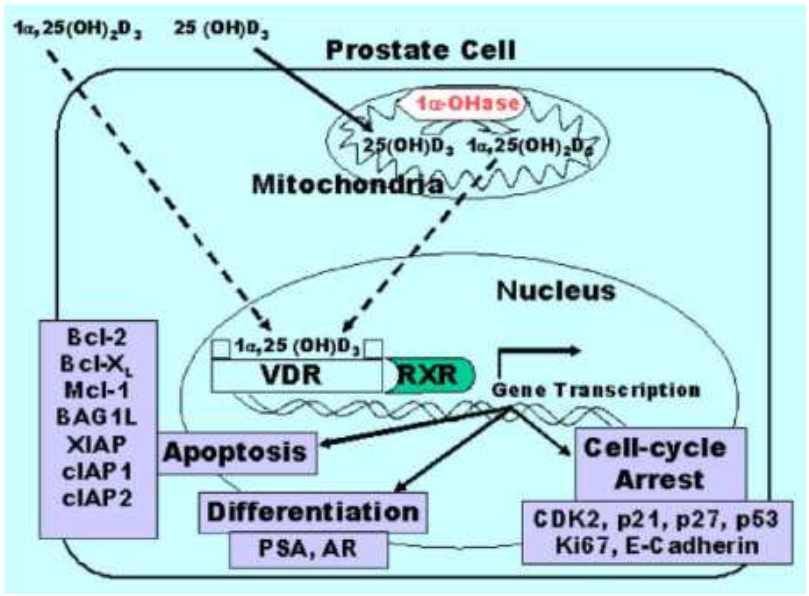
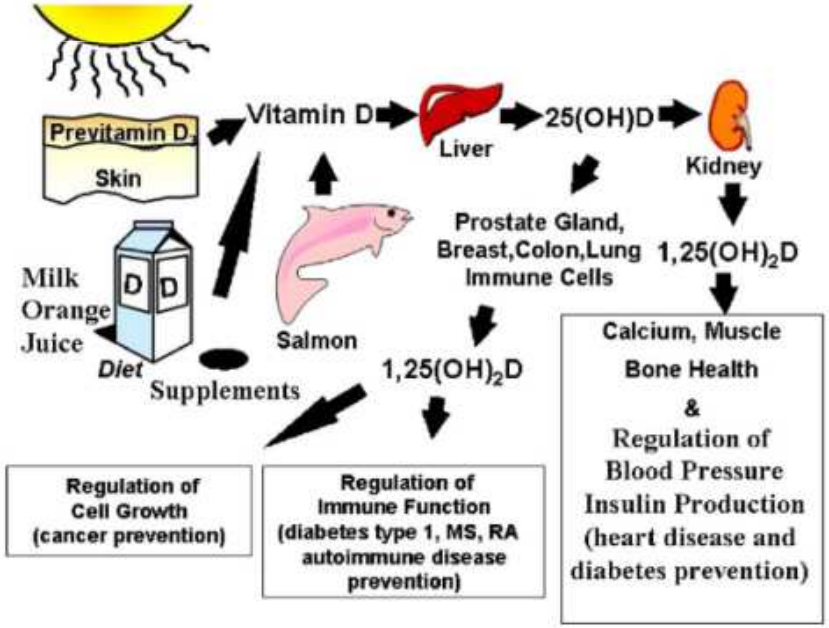


REVIEW ARTICLE

# Vitamin D, cardiovascular disease and mortality

Stefan Pilz*,†, Andreas Tomaschitz*, Winfried März‡,§,¶, Christiane Drechsler**, Eberhard Ritz††, Armin Zittermann‡‡, Etienne Cavalier§§, Thomas R. Pieber*, Joan M. Lappe¶¶, William B. Grant***, Michael F. Holick††† and Jacqueline M. Dekker†

**Table 1.** Population-based studies on the association of 25(OH)D with cardiovascular (CV) events and mortality

| First author (References) | Country | Age, years | Males (%) | No. of subjects | Follow-up, years | Event type | No. of events | Main analysis [25(OH)D in nM] | Adjusted relative risk (95% CI) |
|---|---|---|---|---|---|---|---|---|---|
| Wang[67] | USA | 59 | 45 | 1739 | 5·4 | CV events | 120 | <37·5 *vs* ≥37·5 | 1·66 (1·13–2·43) |
| Giovannucci[69] | USA | 64 | 100 | 1354 | 10 | Myocardial infarction | 454 | ≤37·5 *vs* ≥75 | 2·09 (1·24–3·54) |
| Melamed[70]* | USA | 45 | 47 | 13 331 | 8·7 | CV mortality | 777 | <44·4 vs >80·1 | 1·20 (0·87–1·64) |
| Semba[76] | Italy | 74 | 75 | 1006 | 6·5 | CV mortality | 107 | <26·2 *vs* >63·9 | 2·64 (1·14–4·79) |
| Pilz[68] | The Netherlands | 70 | 49 | 614 | 6·2 | CV mortality | 20 | first *vs* highest three quartiles | 5·33 (1·97–14·45) |
| Kilkkinen[71] | Finland | 49 | 45 | 6219 | 27·1 | CV mortality | 933 | ≥62 *vs* ≤28 | 0·76 (0·61–0·95) |
| Bolland[74] | New Zealand | 74 | 0 | 1471 | 5 | CV events | 110 | <50 vs ≥50 | 1·2 (0·8–1·8) |
| Hutchinson[93]† | Norway | 59 | 38 | 4751 | 11·8 | CV | 325 | First *vs* fourth | 1·08 (0·79–1·48) |
| | | | 41 | 2410 | 11·4 | mortality | 188 | quartile | 0·93 (0·61–1·44) |
| Fiscella[78]* | USA | 44 | 48 | 15 363 | 9 | CV mortality | 933 | >79·9 *vs* <44·9 | 0·79 (0·62–1·01) |
| Cawthon[72] | USA | 74 | 100 | 1490 | 7·3 | CV mortality | 110 | <50 vs ≥75 | 1·51 (0·83–2·80) |
| Jassal[75] | USA | 74 | 38 | 1073 | 6·4 | CV mortality | 111 | Per SD = 35 | 1·07 (0·86–1·33) |
| Michaëlsson[73]‡ | Sweden | 71 | 100 | 1194 | 12·7 | CV mortality | 177 | <46 *vs* 46–93 | 1·53 (0·97–2·41) |
| Virtanen[79] | Finland | 62 | 49 | 1136 | 9·1 | CV mortality | 35 | ≤34·0 *vs* ≥34·1 | 2·70 (1·31–5·56) |
| Messenger[80]‡ | USA | 76 | 100 | 813 | 4·4 | CV events | 140 | ≤50·2 *vs* ≥75·1 | 1·18 (0·69–2·03) |

*Both reports on the same study: Third National Health and Nutrition Examination Survey (NHANES-III).
†Separate reports for non-smokers (upper line) and smokers (lower line).
‡Both reports on the same study: Osteoporotic Fractures in Men (MrOS) study.

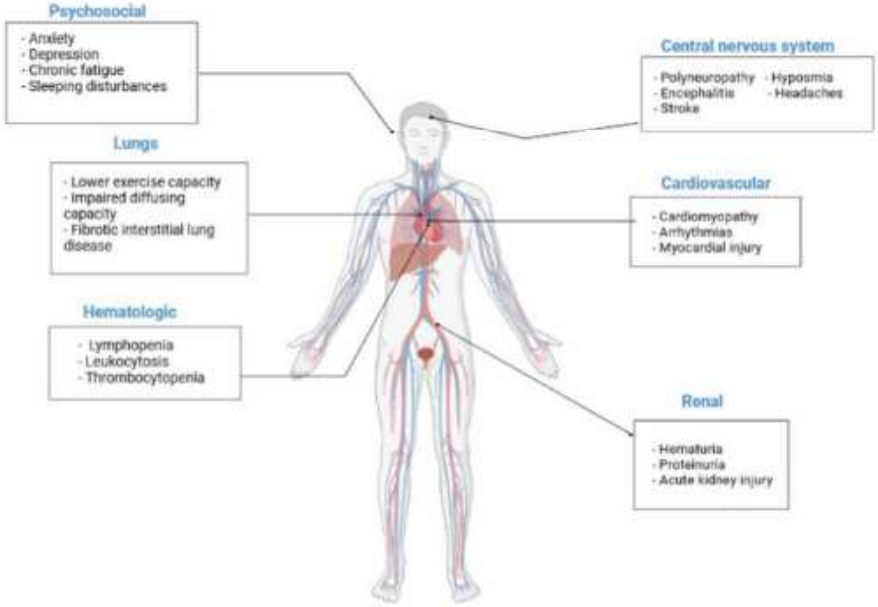
*nutrients*

MDPI

*Review*

# Vitamin D: A Role Also in Long COVID-19?

**Luigi Barrea [1,2,†], Ludovica Verde [2,†], William B. Grant [3,†], Evelyn Frias-Toral [4], Gerardo Sarno [5], Claudia Vetrani [6], Florencia Ceriani [7], Eloisa Garcia-Velasquez [8], José Contreras-Briceño [9], Silvia Savastano [2,6], Annamaria Colao [2,6,10] and Giovanna Muscogiuri [2,6,10,*]**



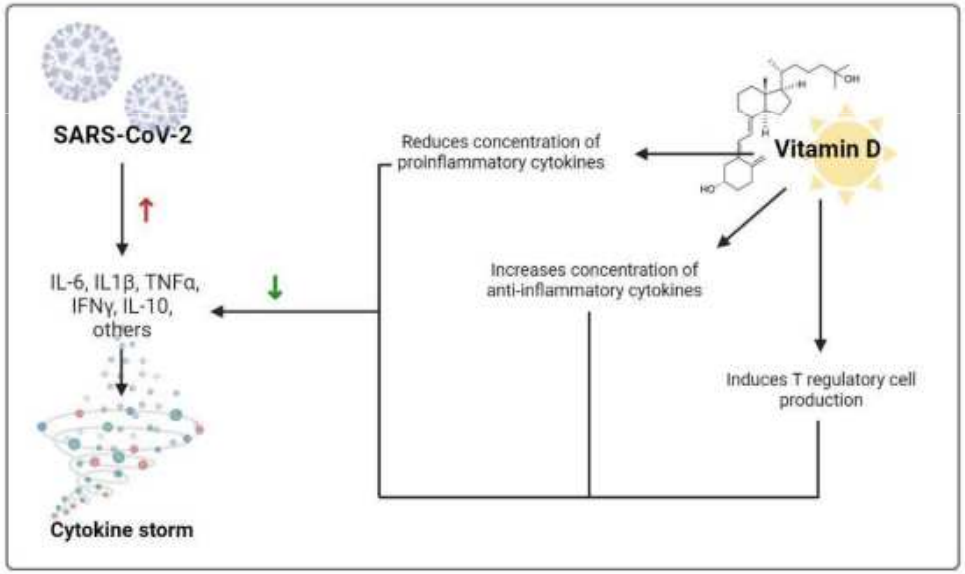



**Table 1.** Proposed mechanisms whereby vitamin D reduces risk of COVID-19 (note, order of mechanisms should be carefully considered, perhaps placing more important ones near the beginning).

| Effect | Mechanism | Reference |
|---|---|---|
| Inactivates viruses | Induction of cathelicidin | [47] |
| Reduces risk of cytokine storm | Reduces concentration of proinflammatory cytokines and increases concentration of anti-inflammatory cytokines | [24] |
| Reduces risk of cytokine storm | Induces T regulatory cell production | [27] |
| Reduces risk of pneumonia | Reduces risk of endothelial dysfunction | [48] |
| Increases the metabolic tolerance of the host to damage inflicted by the pathogen infection | Reduces matrix metalloproteinase-9 concentrations | [49] |
| Reduces free SARS-CoV-2 concentrations | Increases soluble ACE2 concentrations that can bind to SARS-CoV-2 | [50] |
| Anti-viral effects | Balanced differentiation of effector CD8 and CD4 T cells | [51] |
| Reduces risk of myocarditis | Reduces concentration of catecholamines | [52] |
| Reduces risk of myocarditis | Inhibits RAS | [53] |
| Reduces risk of vascular dilation and permeability and hypotensin | Inhibits RAS-mediated bradykinin storm | [46] |
| Protects against the effects of histamines such as acute immune-mediated reactions [54], lung dysregulation [55], increase in Th2 and decrease in Th1 cytokines [56], and thus susceptibility to respiratory tract infections [57] | Preserves stability of mast cells, which can release histamine when activated. | [58] |
| Promotes adaptive immunity | Regulations of T cell proliferation | [27] |
| Neuroprotection | Reduces inflammation and oxidative stress | [59] |
| Protection against exacerbation by other viruses | Reduces risk of Epstein–Barr virus infection | [60] |

Abbreviations: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; ACE2 = angiotensin-converting enzyme 2; RAS = renin angiotensin system.

# Pourquoi donner de la vitamine D dans les rhumatismes inflammatoires?

- Pour prévenir la COVID?
- Pour éviter le développement de la polyarthrite chez des pairs?
- Pour diminuer l’activité inflammatoire?
- Pour éviter les fractures?

# Pour diminuer l’activité inflammatoire?

# A randomised, double-blind, placebo-controlled study assessing the efficacy of high doses of vitamin D on functional disability in patients with rheumatoid arthritis

M. Soubrier[1], C. Lambert[2], B. Combe[3], P. Gaudin[4], T. Thomas[5], J. Sibilia[6], M. Dougados[7], J-J. Dubost[1]

Clinical and Experimental Rheumatology 2018; **36**: 1056-1060.

- RA according to the revised 1987 ACR criteria
- be in non-remission (DAS28 >2.6)
- display serum 25[OH] D levels <30 ng/mL

- Patients were randomised according to a 1:1 ratio to receive either vitD (100,000IU vial) or placebo
- After administering the loading dose, all patients were given 1 vial every 4 weeks until the 24th week. Patients were assessed at Week 24

- **HAQ at 6 month**

# A randomised, double-blind, placebo-controlled study assessing the efficacy of high doses of vitamin D on functional disability in patients with rheumatoid arthritis

M. Soubrier[1], C. Lambert[2], B. Combe[3], P. Gaudin[4], T. Thomas[5], J. Sibilia[6], M. Dougados[7], J-J. Dubost[1]

Clinical and Experimental Rheumatology 2018; **36**: 1056-1060.

- 59 RA patients were enrolled in the study, 30 of whom were assigned to placebo group and 29 to vitD group

- At 6 months, when no adjustments were made, there **was no significant difference** between the vitD and placebo groups as regards with the primary efficacy parameter, namely the HAQ score

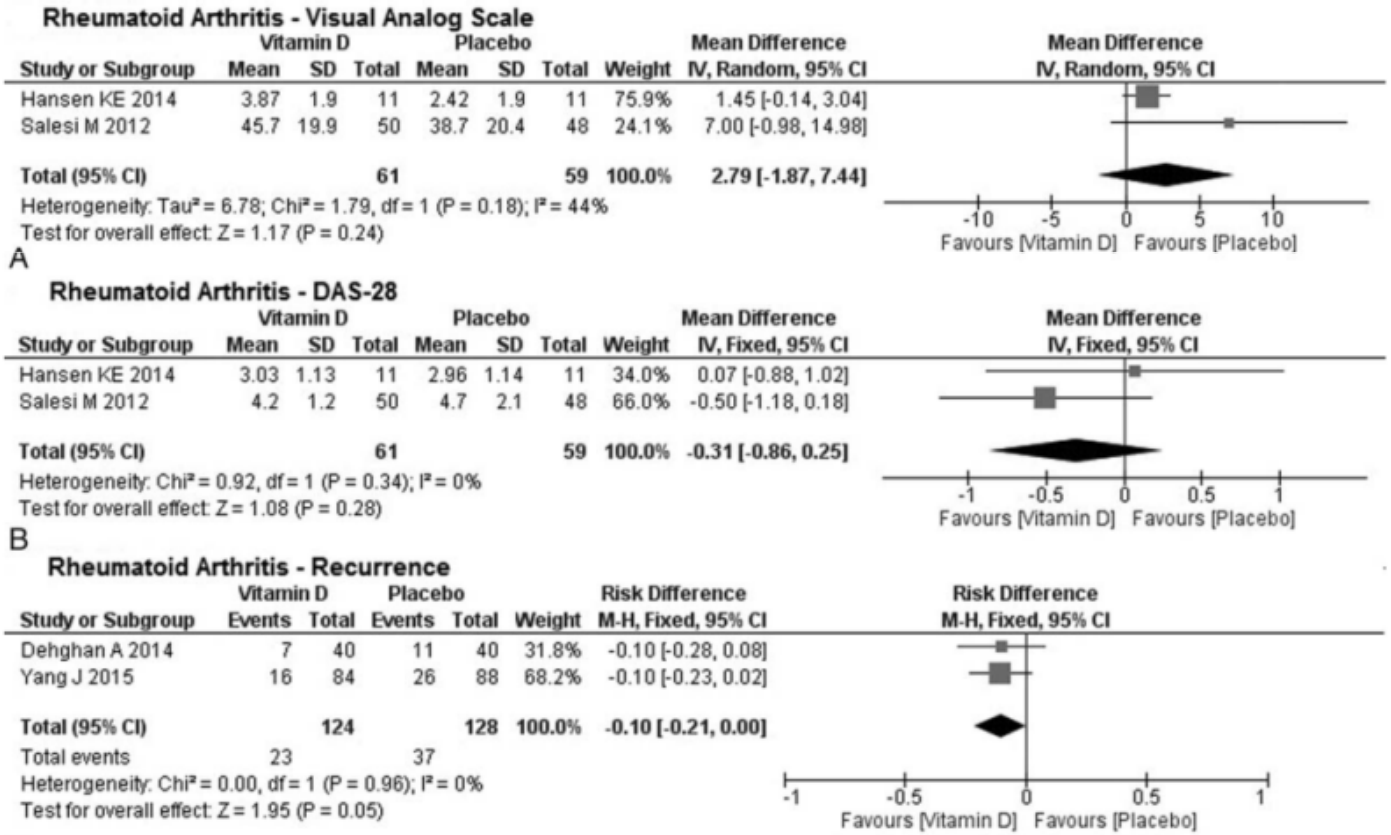
- After **adjusting for age, gender, season, and initial vitD status**, the between-group difference achieved statistically significance (Vit D group **-0.03±0.23 vs. 0.08**±0.25 placebo group, p=0.046) pas cliniquement significatif

- **In the subgroup** of patients exhibiting serum 25[OH]D levels <20ng/mL, there was a significant decrease in HAQ score observed at 6 months in patients given vitD (-0.12 [-0.19, +0.19]), as compared to those receiving placebo (+0.12 [-0.06, 0.25]) (p=0.03)

# Vitamin D supplementation and disease activity in patients with immune-mediated rheumatic diseases

## A systematic review and meta-analysis

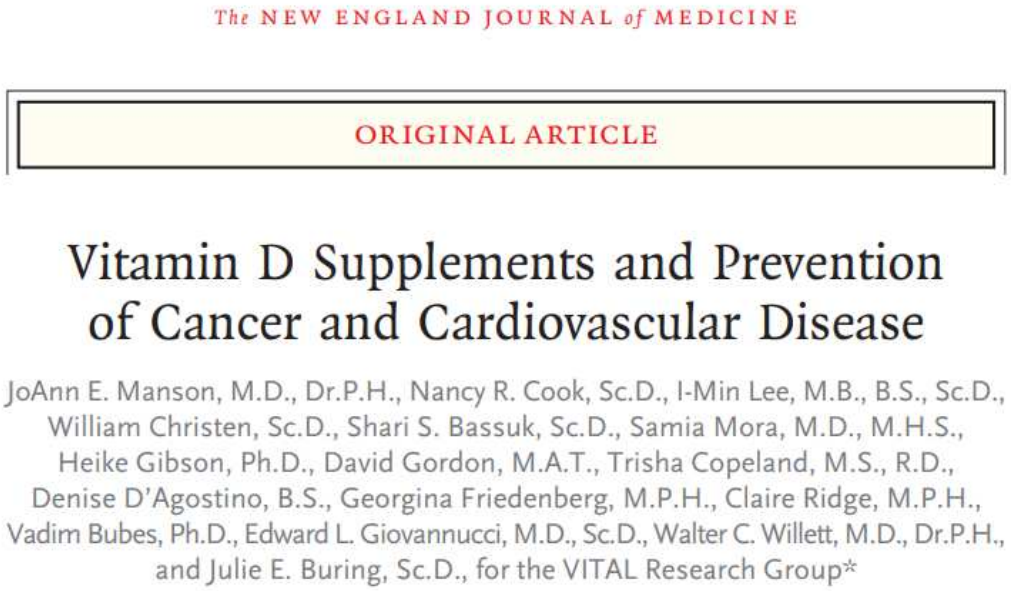
André Silva Franco, MD[a], Thiago Quadrante Freitas[a], Wanderley M. Bernardo, MD, PhD[b], Rosa Maria R. Pereira, MD, PhD[a,*]



# Pour éviter le développement d’une polyarthrite?

# Etude VITAL

- The VITamin D and OmegA-3 TriaL (VITAL) is a randomized clinical trial in 25,871 U.S. men and women investigating whether taking daily **dietary supplements of vitamin D3 (2000 IU)** or **omega-3 fatty acids (Omacor® fish oil, 1 gram)** reduces the **risk of developing cancer, heart disease, and stroke in people who do not have a prior history of these illnesses**


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Vitamin D Supplements and Prevention of Cancer and Cardiovascular Disease

JoAnn E. Manson, M.D., Dr.P.H., Nancy R. Cook, Sc.D., I-Min Lee, M.B., B.S., Sc.D., William Christen, Sc.D., Shari S. Bassuk, Sc.D., Samia Mora, M.D., M.H.S., Heike Gibson, Ph.D., David Gordon, M.A.T., Trisha Copeland, M.S., R.D., Denise D'Agostino, B.S., Georgina Friedenberg, M.P.H., Claire Ridge, M.P.H., Vadim Bubes, Ph.D., Edward L. Giovannucci, M.D., Sc.D., Walter C. Willett, M.D., Dr.P.H., and Julie E. Buring, Sc.D., for the VITAL Research Group*

# Méthodologie

- Population incluse :
  - 25,871 participants
  - Pas d'antécédents de cancer ou pathologies cardiovasculaire

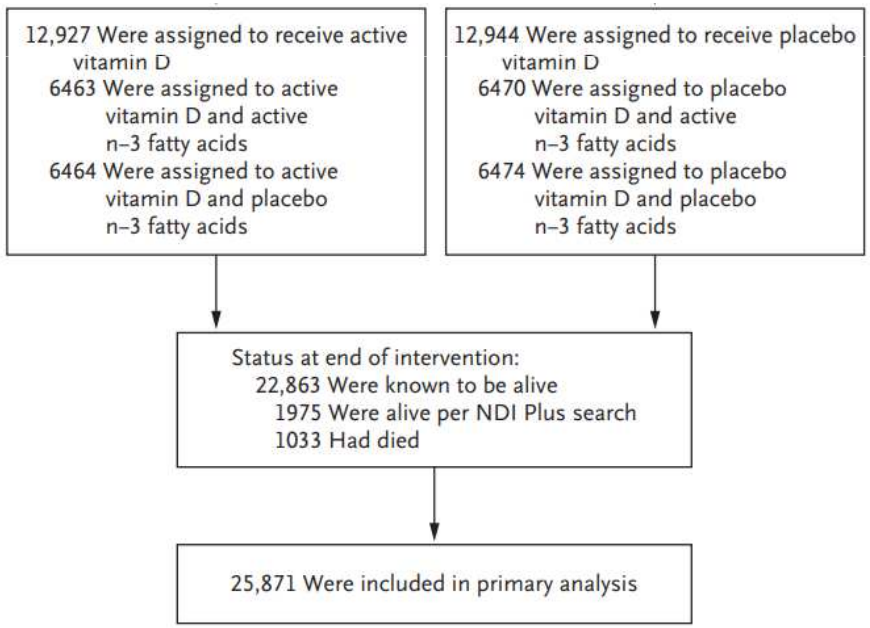


**Table 1. Characteristics of the Participants at Baseline, According to Randomized Assignment to Vitamin D or Placebo.***

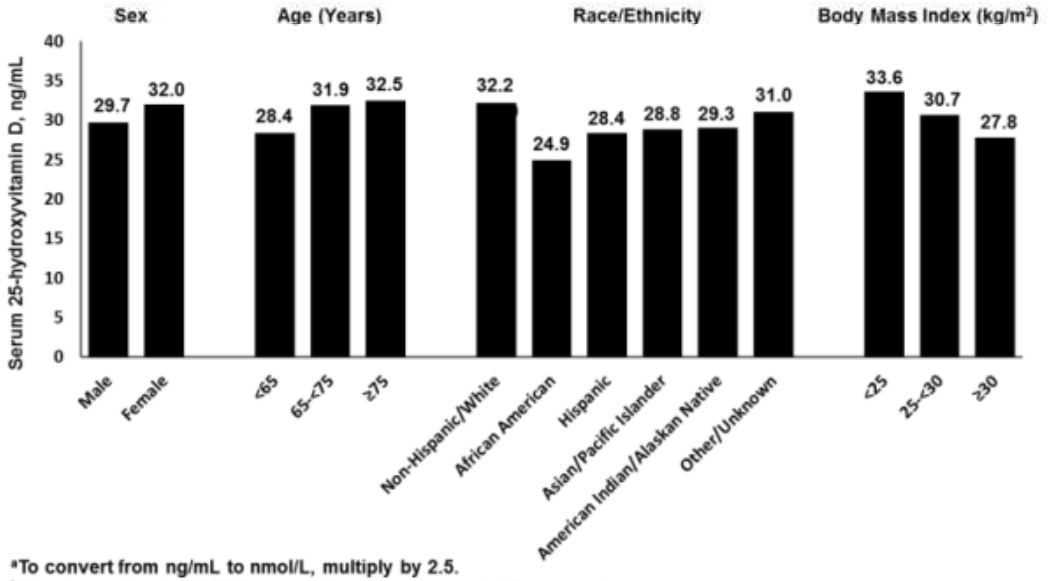
| Characteristic | Total (N = 25,871) | Vitamin D Group (N = 12,927) | Placebo Group (N = 12,944) |
|---|---|---|---|
| Female sex — no. (%) | 13,085 (50.6) | 6547 (50.6) | 6538 (50.5) |
| Age — yr | 67.1±7.1 | 67.1±7.0 | 67.1±7.1 |
| Race or ethnic group — no./total no. (%)† | | | |
| Non-Hispanic white | 18,046/25,304 (71.3) | 9013/12,647 (71.3) | 9033/12,657 (71.4) |
| Black | 5106/25,304 (20.2) | 2553/12,647 (20.2) | 2553/12,657 (20.2) |
| Nonblack Hispanic | 1013/25,304 (4.0) | 516/12,647 (4.1) | 497/12,657 (3.9) |
| Asian or Pacific Islander | 388/25,304 (1.5) | 188/12,647 (1.5) | 200/12,657 (1.6) |
| Native American or Alaskan native | 228/25,304 (0.9) | 118/12,647 (0.9) | 110/12,657 (0.9) |
| Other or unknown | 523/25,304 (2.1) | 259/12,647 (2.0) | 264/12,657 (2.1) |
| Body-mass index‡ | 28.1±5.7 | 28.1±5.7 | 28.1±5.8 |
| Current smoking — no./total no. (%) | 1836/25,485 (7.2) | 921/12,729 (7.2) | 915/12,756 (7.2) |
| Hypertension treated with medication — no./total no. (%) | 12,791/25,698 (49.8) | 6352/12,834 (49.5) | 6439/12,864 (50.1) |
| Current use of cholesterol-lowering medication — no./total no. (%) | 9524/25,428 (37.5) | 4822/12,700 (38.0) | 4702/12,728 (36.9) |
| Diabetes — no./total no. (%) | 3549/25,828 (13.7) | 1812/12,903 (14.0) | 1737/12,925 (13.4) |

* Plus–minus values are means ±SD. Percentages may not sum to 100 because of rounding. There were no significant differences between the groups with regard to the baseline characteristics.
† Race and ethnic group were reported by the participants.
‡ The body-mass index is the weight in kilograms divided by the square of the height in meters. Data were missing for 2.4% of the participants.

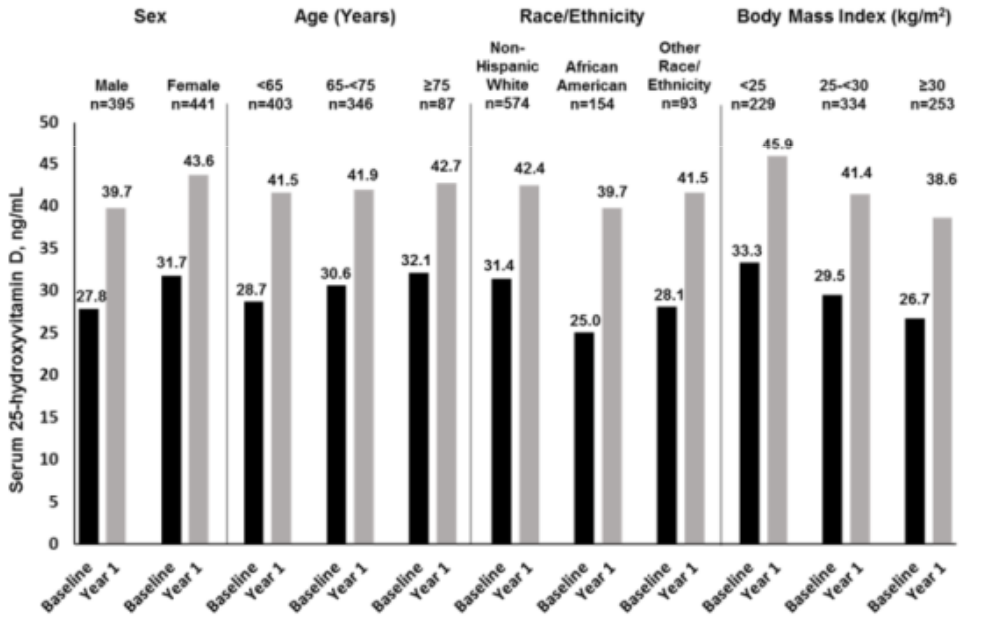
# Effet sur la vitamine D

- most groups had 25-hydroxyvitamin D levels close to, or above, 40 ng per milliliter (100 nmol per liter) after 1 year of supplementation with vitamin D

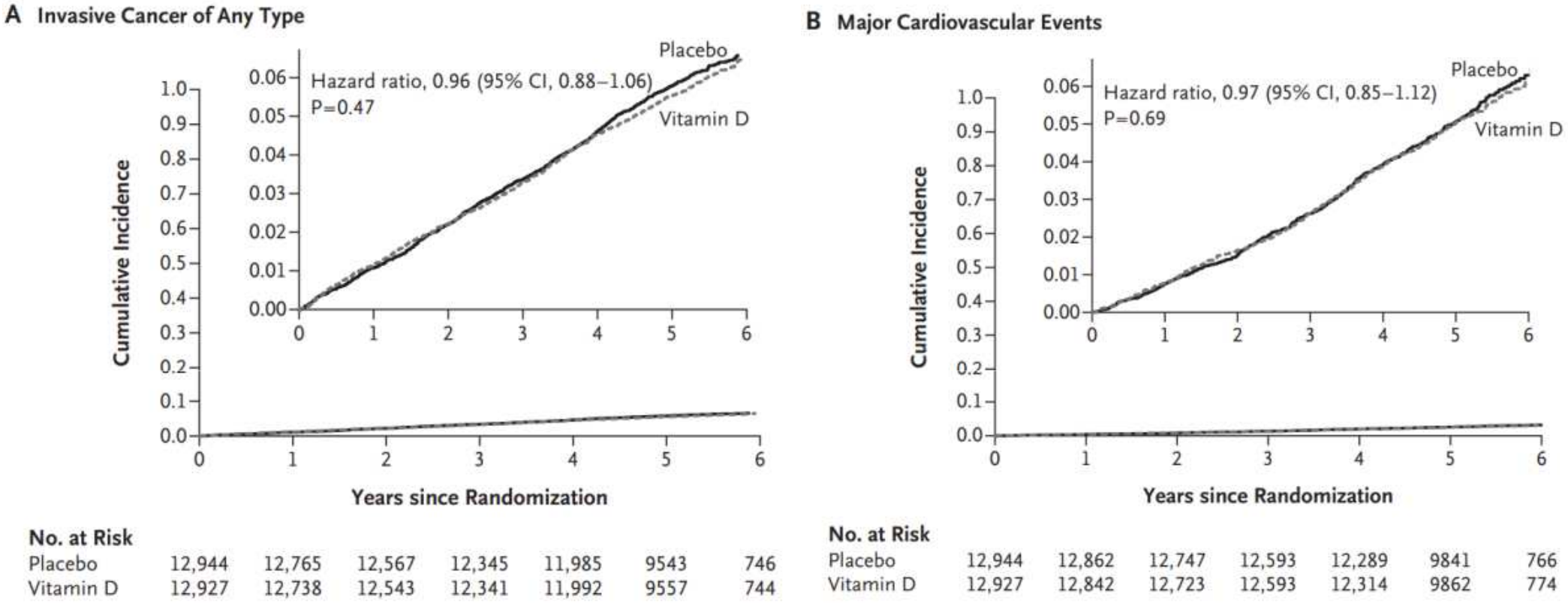
**Figure S1(A). Mean Baseline Serum 25-hydroxyvitamin D Levels (ng/mL)[a] by Demographic Variables (Sex, Age, Race/Ethnicity) and Body Mass Index.[b]**




[a]To convert from ng/mL to nmol/L, multiply by 2.5.
[b]Blood samples (n=15,787) were collected year-round (all seasons).




[a]To convert from ng/mL to nmol/L, multiply by 2.5.
[b]Blood samples (n=1,644) were collected primarily in the winter and spring. Only the treatment group is graphed




Ancillary studies addressing treatment effects on diabetes, heart failure, cognition, autoimmune disorders, and other outcomes will inform the overall benefit–risk balance of high dose supplementation

## Effect of Vitamin D3 and Omega-3 Fatty Acid Supplementation on Risk of Frailty: An Ancillary Study of a Randomized Clinical Trial

**Conclusions and relevance:** In this ancillary study of the VITAL randomized clinical trial, treatment with vitamin D3 or omega-3 fatty acid supplementation, compared with placebo, did not affect the rate of frailty change or incidence over time. These results do not support routine use of either vitamin D3 or omega-3 fatty acid supplementation for frailty prevention in generally healthy community-dwelling older adults not selected for vitamin D3 deficiency.

## Effect of Long-term Supplementation With Marine Omega-3 Fatty Acids vs Placebo on Risk of Depression or Clinically Relevant Depressive Symptoms and on Change in Mood Scores: A Randomized Clinical Trial

**Conclusions and relevance:** Among adults aged 50 years or older without clinically relevant depressive symptoms at baseline, treatment with omega-3 supplements compared with placebo yielded mixed results, with a small but statistically significant increase in risk of depression or clinically relevant depressive symptoms but no difference in mood scores, over a median follow-up of 5.3 years. These findings do not support the use of omega-3 supplements in adults to prevent depression.

## Effect of vitamin D on cognitive decline: results from two ancillary studies of the VITAL randomized trial

Thus, vitamin D3 (2000 IU/day cholecalciferol) supplementation was not associated with cognitive decline over 2-3 years among community-dwelling older participants but may provide modest cognitive benefits in older Black adults, although these results need confirmation.

## Effect of vitamin D supplementation on urinary incontinence in older women: ancillary findings from a randomized trial

**Conclusion:** Vitamin D supplementation compared to placebo for 2 to 5 years was not associated with differences in the prevalence, incidence, or progression of urinary incontinence in older women with and without adequate serum vitamin D levels, with inconsistent differences among subgroups. The findings showed that the broad use of moderate doses of vitamin D supplementation did not reduce urinary incontinence in older women.

# La vitamine D dans la prévention des MAI

- Il n'existe pas de traitement préventif des maladies auto-immunes, qui représentent une des principales causes de morbi-mortalité des femmes < 65 ans
- Les arguments pour prévenir les maladies auto-immunes par apport en vitamine D et oméga 3

**1. La vitamine D**

- Elle régule l'expression de gènes impliqués de l'immunité innée et adaptative
- Des taux plasmatiques élevés de vitamine D et le fait d'habiter dans une région exposée aux UV sont associés à un moindre risque de PR dans l'étude NHS *(Nurses' Health Study)*[1]

**2. Les oméga 3**

- Ils ont des propriétés anti-inflammatoires in vitro et in vivo
- Une consommation élevée en oméga 3 avec des proportions élevées d'oméga 3 dans les membranes cellulaires des globules rouges sont associées à un moindre risque de développer une PR[2]


1. *Hiraki LT et al. Rheumatology 2014;53(12):2243-8 ; Arkema EV et al. Ann Rheum Dis 2013;72(4):506-11*
2. *Pedersen M et al. J Rheumatol 2005;32(7):1249-52 ; Gan RW et al. Rheumatology 2017;56(12):2229-36*

## Vitamin D and marine omega 3 fatty acid supplementation and incident autoimmune disease: VITAL randomized controlled trial

Jill Hahn,[1,2,3] Nancy R Cook,[1,4] Erik K Alexander,[5] Sonia Friedman,[6] Joseph Walter,[4] Vadim Bubes,[4] Gregory Kotler,[4] I-Min Lee,[1,4] JoAnn E Manson,[1,4] Karen H Costenbader[2]

- The primary endpoint was **total confirmed autoimmune disease** incidence
  - Rheumatoid arthritis
  - polymyalgia rheumatica
  - autoimmune thyroid disease
  - Psoriasis
  - inflammatory bowel disease,
  - space to write in all other new onset autoimmune diseases

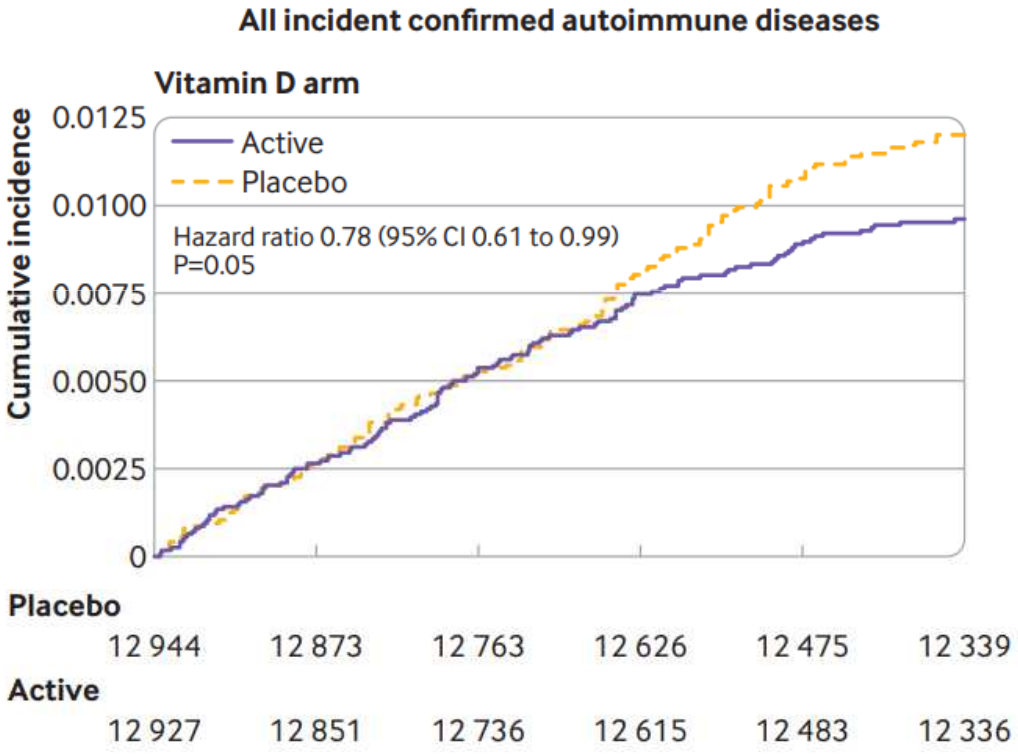
- Autodélcaration par le patient puis étude du dossier par 2 évaluateurs
- Si possible vu de dossier mais pas de preuve = « possible maladie auto-immune »

**Table 2 | Hazard ratios and 95% confidence intervals for primary and secondary endpoints according to randomized assignment to vitamin D or placebo**

| Endpoint | Vitamin D group (n=12 927) | Placebo group (n=12 944) | Hazard ratio (95% CI) | P value |
|---|---|---|---|---|
| **Primary endpoint** | | | | |
| Confirmed autoimmune diseases | 123 | 155 | 0.78 (0.61 to 0.99) | 0.05 |
| **Secondary endpoints** | | | | |
| Confirmed+probable autoimmune diseases | 210 | 247 | 0.85 (0.70 to 1.02) | 0.09 |
| **Analyses excluding all prerandomization autoimmune diseases** | | | | |
| Confirmed autoimmune diseases | 102 | 128 | 0.79 (0.61 to 1.03) | 0.08 |
| Confirmed+probable autoimmune diseases | 170 | 209 | 0.81 (0.66 to 1.00) | 0.05 |
| **Analyses excluding first two years of follow-up** | | | | |
| Confirmed autoimmune diseases | 54 | 87 | 0.61 (0.43 to 0.86) | 0.005 |
| Confirmed+probable autoimmune diseases | 94 | 133 | 0.69 (0.53 to 0.90) | 0.007 |
| **Individual autoimmune diseases** | | | | |
| Confirmed rheumatoid arthritis | 15 | 24 | 0.58 (0.30 to 1.13) | 0.11 |
| Confirmed+probable rheumatoid arthritis | 18 | 27 | 0.63 (0.34 to 1.15) | 0.13 |
| Confirmed polymyalgia rheumatic* | 31 | 43 | 0.70 (0.44 to 1.12) | 0.14 |
| Confirmed+probable polymyalgia rheumatica | 32 | 43 | 0.72 (0.46 to 1.15) | 0.17 |
| Confirmed autoimmune thyroid disease | 21 | 11 | 1.63 (0.77 to 3.45) | 0.20 |
| Confirmed+probable autoimmune thyroid disease | 99 | 94 | 1.05 (0.78 to 1.41) | 0.74 |
| Confirmed psoriasis† | 15 | 23 | 0.72 (0.37 to 1.39) | 0.32 |
| Confirmed+probable psoriasis | 17 | 25 | 0.70 (0.37 to 1.32) | 0.27 |
| Confirmed other autoimmune disease | 40 | 56 | 0.74 (0.49 to 1.11) | 0.15 |
| Confirmed+probable other autoimmune disease | 45 | 63 | 0.73 (0.50 to 1.08) | 0.12 |

Analyses were from Cox regression models controlled for age, sex, race, and omega 3 fatty acid randomization group.
*Fourteen participants had confirmed polymyalgia rheumatica without giant cell arteritis, 18 had confirmed giant cell arteritis without polymyalgia rheumatica, and two were confirmed with both.
†No participants had psoriatic arthritis.

# Que se passe-t-il à 3 ans?



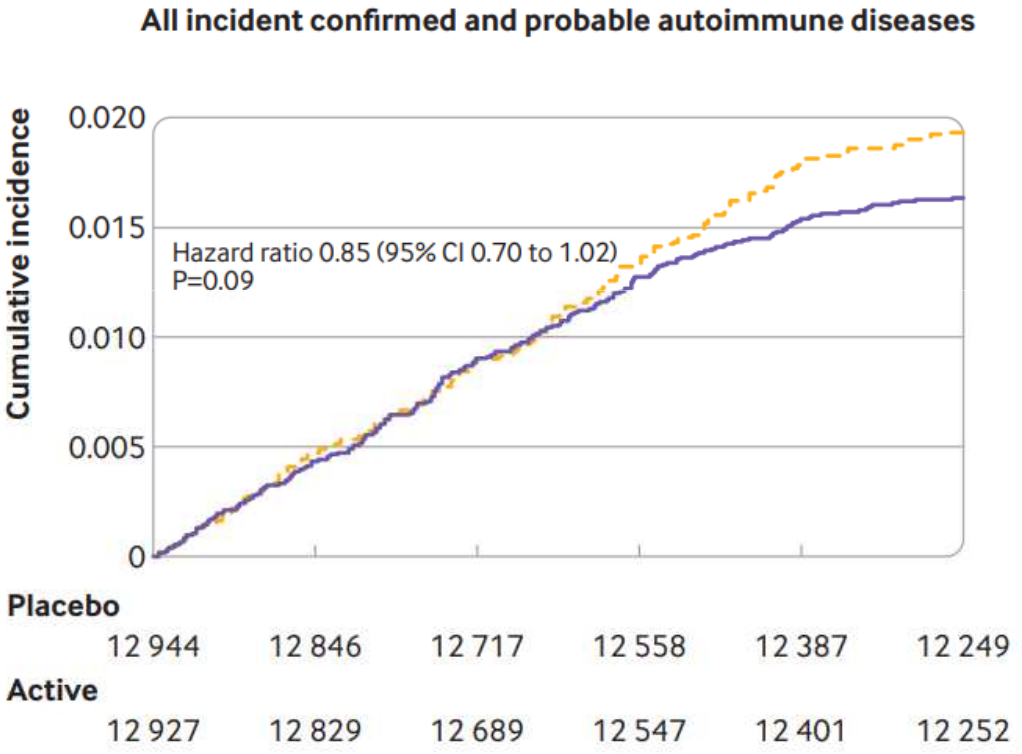
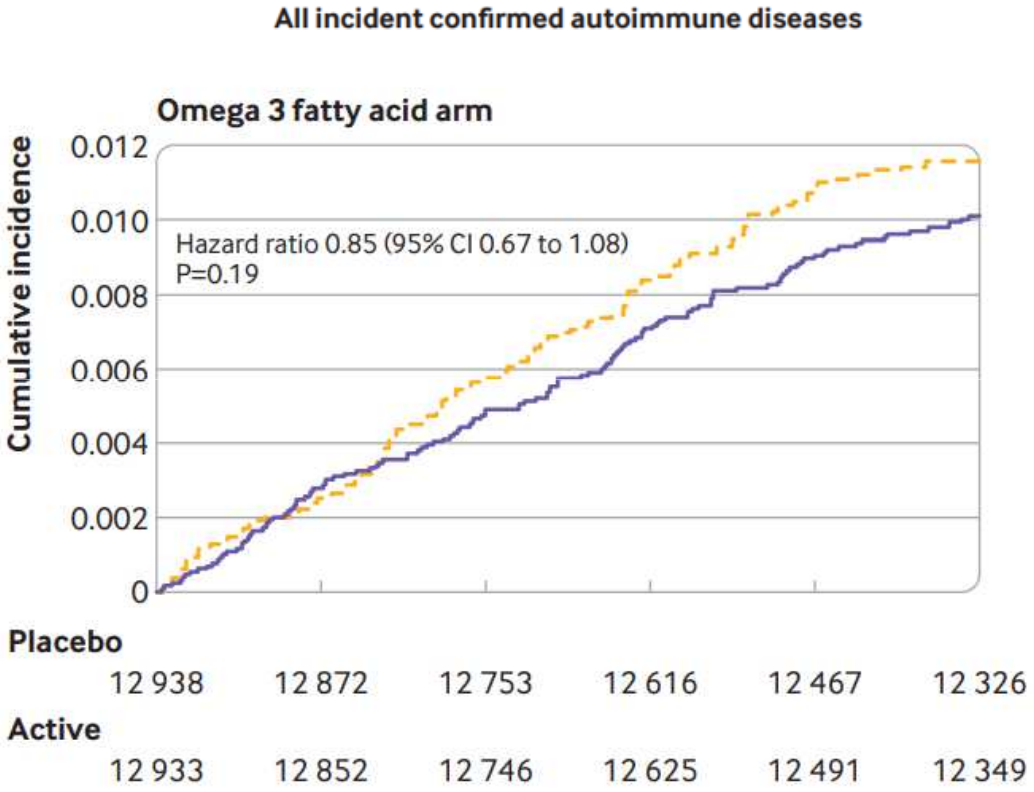



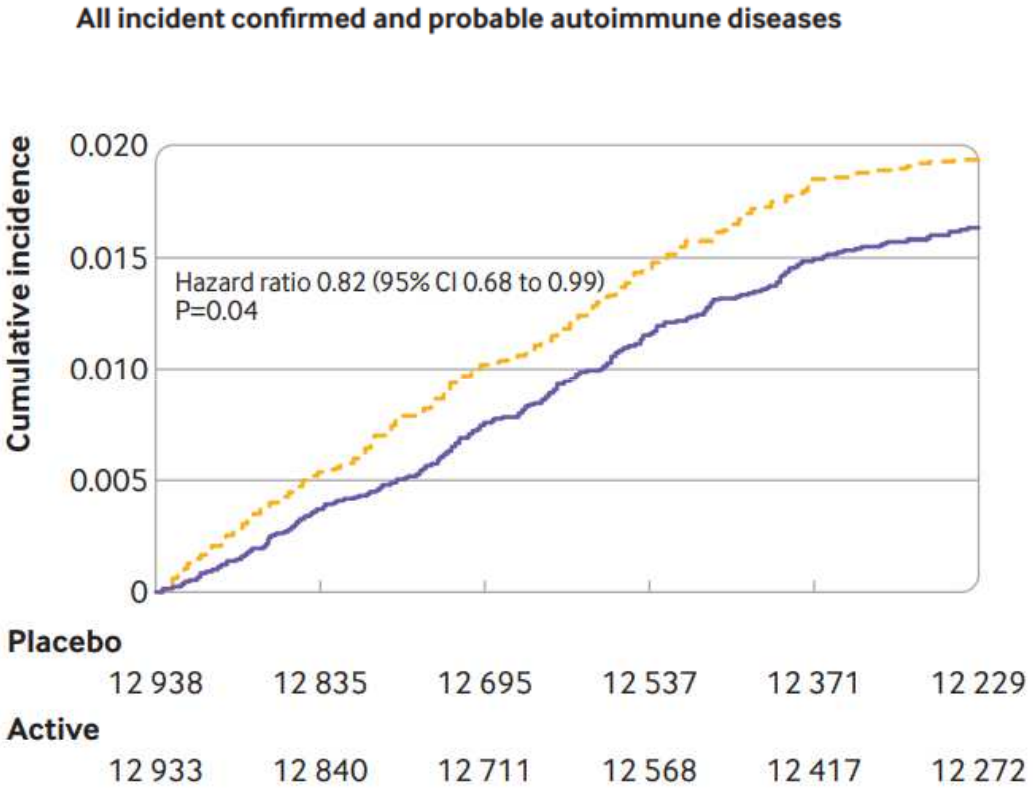
**Table 3 | Hazard ratios and 95% confidence intervals for primary and secondary endpoints according to randomized assignment to omega 3 fatty acids or placebo within VITAL trial in intention-to-treat analyses**

| Endpoint | Omega 3 group (n=12 933) | Placebo group (n=12 938) | Hazard ratio (95% CI) | P value |
|---|---|---|---|---|
| **Primary endpoint** | | | | |
| Confirmed autoimmune disease | 130 | 148 | 0.85 (0.67 to 1.08) | 0.19 |
| **Secondary endpoints** | | | | |
| Confirmed+probable autoimmune disease | 208 | 249 | 0.82 (0.68 to 0.99) | 0.04 |
| **Analyses excluding all prerandomization autoimmune disease** | | | | |
| Confirmed autoimmune disease | 111 | 119 | 0.91 (0.70 to 1.18) | 0.48 |
| Confirmed+probable autoimmune disease | 180 | 199 | 0.90 (0.73 to 1.10) | 0.30 |
| **Analyses excluding first two years of follow-up** | | | | |
| Confirmed autoimmune disease | 67 | 74 | 0.90 (0.64 to 1.26) | 0.54 |
| Confirmed+probable autoimmune disease | 110 | 117 | 0.94 (0.72 to 1.23) | 0.66 |
| **Individual autoimmune diseases** | | | | |
| Confirmed rheumatoid arthritis | 15 | 24 | 0.58 (0.30 to 1.13) | 0.11 |
| Confirmed+probable rheumatoid arthritis | 17 | 28 | 0.57 (0.31 to 1.05) | 0.07 |
| Confirmed polymyalgia rheumatica | 34 | 40 | 0.87 (0.55 to 1.38) | 0.55 |
| Confirmed+probable polymyalgia rheumatica | 34 | 41 | 0.85 (0.54 to 1.34) | 0.48 |
| Confirmed autoimmune thyroid disease | 12 | 20 | 0.53 (0.25 to 1.14) | 0.10 |
| Confirmed+probable autoimmune thyroid disease | 85 | 108 | 0.80 (0.59 to 1.07) | 0.13 |
| Confirmed psoriasis | 23 | 15 | 1.57 (0.80 to 3.07) | 0.19 |
| Confirmed+probable psoriasis | 25 | 17 | 1.44 (0.76 to 2.72) | 0.26 |
| Confirmed other autoimmune disease | 45 | 51 | 0.84 (0.56 to 1.26) | 0.40 |
| Confirmed+probable other autoimmune disease | 48 | 60 | 0.76 (0.52 to 1.12) | 0.17 |

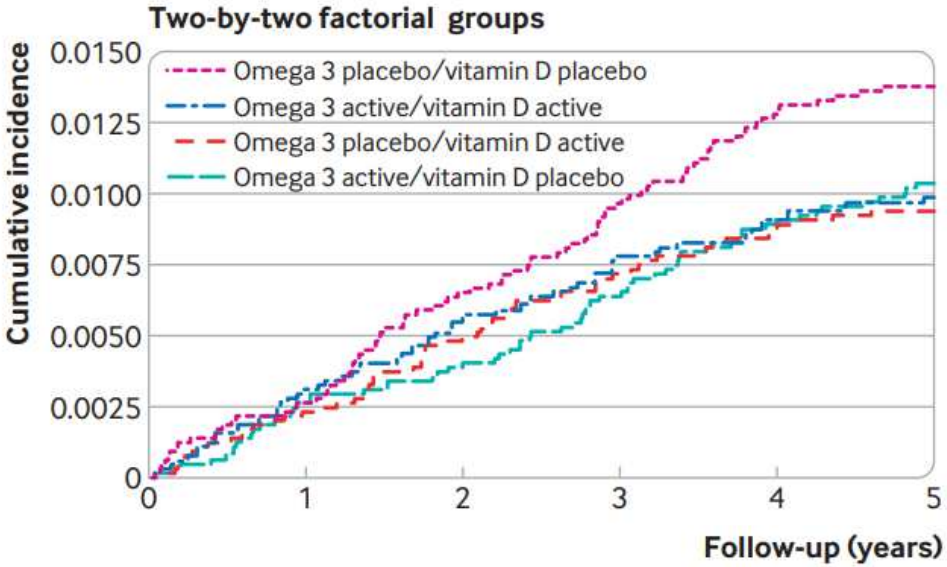
VITAL=vitamin D and omega 3 trial.
Analyses were from Cox regression models controlled for age, sex, race, and vitamin D randomization group.

# Effet de la supplémentation en Omega 3 ?



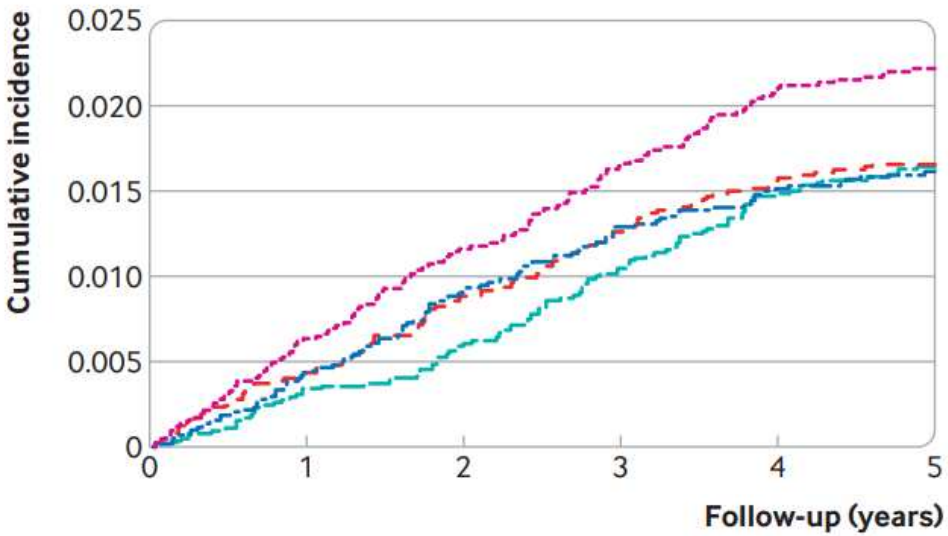
**All incident confirmed autoimmune diseases**




Omega 3 placebo/vitamin D placebo: reference
Omega 3 active/vitamin D active: hazard ratio 0.69 (95% CI 0.49 to 0.96)
Omega 3 placebo/vitamin D active: hazard ratio 0.68 (95% CI 0.48 to 0.94)
Omega 3 active/vitamin D placebo: hazard ratio 0.74 (95% CI 0.54 to 1.03)

| | | | | | |
|---|---|---|---|---|---|
| **Omega 3 placebo/vitamin D placebo** | 6441 | 6379 | 6301 | 6224 | 6157 |
| **Omega 3 active/vitamin D active** | 6420 | 6362 | 6300 | 6240 | 6167 |
| **Omega 3 placebo/vitamin D active** | 6431 | 6374 | 6315 | 6243 | 6169 |
| **Omega 3 active/vitamin D placebo** | 6432 | 6384 | 6325 | 6251 | 6182 |

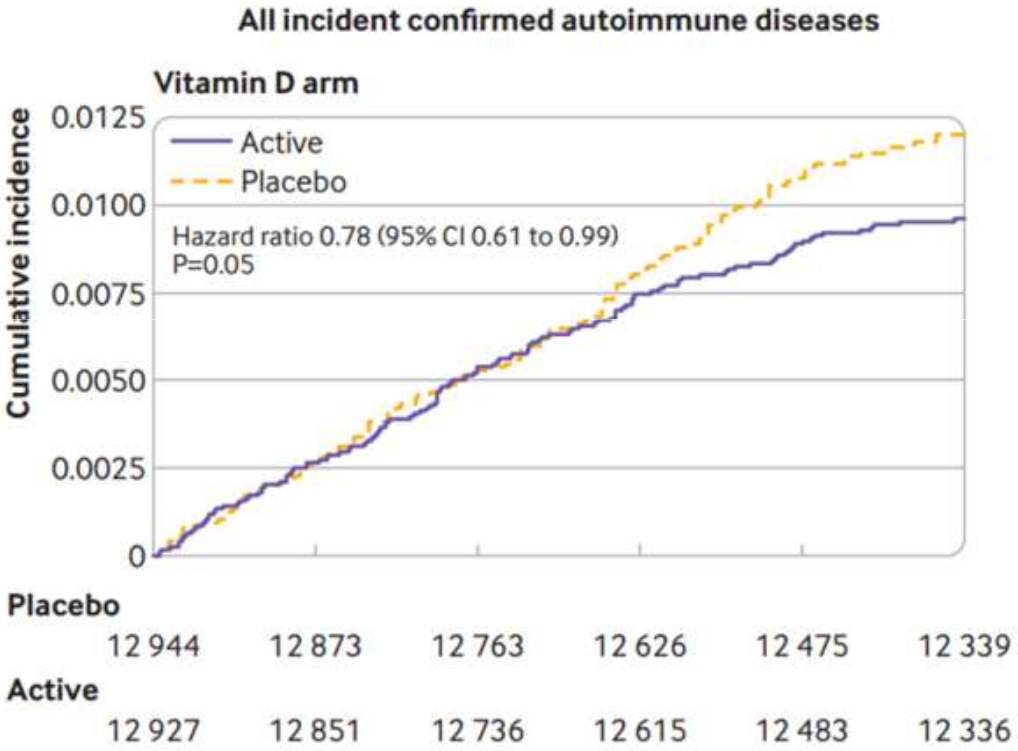
**All incident confirmed and probable autoimmune diseases**




Omega 3 placebo/vitamin D placebo: reference
Omega 3 active/vitamin D active: hazard ratio 0.71 (95% CI 0.55 to 0.92)
Omega 3 placebo/vitamin D active: hazard ratio 0.76 (95% CI 0.59 to 0.99)
Omega 3 active/vitamin D placebo: hazard ratio 0.74 (95% CI 0.57 to 0.96)

| | | | | | |
|---|---|---|---|---|---|
| **Omega 3 placebo/vitamin D placebo** | 6417 | 6346 | 6257 | 6172 | 6104 |
| **Omega 3 active/vitamin D active** | 6411 | 6340 | 6267 | 6202 | 6127 |
| **Omega 3 placebo/vitamin D active** | 6418 | 6349 | 6280 | 6199 | 6125 |
| **Omega 3 active/vitamin D placebo** | 6429 | 6371 | 6301 | 6215 | 6145 |

# Interprétation




Incidence cumulative des MAI à 5 ans

- Vitamine D: 0,95%
- Placebo: 1,19%

Différence absolue : 0,2%
Différence relative -21%
NNT: 500 patients

Interprétation de l'étude par le sauteurs
Si on prend les 3 dernière années, **- 39% de risque de MAI**

➡ Faut-il traiter de manière préventive la population générale par vitamine D?

# Limites

- Patients de 67 en moyenne
- Pas d’antécédent de maladies auto-immunes
- Carence en vitamine D modérée
- Multi groupes
- Etude Ancillaire

- Quid dans les populations à risque ?

ORIGINAL ARTICLE

JBMR®

# Effects of Supplemental Vitamin D on Bone Health Outcomes in Women and Men in the VITamin D and OmegA-3 TriaL (VITAL)

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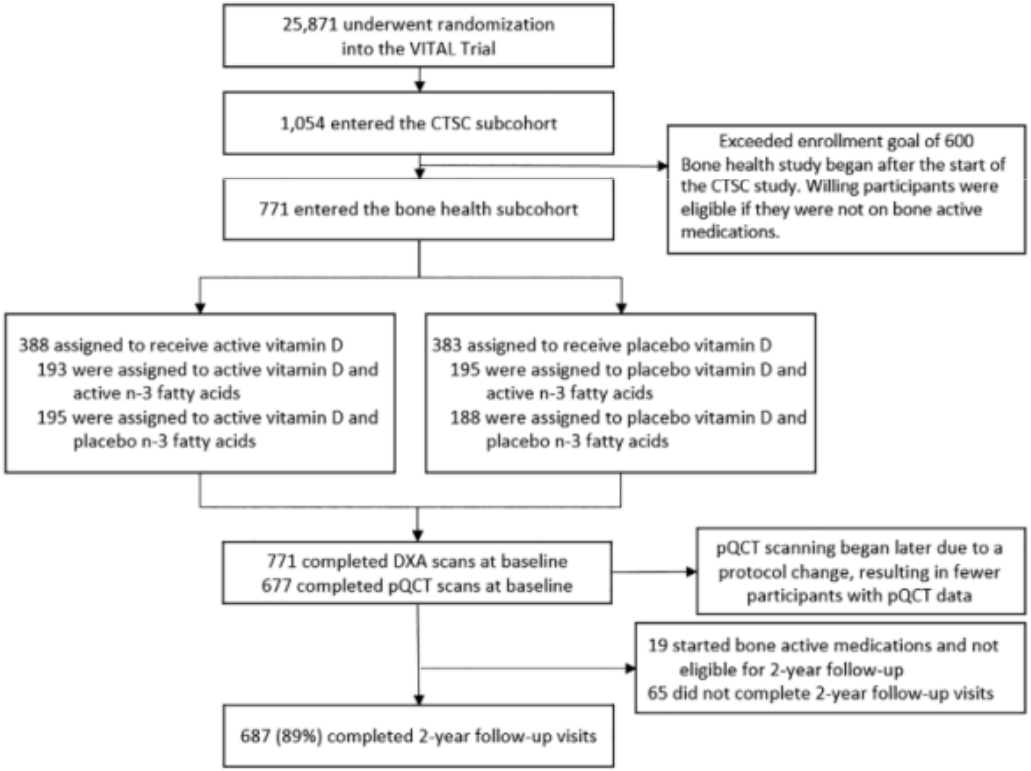

**Table 1.** Characteristics of the Bone Health Subcohort at Baseline According to Randomized Assignment to Vitamin $D_3$ Versus Placebo Groups

| Characteristic | Total ($N = 771$) | Vitamin $D_3$ group ($n = 388$) | Placebo group ($n = 383$) | $p$ Value |
|---|---|---|---|---|
| Female sex, $n$ (%), $N = 771$ | 360 (46.7%) | 179 (46.1%) | 181 (47.3%) | 0.76 |
| Age (years), mean (SD), $N = 771$ | 63.8 (6.1) | 63.7 (6.0) | 63.9 (6.3) | 0.53 |
| Race or ethnic group,[1] $n$ (%) | 755 (97.9%) | | | 0.28 |
| Non-Hispanic white | 630 (83.4%) | 317 (82.8%) | 313 (84.1%) | |
| Black | 67 (8.9%) | 35 (9.1%) | 32 (8.6%) | |
| Nonblack Hispanic | 26 (3.4%) | 11 (2.9%) | 15 (4.0%) | |
| Asian | 15 (2.0%) | 9 (2.4%) | 6 (1.6%) | |
| Native American or Alaskan native | 5 (0.7%) | 2 (0.5%) | 3 (0.8%) | |
| Other or unknown | 12 (1.6%) | 9 (2.4%) | 3 (0.8%) | |
| Body mass index (kg/m$^2$), mean (SD), $N = 771$ | 27.2 (4.8) | 27.2 (4.7) | 27.3 (4.8) | 0.91 |
| Fat mass index(kg/m$^2$), mean (SD), $N = 767$ | 10.27 (3.89) | 10.26 (4.03) | 10.28 (3.74) | 0.94 |
| Leisure time physical activity (hr/wk), median (interquartile range) MET, $N = 767$ | 21.47 (7.86–37.11) | 21.61 (7.86–37.80) | 20.99 (7.97–36.00) | 0.62 |
| Diabetes history, $n$ (%), $N = 770$ | 84 (10.9%) | 44 (11.4%) | 40 (10.4%) | 0.68 |
| Current smoking, $n$ (%), $N = 766$ | 48 (6.3%) | 26 (6.8%) | 22 (5.8%) | 0.33 |
| Any fracture history,[2] $n$ (%), $N = 771$ | 61 (7.9%) | 32 (8.3%) | 29 (7.6%) | 0.73 |
| Parental history of hip fracture, $n$ (%), $N = 733$ | 102 (13.9%) | 54 (14.8%) | 48 (13.0%) | 0.49 |
| Baseline calcium supplement use,[3] $n$ (%), $N = 771$ | 132 (17.1%) | 69 (17.8%) | 63 (16.5%) | 0.62 |
| Baseline vitamin D supplement use,[3] $n$ (%), $N = 771$ | 326 (42.3%) | 157 (40.5%) | 169 (44.1%) | 0.30 |
| Baseline total 25(OH)D (nmol/L),[4] mean (SD), $N = 770$ | 69.1 (22.7) | 67.4 (22.2) | 71.1 (23.2) | 0.025 |
| Baseline free 25(OH)D (pmol/L), mean (SD), $N = 770$ | 14.6 (4.7) | 14.4 (4.5) | 14.8 (4.8) | 0.21 |

[1] Race and ethnic groups self-reported by participants.

[2] Of those who reported fractures, 16 had a history of a fragility fracture (hip, spine, shoulder, and/or forearm fracture).

[3] Calcium supplement intake ≤1200 mg/d; vitamin D intake ≤800 IU/d.

[4] To convert values of 25(OH)D to ng/mL, multiply by 0.4.

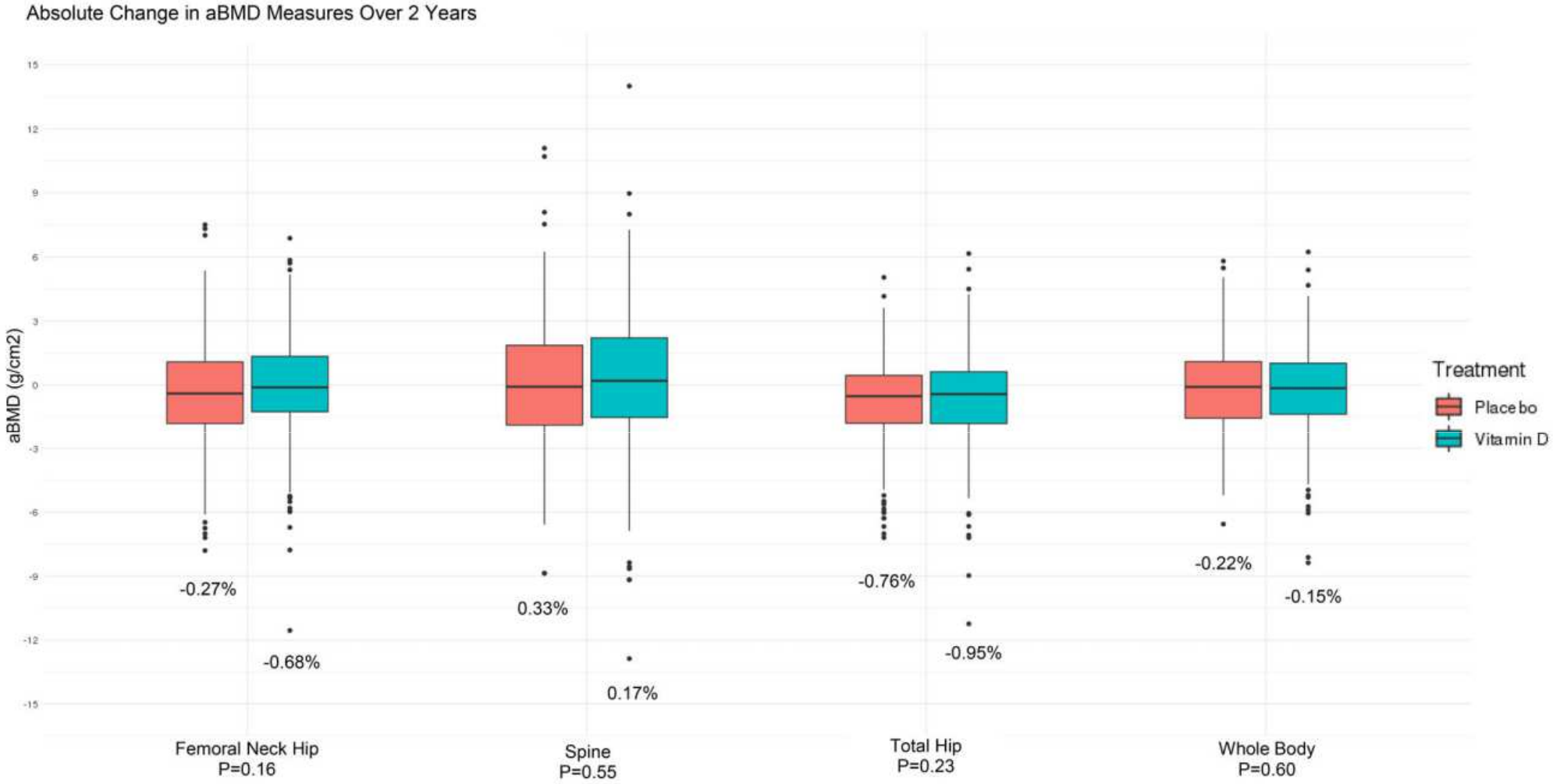


**Fig. 2.** Mean absolute changes in areal bone mineral density (aBMD) from baseline to 2 years in the vitamin $D_3$ and placebo groups. Percentages represent the percent change in aBMD over 2 years. All analyses adjusted for age, sex, and race.

# Faut-il donner de la vitamine D aux RIC

- « Ca fait pas de mal »
- Aucune preuve d'un effet bénéfique sur l'activité inflammatoire
- Effet préventif sur l'apparition de MAI?

- Pas systématique
- Si risque important de déficit (patients âgés, peu d'exposition solaire)
- Pathologie osseuse associée