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Dear Readers

this edition provides an update on some skeletal and extra-skeletal effects of vitamin D. As you know, so-called stress fractures are caused by repetitive loads and mechanical stresses that exceed the bone tissue's ability to repair itself and are especially common among athletes, military personnel and individuals who engage in strenuous physical activity. Well, patients who suffer from it frequently present vitamin D deficiency and it is also known that adequate vitamin D levels accelerate bone callus formation and improve the quality of bone regeneration. This seems to be attributable to a dual role of vitamin D: the immunomodulation role in the first acute inflammatory phase of "fracture healing" and the mineralisation role.

The second article contains an important update on the possible role of vitamin D in reducing the risk of developing type 2 diabetes. The rationale has long been there: vitamin D also has intranuclear receptors in pancreatic beta cells and could therefore play a role in glucose homeostasis. Observational studies have indeed documented an association between hypovitaminosis D and the presence of type 2 diabetes, but interventional studies with vitamin D supplementation have so far reported conflicting results on glycaemic control and insulin resistance in subjects with prediabetes. Furthermore, there were few studies to date in the general population and on the possible role of genetic variants of the vitamin D receptor. Hence the importance of a recent large prospective cohort study that observed a significant association between circulating 25(OH)D levels above 75 nmol/L and reduced risk of developing type 2 diabetes compared to subjects with 25(OH)D levels below 25 nmol/L, regardless of prediabetes status and especially in the presence of certain genetic polymorphisms. This has been considered in the *Endocrine Society's* new vitamin D guidelines<sup>1</sup> that, in recommendation no. 10, suggests vitamin D supplementation, in addition to lifestyle correction, in individuals at high risk of prediabetes to reduce the risk of progression to type 2 diabetes.

The same new guideline<sup>1</sup> recommends for the first time vitamin D supplementation in children and adolescents up to 18 years of age not only to prevent rickets but also to reduce the risk of respiratory tract infections, recognising the specific extra-skeletal benefit of vitamin D.

Another important and original acknowledgement of an extra-skeletal benefit by the same guidelines<sup>1</sup> is the sixth recommendation, which recommends vitamin D supplementation in all individuals over 75 years of age due to the possibility of reducing the risk of mortality. This reminds me of the report I had made to the Italian Medicines Agency (AIFA) in my capacity then as President of the Italian Society of Osteoporosis, Mineral Metabolism and Skeletal Diseases (SIOMMMS) in relation to note 96<sup>2</sup>: I pointed out that the note neglects the elderly by not providing them, regardless of the 25(OH)D determination, with supplementation by the National Health Service, despite the fact that they are understandably and notoriously at risk of chronic deficiency. Among the effects of note 96 on the prescription of vitamin D, as later reported by AIFA<sup>3</sup>, there was indeed a reduction in the use of vitamin D, even in the elderly<sup>3</sup>, a fact

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that I find worrying and not an expression of improved appropriateness of use.

The new recommendation in the recent guidelines <sup>1</sup> on vitamin D supplementation in all elderly people also reminds me of the Project started in the Veneto Region 20 years ago <sup>4</sup>which envisaged vitamin D supplementation in the entire elderly population, particularly during the winter months.

What do you think?

Enjoy reading!

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### References

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1947. <https://doi.org/10.1210/clinem/dgae290>

<sup>2</sup> <https://www.aifa.gov.it/documents/20142/1728113/nota-96.pdf>

<sup>3</sup> MonitoraggioNota96. [https://www.aifa.gov.it/documents/20142/1030827/NOTA\\_96\\_31mesi\\_08.11.2022.pdf](https://www.aifa.gov.it/documents/20142/1030827/NOTA_96_31mesi_08.11.2022.pdf)

<sup>4</sup> <https://bur.regione.veneto.it/BurVServices/pubblica/DetailDgr.aspx?id=184286>