

## VITAMIN D

UpDates

### Editor in Chief

Maurizio Rossini

### Scientific Committee

Andrea Fagiolini

Andrea Giusti

Davide Gatti

Diego Peroni

Francesco Bertoldo

Leonardo Triggiani

Paolo Gisondi

Pasquale Strazzullo

Sandro Giannini

Stefano Lello

### Editorial Assistant

Sara Rossini

### Copyright by

Pacini Editore srl

### Managing Editor:

Patrizia Pacini

### Publisher

Pacini Editore Srl

Via Gherardesca 1 • 56121 Pisa

Tel. 050 313011 • Fax 050 3130300

Info@pacinieditore.it

www.pacinieditore.it

### B.U. Pacini Editore Medicina

Andrea Tognelli

Medical Project - Marketing Director

Tel. 050 3130255

atognelli@pacinieditore.it

### Copy Editor

Lucia Castelli

Tel. 050 3130224

lcastelli@pacinieditore.it

### Graphics and Layout

Massimo Arcidiacono

Tel. 050 3130231

marcidiacono@pacinieditore.it

### Print

Industrie Grafiche Pacini • Pisa

The Publisher remains at the complete disposal of those with rights whom it was impossible to contact, and for any omissions. Photocopies, for personal use, are permitted within the limits of 15% of each publication by following payment to SIAE of the charge due, article 68, paragraphs 4 and 5 of the Law April 22, 1941, n. 633. Reproductions for professional or commercial use or for any other other purpose other than personal use can be made following a written request and specific authorization in writing from AIDRO, Corso di Porta Romana, 108, 20122 Milan, Italy (segreteria@aidro.org - www.aidro.org). Digital Edition December 2019.

# EDITORIAL

## Maurizio Rossini

Department of Medicine, Section of Rheumatology, University of Verona

Dear Colleagues,

As you will see, this issue features two contributions relative to the debate on the possible extra skeletal effects of vitamin D supplementation, in particular on type-2 diabetes (T2DM) and in the field of cancer treatment.

You will note that both authors correctly conclude that in general available trials have not found significant results on these fronts: rather, because they were conducted on populations which on the whole were not vitamin D deficient, they are not able to exclude a protective effect of vitamin D supplementation in subjects who are deficient, especially if we consider that sub-analyses of these subjects actually suggest a positive effect.

We see, for example, that a post-hoc analysis of the randomized clinical trial by Pittas et al. [1] on a small number of participants that had baseline circulating levels of 25-hydroxyvitamin D <1.2 ng/mL (< 30 nmol/L) showed that the risk of developing T2DM was reduced by 60% in subjects treated with cholecalciferol with respect to those given the placebo (hazard ratio [HR] 0.38, 95% IC 0.18-0.80).

We further find that in the study conducted on patients affected by lung tumors vitamin D supplementation did not on the whole produce the expected results. Yet when patients with early stage adenocarcinoma and low vitamin D levels were selected, supplementation in fact reduced mortality by over 60% with respect to the placebo (HR = 0.37; 95% IC 0.15-0.95). [2]

The time required to assess an outcome may also be fundamental: you will see, for example, that the negative conclusion of the VITAL trial [3] would change if the follow-ups of the first 1-2 years were excluded: such an exclusion, in my opinion, would be reasonable, given the biological latency. In that case, vitamin D supplementation shows a significant - 25% - reduction of death by cancer (HR = 0.75; 95% IC 0.59-0.96).

With regard to the documentation on a significant effect of vitamin D supplementation only in subjects with low baseline 25-hydroxyvitamin D3 levels, it is worth remembering that the literature contains numerous other examples, both skeletal and extra skeletal [4]. Figure 1 shows several examples of different effects of supplementation on some extra skeletal risks with respect to baseline serum levels - low and not low - in supplemented patients.

This should not surprise us [5], in view of the fact that vitamin D acts as a nutrient: it is beneficial when lacking, though not so when it is not lacking...

To conclude, I do not believe that we can affirm today that we are overestimating the possible extra skeletal benefits of vitamin D supplementation. Neither do I think that we can deny them, given that the design and results of clinical trials conducted thus far do not allow us to exclude such benefits.

What do you think?

I hope you enjoy reading this issue.

Correspondence

MAURIZIO ROSSINI

maurizio.rossini@univr.it

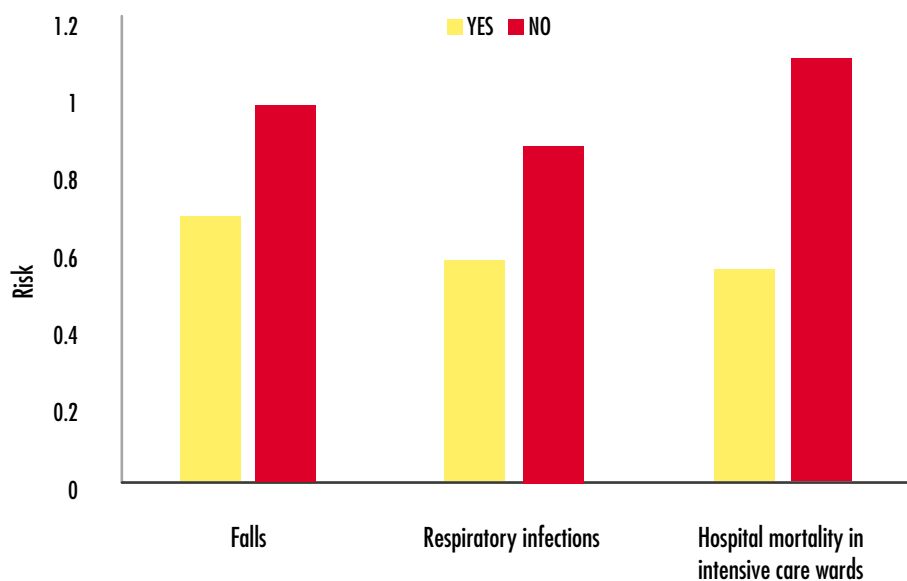
VITAMIN D - UpDates

2019;2(4):106-107

© Copyright by Pacini Editore srl



OPEN ACCESS



**FIGURE 1.**

Effects of vitamin D supplementation on extra skeletal risks (relative risk, odds ratio or hazard ratio) with respect to baseline serum levels of 25-hydroxyvitamin D3, either low (YES) or not low (NO) ( $p < 0.05$  among the groups).

## References

- 1 Pittas AG, Dawson-Hughes B, Sheehan P, et al; D2d Research Group. *Vitamin D supplementation and prevention of type 2 diabetes*. *N Engl J Med* 2019;381:520-530. <https://doi.org/10.1056/NEJMoa1900906>.
- 2 Akiba T, Morikawa T, Odaka M, et al. *Vitamin D supplementation and survival of patients with non-small cell lung cancer: a randomized, double-blind, placebo-controlled trial*. *Clin Cancer Res* 2018;24:4089-97. <https://doi.org/10.1158/1078-0432.CCR-18-0483>.
- 3 Manson JE, Cook NR, Lee IM, et al; VITAL Research Group. *Vitamin D supplements and prevention of cancer and cardiovascular disease*. *N Engl J Med* 2019;380:33-44. <https://doi.org/10.1056/NEJMoa1809944>.
- 4 Scragg R. *Emerging evidence of thresholds for beneficial effects from vitamin D supplementation*. *Nutrients*. 2018;10(5). pii: E561. <https://doi.org/10.3390/nu10050561>.
- 5 Fassio A, Rossini M, Gatti D. *Vitamin D: no efficacy without deficiency. What's new?* *Reumatismo* 2019;71:57-61 <https://doi.org/10.4081/reumatismo.2019.1201>.