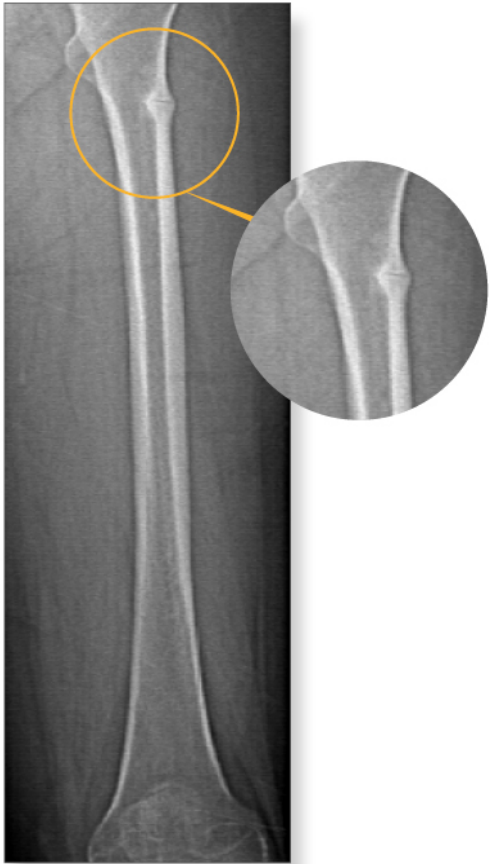


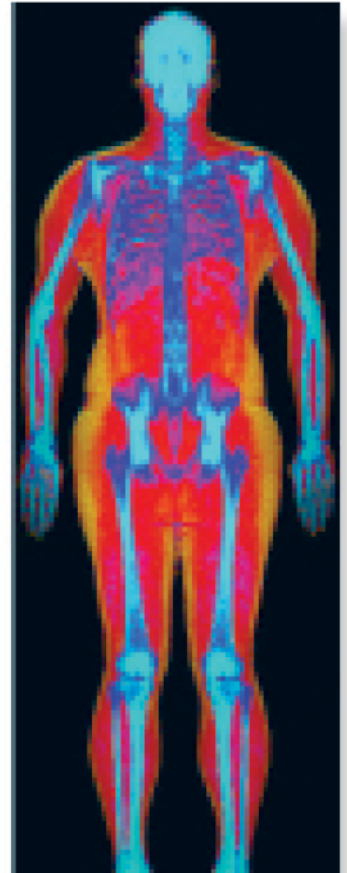
Powerful images. Clear answers.



Manage Patient's concerns about
Atypical Femur Fracture*



Vertebral Fracture Assessment –
a critical part of a complete
fracture risk assessment



Advanced Body Composition®
Assessment – the power to
see what's inside

Contact your Hologic rep today at BSHSalesSupportUS@hologic.com

PAID ADVERTISEMENT

*Incomplete Atypical Femur Fractures imaged with a Hologic densitometer, courtesy of Prof. Cheung, University of Toronto

ADS-02018 Rev 003 (10/19) Hologic Inc. ©2019 All rights reserved. Hologic, Advanced Body Composition, The Science of Sure and associated logos are trademarks and/or registered trademarks of Hologic, Inc., and/or its subsidiaries in the United States and/or other countries. This information is intended for medical professionals in the U.S. and other markets and is not intended as a product solicitation or promotion where such activities are prohibited. Because Hologic materials are distributed through websites, eBroadcasts and tradeshows, it is not always possible to control where such materials appear. For specific information on what products are available for sale in a particular country, please contact your local Hologic representative.

www.hologic.com | dxaperformance.com | 1.800.442.9892

Calcifediol Is Not Superior to Cholecalciferol in Improving Vitamin D Status in Postmenopausal Women

Manuel Sosa-Henríquez,^{1,2} M.a Jesús Gómez de Tejada-Romero,³ M.a Jesús Cancelo-Hidalgo,⁴ Guillermo Martínez Díaz-Guerra,⁵ Íñigo Etxebarria Foronda,⁶ Francisco José Tarazona-Santabalbina,⁷ Óscar Torregrosa-Suau,⁸ and Carmen Valdés-Llorca⁹

¹University of Las Palmas de Gran Canaria, Investigation Group on Osteoporosis and Bone and Mineral Diseases, Las Palmas de Gran Canaria, Spain

²Bone Metabolic Unit, Hospital University Insular, Las Palmas de Gran Canaria, Spain

³Department of Medicine, University of Seville, Seville, Spain

⁴University Hospital of Guadalajara, Alcalá University, Madrid, Spain

⁵University Hospital 12 de Octubre. Madrid, University Complutense, Madrid, Spain

⁶Department of Orthopaedic, Alto Deba Hospital, Mondragon, Spain

⁷Geriatric Service, University Hospital La Ribera, Alzira, Spain

⁸Bone Metabolic Unit. Service of Internal Medicine, University General Hospital, Elche, Spain

⁹Health Center of Fuencarral. SERMAS, Madrid, Spain

To the Editor:

We have read with interest the article published in the *Journal of Bone and Mineral Research* (the *JBMR*) by Pérez Castrillón and colleagues,⁽¹⁾ comparing the efficacy and safety of calcifediol versus cholecalciferol in improving vitamin D status in postmenopausal women.

We would point out a series of inaccuracies that question the validity and certainty of their conclusions. Due to limitations we cannot cite them all, but we describe the most relevant:

- The women studied are postmenopausal with hypovitaminosis or vitamin D deficiency (25(OH) vitamin D levels less than 20 ng/mL). Therefore, the results cannot be extrapolated to all postmenopausal women, as the title suggests.
- The cholecalciferol doses prescribed are not those recommended for subjects with vitamin D deficiency. The authors justify the monthly dose of cholecalciferol (25,000 IU) recommended by Kanis and colleagues⁽²⁾ and Pludowski and colleagues.⁽³⁾ However, in Kanis and colleagues⁽²⁾ guidelines, the doses are for treating osteoporosis, not for vitamin D deficiency, so not applicable here. Furthermore, the Pludowski and colleagues⁽³⁾ guidelines indicate that “for patients with a laboratory confirmed vitamin D deficiency, ie, 25(OH)D concentration lower than 20 ng/mL (50 nmol/L), a vitamin D treatment should be implemented. (...). The dosage should

be as follows (...): for adults and the elderly 7000–10,000 IU/ day (175–250 mg/day) or 50,000 IU/week (1250 mg/week).” Clearly, the cholecalciferol dose was not adequate, but markedly lower than those recommended in this latest, reported guideline. Therefore, the cholecalciferol treatment group was underdosed.

Other guidelines recommend that, regarding vitamin D deficiency, defined by levels of 25(OH) vitamin D below 20 ng/mL, higher doses than those indicated here should be prescribed. The Endocrine Society recommends cholecalciferol doses administered at 50,000 IU weekly for 8 weeks (alternatively 6000 IU daily), followed by 1500–2000 daily maintenance IU⁽⁴⁾; the National Osteoporosis Society recommends 2000 IU daily,⁽⁵⁾ between 45,000 and 60,000 IU monthly of cholecalciferol. More recently, the American Association of Clinical Endocrinologists (AACE) recommended 5000 IU daily for 8 to 12 weeks⁽⁶⁾; ie, 150,000 IU monthly.

Thus, 25,000 IU of cholecalciferol administration once a month used by Pérez Castrillón and colleagues⁽¹⁾ is insufficient and explains why they deem cholecalciferol “inferior” to calcifediol.

- The article reflects partial results at 4 months in a study designed for 1 year. This should have been reflected in the title. According to the reported dates, the last patient would have completed his annual visit on June 25, 2020 (visit at

This is an open access article under the terms of the [Creative Commons Attribution](#) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

Received in original form January 31, 2022; revised form March 5, 2022; accepted March 13, 2022.

Address correspondence to: Manuel Sosa-Henríquez, MD, PhD, University of Las Palmas de Gran Canaria, Paseo Blas Cabrera Felipe s/n. 35016, Las Palmas de Gran Canaria, Canary Islands, Spain. E-mail: manuel.sosa@ulpgc.es

[The copyright line for this article was changed on 29 June 2022 after original online publication]

Journal of Bone and Mineral Research, Vol. 37, No. 7, July 2022, pp 1411–1412.

DOI: 10.1002/jbmr.4560

© 2022 The Authors. *Journal of Bone and Mineral Research* published by Wiley Periodicals LLC on behalf of American Society for Bone and Mineral Research (ASBMR).

4 months: October 25, 2019). The article with the results at 4 months was sent to the journal in February 2021. What happened in those remaining 8 months? Why have those data not been shown?

It is important to know the percentage of patients who, in this 4–12-month window, develop 25(OH) vitamin D levels above the optimal desirable range of 30–50 ng/mL.⁽⁷⁾ It would be interesting to know the speed with which the levels of 25(OH) vitamin D fall again after discontinuing calcifediol at 4 months (group A.2). The authors have not included a similar group of cholecalciferol that would permit comparisons. Also, not all clinically relevant results were taken into account, because although it is important to correct low vitamin D levels, the ultimate benefit is to prevent hypovitaminosis complications. The time in which vitamin D levels remain stable after treatment is not specified; it only focuses on correcting levels and the speed with which correction occurs. A quick correction would not be useful if after 4 months complications begin to appear. The expected benefits do not currently outweigh the risks and costs, because the long-term adverse effects of calcifediol are not known and cholecalciferol treatment has so far been effective, safe, and cheap.^(8,9)

In our opinion, this study of Pérez Castrillón and colleagues⁽¹⁾ holds some issues of concern that could invalidate the results shown and could mislead readers to a false understanding.

Author Contributions

Manuel Sosa-Henríquez: Conceptualization; investigation; methodology; supervision; validation; visualization; writing – original draft; writing – review and editing. **M.a Jesús Gómez de Tejada-Romero:** Conceptualization; methodology; supervision; validation; visualization; writing – original draft. **M.a Jesús Cancelo-Hidalgo:** Conceptualization; methodology; supervision; validation; visualization. **Guillermo Martínez Díaz-Guerra:** Conceptualization; supervision; validation; visualization. **Íñigo Etxebarria Foronda:** Conceptualization; investigation;

supervision; validation; visualization. **Francisco José Tarazona-Santabalbina:** Conceptualization; supervision; validation; visualization. **Óscar Torregrosa-Suau:** Conceptualization; methodology; supervision; validation; visualization. **Carmen Valdés-Llorca:** Conceptualization; investigation; resources; supervision; validation; visualization.

References

1. Pérez Castrillón JL, Dueñas-Laita A, Brandi ML, et al. Calcifediol is superior to cholecalciferol in improving vitamin D status in postmenopausal women: a randomized trial. *J Bone Miner Res.* 2021;36(10):1967-1978.
2. Kanis JA, Cooper C, Rozzoli R, et al. European guidance for the diagnosis and management of osteoporosis in postmenopausal women. *Osteoporos Int.* 2019;30:3-44.
3. Pludowski P, Holick MF, Grant WB, et al. Vitamin D supplementation guidelines. *J Steroid Biochem Mol Biol.* 2018;175:125-135.
4. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2011;96:1911-1930.
5. Aspray TJ, Bowring C, Fraser W, et al. National Osteoporosis Society vitamin D guideline summary. *Age Ageing.* 2014;43:592-595.
6. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists/American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis: 2020 update executive summary. *Endocr Pract.* 2020;26(5):564-570.
7. Gaksch M, Jorde R, Grimnes G, et al. Vitamin D and mortality: individual participant data meta-analysis of standardized 25-hydroxyvitamin D in 26916 individuals from a European consortium. *PLoS One.* 2017;12(2):e0170791.
8. Schleck ML, Souberbielle JC, Jandrain B, et al. A randomized, double-blind, parallel study to evaluate the dose-response of three different vitamin D treatment schemes on the 25-hydroxyvitamin D serum concentration in patients with vitamin D deficiency. *Nutrients.* 2015;7:5413-5422.
9. Vieth R, Chan PC, MacFarlane GD. Efficacy and safety of vitamin D3 intake exceeding the lowest observed adverse effect level. *Am J Clin Nutr.* 2001;73(2):288-294.