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Effetti cardiovascolari della vitamina D

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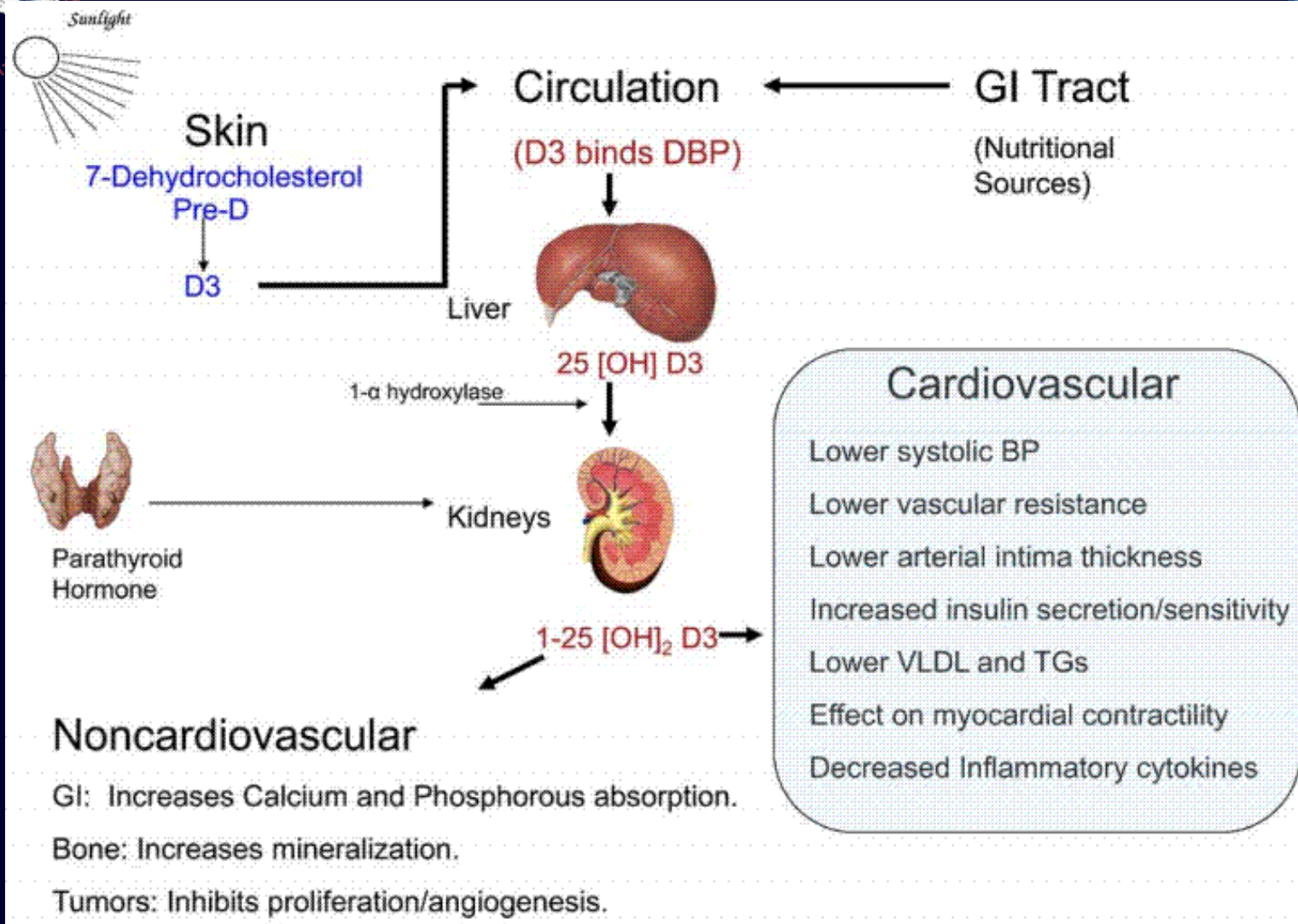
Via Antico Corso
Catania, Sicilia
Street View



U.O.C. Cardiologia Pediatrica Ospedale Santo Bambino CT

Vitamin D







Calcium 600 +D
Essential For Your Health
70 Capsules

Vitamin D might help lower heart disease risks!

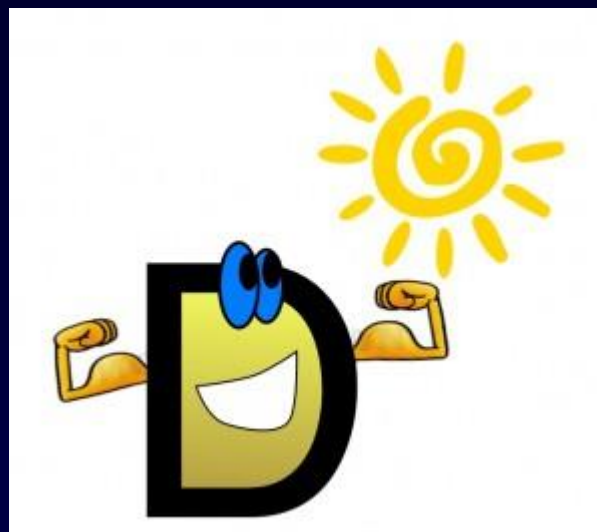
Mountainside Medical Equipment

II. Questioning & problem solving

1. Questioning:

Vitamin D deficiency → heart disease





La ricerca sugli effetti della vitamina D sulla salute è in continua espansione.

Il numero di pubblicazione, comparse su pubmed, riportanti “*vitamin D*” nel titolo è passato da:

3119 nel 2011 a 3919 nel 2014!!!

Letter

Vitamin D Deficiency Contributed to Mozart's Death

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Top Vitamin D Research of 2014

Higher vitamin D blood levels may reduce the risk of many types of disease including autoimmune diseases, cancers, cardiovascular disease, dementia, diabetes mellitus and fractures. (*OMNS Feb 3, 2015*)

Randomized Control Trials (RCT) in 2014

–Vitamin D3 supplementation in patients with chronic obstructive pulmonary disease [Martineau, 2014]

A vitamin D trial in the UK in which patients with chronic obstructive pulmonary disease (COPD) were given 120,000 IU vitamin D3 every two months for a year found that vitamin D3 supplementation was protective against moderate or severe exacerbation in those with baseline 25(OH)D concentrations < 50 nmol/L (20 ng/mL) but not for those with concentrations > 50 nmol/L. Vitamin D3 supplementation had no effect on upper respiratory infections. This is consistent with previous RCTs that used high doses at infrequent intervals, every 2 months in this case; however other trials that used an adequate dose given daily have shown reduction in upper respiratory tract infections.

–Vitamin D promotes vascular regeneration [Wong, 2014]

This study demonstrated that vitamin D improved cardiovascular disease. The German team investigated this effect several ways. They showed that supplementation with 4000 IU/day of vitamin D3 increased the number of circulating angiogenic myeloid cells, which promote growth and vascular regeneration necessary for a healthy cardiovascular system. A similar result was found in a mouse model, which also demonstrated restoration of impaired angiogenesis (new vessel formation) function. They also examined the mechanisms by which vitamin D acted.

Vitamin D and depression: a systematic review and meta-analysis comparing studies with and without biological flaws. [Spedding, 2014]

This paper reported on a statistical average of many studies of vitamin D RCTs without methodological flaws and found that vitamin D supplementation resulted in a statistically significant improvement in clinical depression. However, the same analysis of vitamin D RCTs with methodological flaws found a statistically significant worsening of depression. The major flaws identified included not increasing 25(OH)D concentrations and not measuring baseline or final 25(OH)D concentrations. Vitamin D supplementation of > 800 IU/d was somewhat favorable in the management of depression.

–Effect of vitamin D supplementation on antibiotic use: a randomized controlled trial. [Tran, 2014]

A post hoc (conducted after the study was completed) analysis of a vitamin D RCT involving 644 Australian residents aged 60-84 years found a significant reduction in prescribed antibiotics if they were over the age of 70 years and taking 60,000 IU of vitamin D3 monthly compared with the placebo groups. The effect was not significant for those < 70 years of age. This study suggests that taking an average of 2000 IU/day vitamin D3 reduces the risk of infections, most likely respiratory infections, in older adults.

–Observational studies of Vitamin D

Observational studies provide some of the strongest evidence to date for beneficial health outcomes related to vitamin D. Observational studies measure vitamin D status and health outcomes for every participant. Blood samples are taken at the time of enrollment and people are followed for several years. Vitamin D is said to be effective if positive health outcomes result.

–Vitamin D and risk of cause specific death: systematic review and meta-analysis of observational cohort and randomised intervention studies [Chowdhury, 2014]

This paper was a review of observational and RCT studies that showed a correlation between vitamin D and specific mortality outcomes. One conclusion was that supplementation with vitamin D3 significantly reduces overall mortality among older adults. They used data from 73 cohort studies (849,412 participants) and 22 RCTs (30,716 participants). In the RCTs, all cause mortality rate was reduced by 11% for vitamin D3 supplementation but increased by 4% for vitamin D2 supplementation. In addition, their meta-analysis of cancer-specific incidence and mortality rates comparing those who started in the lowest third of vitamin D blood concentrations against those in the highest third suggests that vitamin D may have a much stronger impact on survival after developing cancer than on reducing the risk of developing cancer to start with.

–Meta-analysis of all-cause mortality according to serum 25-hydroxyvitamin D [Garland, 2014]

An analysis of 32 observational studies found that as 25(OH)D concentrations increased from 13 nmol/L (5 ng/ml) to 90 nmol/L (36 ng/ml) there is a linear reduction in all-cause mortality. At concentrations greater than 90 nmol/L (36 ng/ml), no further improvement was observed. This finding is important in that it did not find any evidence for a U-shaped relationship showing higher risk for both low and high 25(OH)D concentrations as has been reported in some studies. Furthermore, the risk for all-cause mortality rate for those with 25(OH)D concentration < 25 nmol/L (10 ng/mL) was 1.9 compared to that for those with concentrations > 100 nmol/L (40 ng/mL).

–Avoidance of sun exposure is a risk factor for all-cause mortality: results from the MISS cohort [Lindqvist, 2014]

An observational study in Sweden involving 29,518 women followed for up to 20 years with 2,545 reported deaths found that the mortality rate for those who avoided sun exposure was approximately twice as high as those who were most exposed to the sun. This difference explained 3% of all deaths and is important since UVB doses in Sweden are generally low and virtually absent for six months of the year. Production of vitamin D may explain most of the differences between sun exposure amounts, although other beneficial effects of solar UV exist, such as release of nitric oxide resulting in reduction of blood pressure, as well as vitamin D-independent effects on the immune system.

–Meta-analysis of vitamin D sufficiency for improving survival of patients with breast cancer [Mohr, 2014]

Two meta-analyses found significantly increased cancer survival rates with higher concentration of 25(OH)D at time of diagnosis. For breast cancer, results from five studies found that those with 25(OH)D concentration of 75 nmol/L (30 ng/mL) had half the 5-20 year mortality rate as those with a lower concentration of 30 nmol/L (12 ng/mL).

–Reduced 25-hydroxyvitamin D and risk of Alzheimer's disease and vascular dementia [Afzal, 2014]

–Two papers reported that those with low 25(OH)D concentrations had increased risk of developing vascular dementia and Alzheimer's disease. This first one is from Denmark. A study involving 418 people followed for 30 years found a 25% increased risk of Alzheimer's disease and a 22% increased risk of vascular dementia for those with baseline 25(OH)D concentration < 25 nmol/L (10 ng/ml) compared to > 50 nmol/L (20 ng/ml)

Pregnancy

There is considerable interest in the role of vitamin D during pregnancy

Post-hoc comparison of vitamin D status at three time points during pregnancy demonstrates lower risk of preterm birth with higher vitamin D closer to delivery [Wagner, 2014]

–In a reanalysis of results from two maternal vitamin D supplementation trials conducted in South Carolina, it was found that: *"(1) maternal vitamin D status closest to delivery date was more significantly associated with preterm birth, suggesting that later intervention as a rescue treatment may positively impact the risk of preterm delivery, and (2) a serum concentration of 100 nmol/L (40ng/mL) in the 3rd trimester was associated with a 47% reduction in preterm births."*

–Vitamin D in fetal development: Findings from a birth cohort study [Hart, 2014]

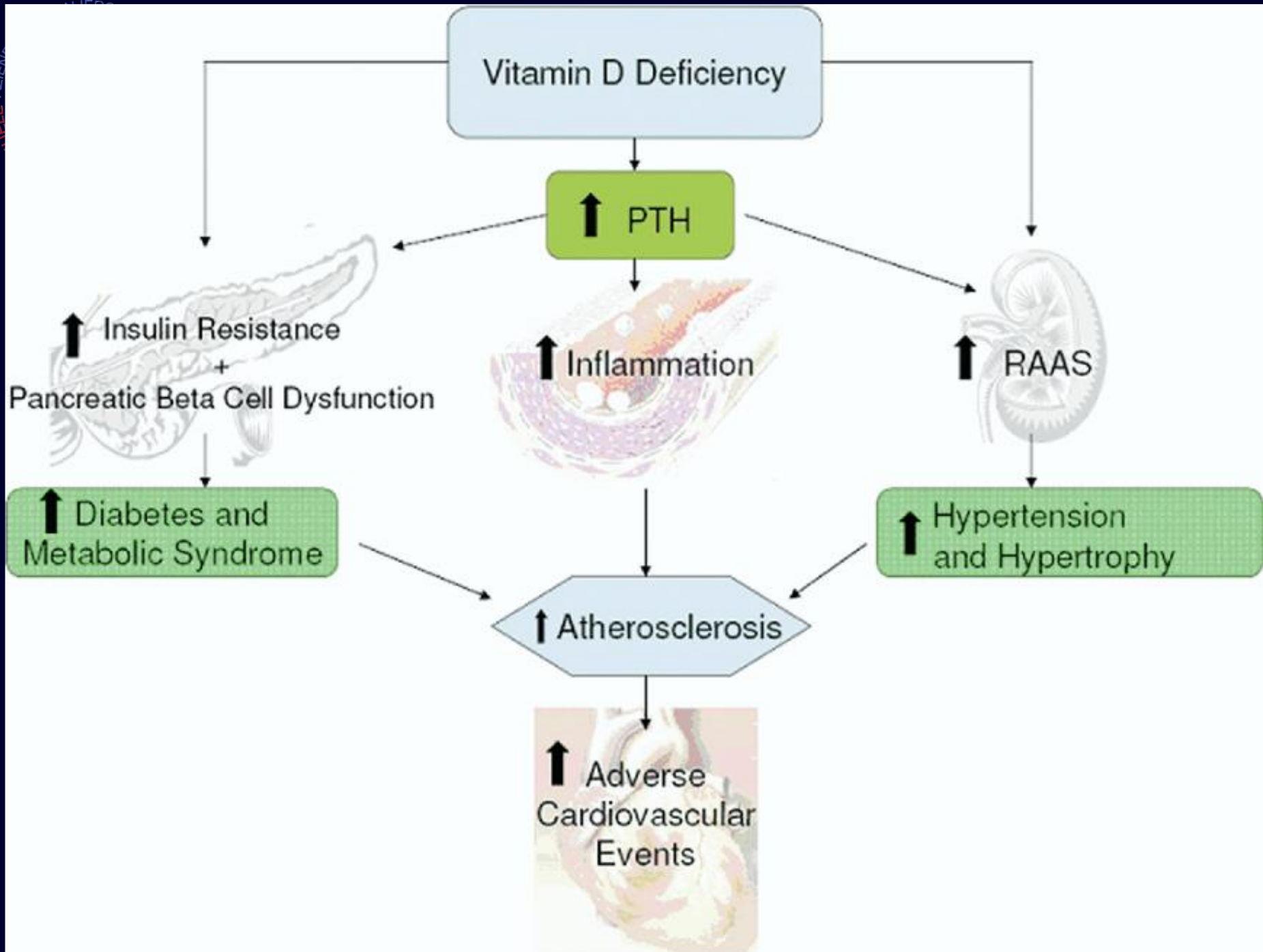
–A study in Australia compared maternal 25(OH)D concentration at 18 weeks' pregnancy with outcomes of the children years later. The authors found that "maternal vitamin D deficiency during pregnancy was associated with impaired lung development in 6-year-old offspring, neurocognitive difficulties at age 10, increased risk of eating disorders in adolescence, and lower peak bone mass at 20 years."

–Vitamin D and pre-eclampsia: original data, systematic review and meta-analysis [Hypponen, 2014]

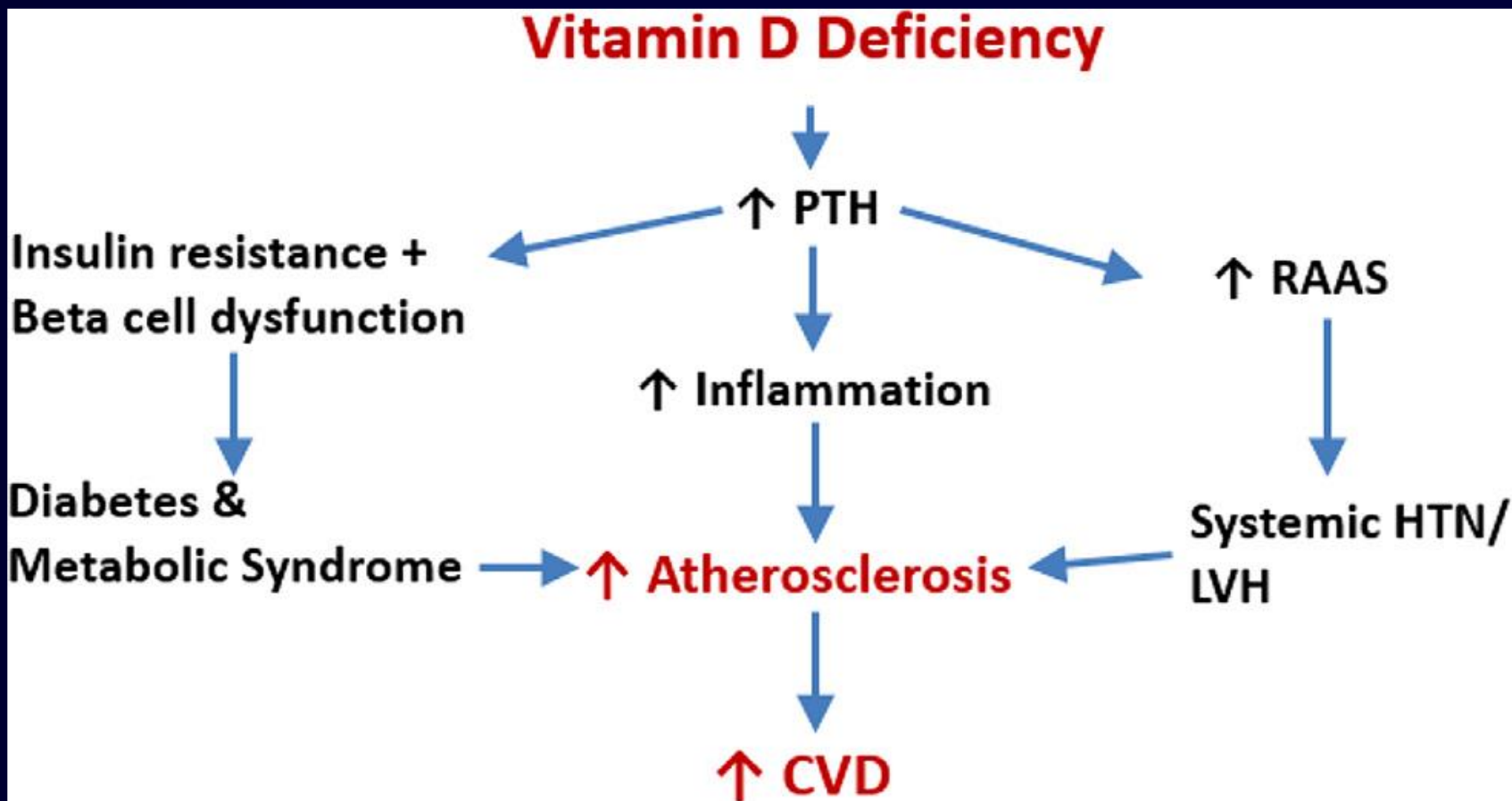
–A review of vitamin D supplementation and 25(OH)D concentrations during pregnancy found vitamin D reduces the risk of pre-eclampsia. For 25(OH)D concentration, the combined risk reduction was 48% with higher level circulating vitamin D. For vitamin D RCTs, the combined risk reduction was 34% for vitamin D supplementation vs. a placebo. This review provides further support for the importance of vitamin D supplementation and raising 25(OH)D concentrations during pregnancy.

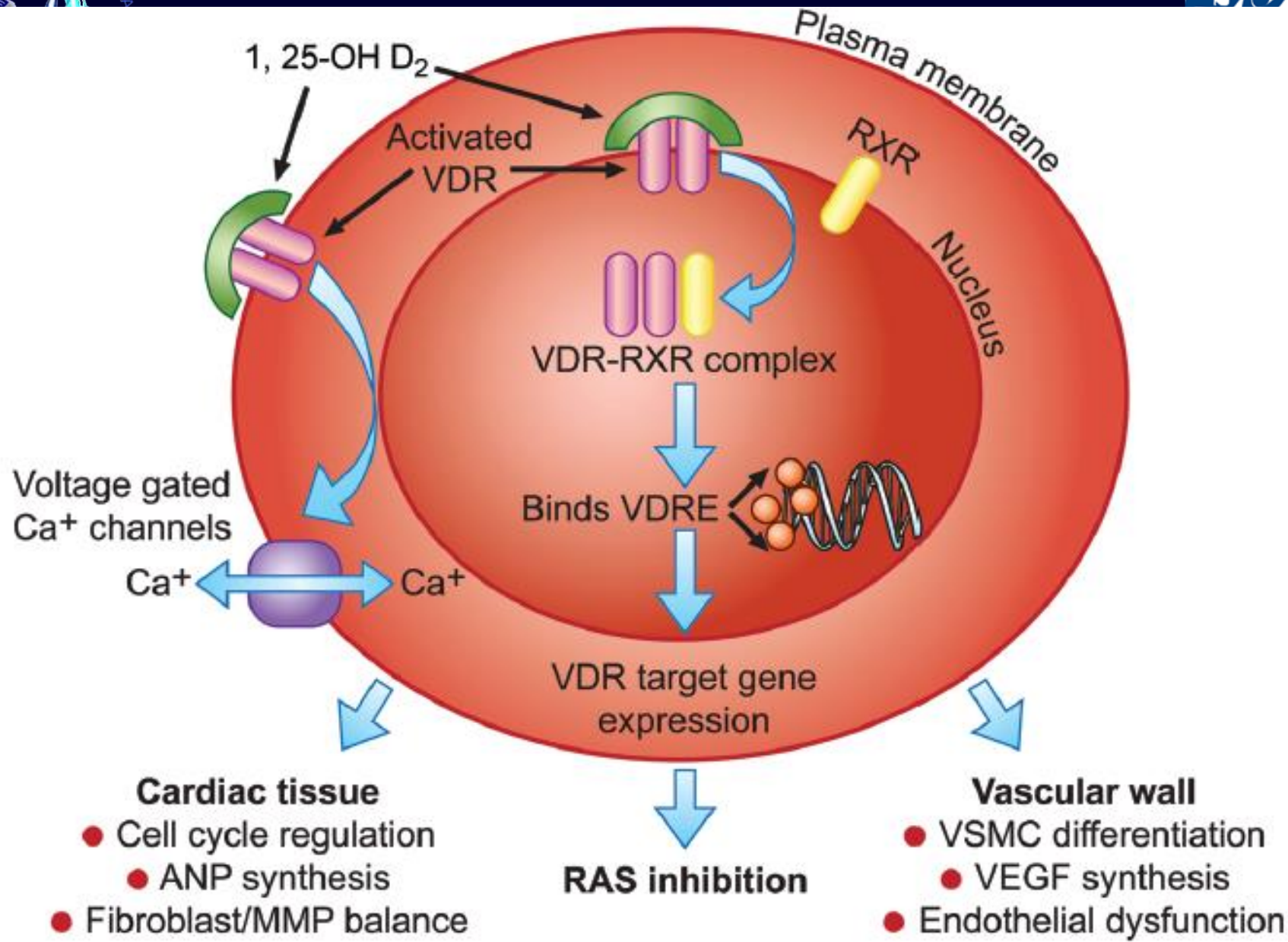


Ma come agisce la vitamina D sul cuore???



The mechanisms of Vitamin D deficiency leading to atherosclerotic vascular disease.





Childhood 25-OH Vitamin D Levels and Carotid Intima-Media Thickness in Adulthood: The Cardiovascular Risk in Young Finns Study

Context: Low vitamin D levels in adulthood have been associated with cardiovascular disease.

Objective: To investigate if low vitamin D levels in childhood are related with increased carotid artery intima-media thickness (IMT) in adulthood.

Design, Setting, and Participants: The analyses included 2148 subjects from the Cardiovascular Risk in Young Finns Study, aged 3–18 years at baseline (in 1980). Subjects were re-examined at age 30–45 years (in 2007). Childhood levels of 25-hydroxy-vitamin D were measured from stored serum in 2010.

Main Outcome Measure: The carotid artery IMT from 2007 was used.

Conclusions: Low 25-OH vitamin D levels in childhood were associated with increased carotid IMT in adulthood. (*J Clin Endocrinol Metab* 100: 0000–0000, 2015)

Vitamin D and risk of cause specific death: systematic review and meta-analysis of observational cohort and randomised intervention studies **BMJ** 1 april 2014

Objective To evaluate the extent to which circulating biomarker and supplements of vitamin D are associated with mortality from cardiovascular, cancer, or other conditions, under various circumstances.

Design Systematic review and meta-analysis of observational studies and randomised controlled trials.

Data extraction Data were extracted by two independent investigators, and a consensus was reached with involvement of a third. Study specific relative risks from 73 cohort studies (849 412 participants) and 22 randomised controlled trials (vitamin D given alone versus placebo or no treatment; 30 716 participants) were meta-analysed using random effects models and were grouped by study and population characteristics.

Conclusions Evidence from observational studies indicates inverse associations of circulating 25-hydroxyvitamin D with risks of death due to cardiovascular disease, cancer, and other causes. Supplementation with vitamin D₃ significantly reduces overall mortality among older adults; however, before any widespread supplementation, further investigations will be required to establish the optimal dose and duration and whether vitamin D₃ and D₂ have different effects on mortality risk.

What is already known on this topic

Vitamin D may be associated with many extraskeletal disease conditions, including overall mortality outcomes

However, associations of vitamin D concentrations with risk of death from a broad range of causes, under different circumstances, and across primary and secondary prevention settings, remain less well understood

What this study adds

Updated meta-analyses of observational studies indicate inverse associations of circulating vitamin D concentrations with risks of deaths from cardiovascular disease, cancer, and other causes

Combined data from all relevant randomised intervention studies show that, when given alone, vitamin D supplementation may not reduce overall mortality significantly among older adults

When data were stratified by type of supplementation, vitamin D₃, given singly, reduced mortality significantly by 11%

By contrast, supplementation with vitamin D₂ alone had no overall effect on mortality

Vitamin D and mortality: meta-analysis of individual participant data from a large consortium of cohort studies from Europe and the United States

Abstract

Objective To investigate the association between serum 25-hydroxyvitamin D concentrations (25(OH)D) and mortality in a large consortium of cohort studies paying particular attention to potential age, sex, season, and country differences.

Design Meta-analysis of individual participant data of eight prospective cohort studies from Europe and the US.

Setting General population.

Participants 26 018 men and women aged 50-79 years

Conclusions Despite levels of 25(OH)D strongly varying with country, sex, and season, the association between 25(OH)D level and all-cause and cause-specific mortality was remarkably consistent. Results from a long term randomised controlled trial addressing longevity are being awaited before vitamin D supplementation can be recommended in most individuals with low 25(OH)D levels.

What is already known on this subject

Mean serum 25-hydroxyvitamin D (25(OH)D) concentrations vary by country, sex, age, and season of blood draw

Vitamin D deficiency has been linked to all-cause and cardiovascular mortality, whereas results on cancer mortality have been inconsistent

What this study adds

In this large consortium of eight cohort studies from Europe and the United States, the bottom 25(OH)D quintile was associated with increased all-cause and cardiovascular mortality and with cancer mortality in subjects with a history of cancer but not in subjects without a history of cancer. These relationships were compellingly consistent across countries, sexes, age groups, and seasons of blood draw, although cut-off values for the 25(OH)D quintiles varied among the analyses

In clinical practice, cut-off values for vitamin D deficiency might need to be made region-, sex-, and season-specific to identify those in the population with the relatively lowest 25(OH)D concentrations



Evidence for a U-Shaped Relationship Between Prehospital Vitamin D Status and Mortality: A Cohort Study

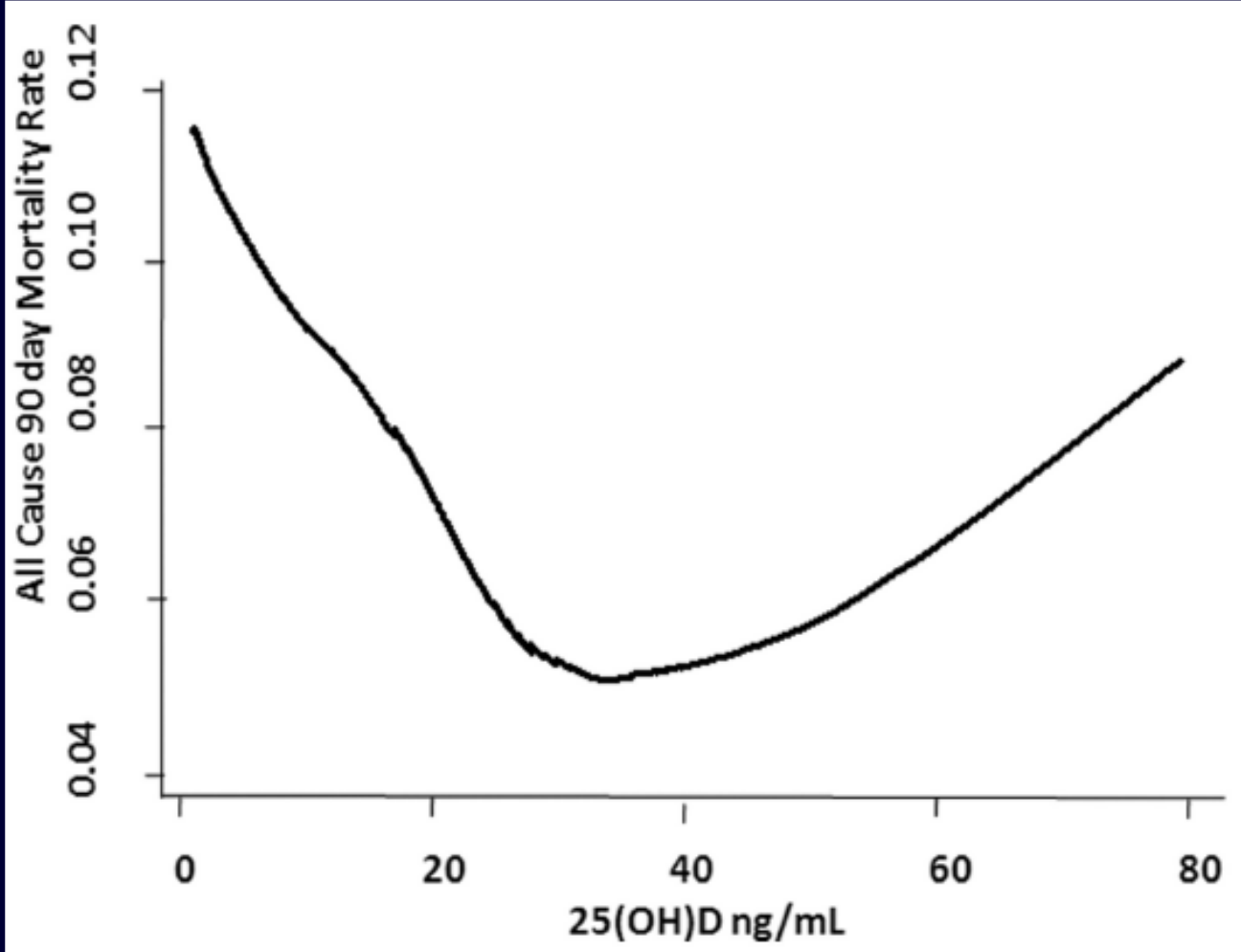
Objective: The objective of the study was to examine the association between prehospital serum 25-hydroxyvitamin D [25(OH)D] and the risk of mortality after hospital admission.

Design: We performed a retrospective cohort study of adults hospitalized for acute care between 1993 and 2011.

Setting: The study was conducted at two Boston teaching hospitals.

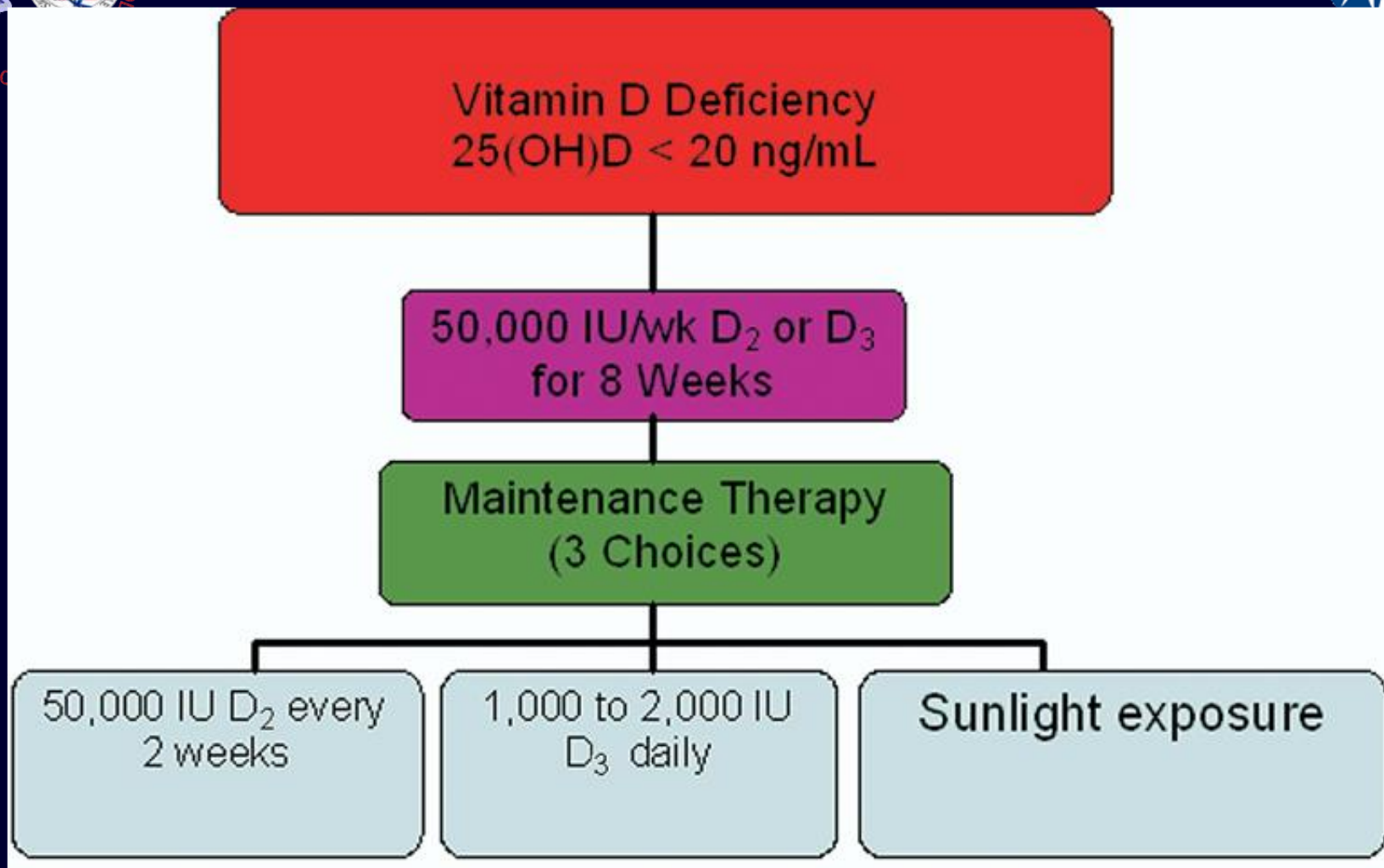
Patients: A total of 24 094 adult inpatients participated in the study.

Conclusions: Analysis of 24 094 adult patients showed that 25(OH)D levels less than 20 ng/mL and 60 ng/mL or greater before hospitalization were associated with an increased odds of 90-day mortality. Although previous reports have suggested an association between low vitamin D status and mortality, these data raise the issue of potential harm from high serum 25(OH)D levels, provide a rationale for an upper limit to supplementation, and emphasize the need for caution in the use of extremely high doses of vitamin D among patients. (*J Clin Endocrinol Metab* 99: 1461–1469, 2014)



... Allora iniziare una supplementazione con vitamina D potrebbe prevenire o ridurre l'insorgenza di malattie cardio vascolari???







La verità è raramente chiara, mai semplice!

Oscar Wilde

Vitamin D and Cardiovascular Disease

Time for Large Randomized Trials*

Carlos A. Camargo, JR, MD, DRPH

Boston, Massachusetts

...In summary, for those who believe that the inverse association between vitamin D and CVD risk is probably causal, and that the association will prove modifiable, the next steps are clear: widespread serum 25-OHD testing and vitamin D supplementation to achieve a specific 25-OHD target.

Proviamo a fare qualche considerazione insieme?



I dati della letteratura non sono univoci nel consigliare una supplementazione di massa di vitamina D al fine di prevenire l'insorgenza di malattie cardiovascolari.

Modificare la pratica clinica e le politiche sanitarie attuali, con significativi maggiori oneri sociali, non sembra, allo stato attuale, giustificabile.

Abbiamo bisogno di ulteriori, definitivi dati...

ViDA (Vitamin D Assessment) trial in New Zealand and the VITAL (Vitamin D and Omega-3 Trial) in the United States.

Table 1 Large, Population-Based, Randomized, Double-Blind, Placebo-Controlled Trials on the Health Effects of Vitamin D Supplementation (as of August 2011)

	ViDA	VITAL
Country	New Zealand	United States
Principal investigator(s)	Scragg and Camargo	Manson and Buring
Target sample size	5,100	20,000
Age range	50–84 yrs (both men and women)	Men: ≥50 yrs; women: ≥55 yrs
Vitamin D ₃ intervention	100,000 IU/month (about 3,300 IU/day); subjects also are given an extra 100,000 IU at the start of the trial and every autumn	2,000 IU/day; part of a 2 × 2 factorial trial in which the other intervention is 1 g/day of specific omega-3 fatty acids
Primary outcomes	CVD, infection, fractures	Cancer, CVD
Year enrollment started	2011	2011
Expected year of results	2017	2017
Trial registration	ACTRN12611000402943	NCT01169259

Nei prossimi anni ViDA e VITAL saranno, probabilmente, in grado di chiarire definitivamente questo importante e controverso capitolo della medicina...

Allora ci vediamo alla prossima puntata!



–Grazie per l'attenzione!!!