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TOOLS FOR PRACTICE #400 | October 27, 2025

TOOLS FOR PRACTICE

PEER PATIENTS EXPERIENCE EVIDENCE RESEARCH

Vitamin D and Mortality-Don't bet your life on it!

CLINICAL QUESTION

Does vitamin D supplementation reduce mortality, cardiovascular disease, or cancer in adults?

BOTTOM LINE

Vitamin D supplementation does not reduce all-cause mortality, cardiovascular events, or cancer incidence. Effects on cancer mortality are inconsistent with most systematic reviews and the largest randomized controlled trials (RCTs) showing no effect.

EVIDENCE

- 11 systematic reviews[1-11] from the last 3 years, 12-80 RCTs, 70,278-182,804 patients. Adults (most RCTs average age >50, some "healthy" populations, some including chronic diseases), vitamin D (varying doses, example 400 international units (IU) daily to 100,000 IU monthly) compared to placebo/no treatment. Follow-up ~5 years (range 7 months-12 years).
- All-cause mortality :[1-5]
    - Four systematic reviews:[1-4] no difference from placebo. One other[5] had an Odds Ratio 0.95 (95%CI 0.93-0.99) (event rates not reported). Insufficient details provided to evaluate why results differ.
- Cardiovascular disease (RCTs included patients with/without cardiovascular disease):
    - Cardiovascular events:[1-3,9-11] No difference.

    - Cardiovascular mortality:[3,5,9-11] No difference.
- Cancer (RCTs included patients with/without cancer):
    - Cancer Incidence:[1,2,4,9,10] No difference.
    - Cancer mortality:[1,4,9-11] Inconsistent results:
        - Four systematic reviews:[1,4,9,11] No difference. One systematic review[10] not including largest RCT of bolus-dosing found difference, but event rates not provided, and largest RCTs showed no effect.
            - Subgroup analysis of daily versus bolus-dosing:[4,9,10] No difference.
- Adverse events: No difference.
- Limitations: Some systematic reviews missing metagraphs, heterogeneous populations, different dosages (daily versus boluses; various doses).

CONTEXT

- Guideline[12] suggests supplementation in those >75 years old based on a non-statistically different sub-group analysis.[2]
- In the general population and in those with low vitamin D levels, vitamin D does not prevent fractures[13] or respiratory infections.[14] High-dose bolus vitamin D may increase fracture risk.[15]
- Other interventions may have a larger impact on cancer mortality. Exercise interventions of 2-32 weeks with observational follow-up of 1-96 months reduce cancer mortality from 22% to 14% and cancer recurrence from 14% to 7%.[16]

REFERENCES

1. O'Connor EA, Evans CV, Ivlev I, *et al.* JAMA. 2022 Jun 21;327(23):2334-2347.
2. Shah VP, Nayfeh T, Alsawaf Y, *et al.* J Clin Endocrinol Metab. 2024 Jul 12;109(8):1961-1974.
3. Mirza AMW, Almansouri NE, Muslim MF, *et al.* Ann Med Surg (Lond). 2024 Aug 14;86(11):6665-6672.
4. Cheema HA, Fatima M, Shahid A, *et al*. Heliyon. 2022 Oct 28;8(11):e11290.
5. Ruiz-García A, Pallarés-Carratalá V, Turégano-Yedro M, *et al.* Nutrients. 2023 Apr 7;15(8):1810.
6. Pei YY, Zhang Y, Peng XC, *et al.* Nutrients. 2022 Jul 30;14(15):3158
7. Mattumpuram J, Maniya MT, Faruqui SK, *et al*. Curr Probl Cardiol. 2024 Jan;49(1 Pt C):102119.
8. Rasouli MA, Darvishzadehdaledari S, Alizadeh Z, *et al.* J Res Health Sci. 2023 Dec 29;23(4):e00594.
9. Zhang R, Zhang Y, Liu Z, *et al.* Cancers (Basel). 2022 Jul 30;14(15):3717.

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10. Guo Z, Huang M, Fan D, *et al.* Crit Rev Food Sci Nutr. 2023;63(26):8428-8442.
11. Kuznia S, Zhu A, Akutsu T, *et al.* Ageing Res Rev. 2023 Jun;87:101923.
12. Demay MB, Pittas AG, Bikle D *et al*. J Clin Endocrinol Metab. 2024 Jul 12;109(8):1907-1947.
13. Young J, Braschi E. Tools for Practice #374 Vitamin D and Fracture Prevention: Not what it's cracked up to be? Available at https://cfpclearn.ca/tfp374/ Accessed April 3, 2025
14. Braschi, E, Young J Tools for Practice #394 Vitamin D and Respiratory Tract Infections: Does the sun's vitamin chase the cold? Available at https://cfpclearn.ca/tfp394/ Accessed July 24, 2025
15. de Souza MM, Moraes Dantas RL, Leão Durães V, *et al.* J Gen Intern Med. 2024 Jul 12.
16. Morishita S, Hamaue Y, Fukushima T, *et al.* Integr Cancer Ther. 2020 Jan-Dec:19:1534735420917462.

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