

CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

# Vitamin D Supplementation for the General Population: Clinical Evidence and Guidelines

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## Research Questions

1. What is the clinical evidence regarding routine vitamin D supplementation in the general population?
2. What are the evidence-based guidelines regarding vitamin D supplementation in the general population?

## Key Findings

Ten systematic reviews with meta-analyses and one evidence-based guideline were identified regarding vitamin d supplementation for the general population. No evidence-based guidelines were identified.

## Methods

A limited literature search was conducted on key resources including PubMed, the Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. A focused search of intervention (i.e., vitamin D) terms was conducted, with main concepts appearing in title or major subject heading, and methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2013 and October 23, 2018. Internet links were provided, where available.

## Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

**Table 1: Selection Criteria**

<b>Population</b>	Healthy adults, adolescents or children Subgroup of interest: Canada or other Northern countries
<b>Intervention</b>	Routine Vitamin D supplementation
<b>Comparator</b>	No supplementation
<b>Outcomes</b>	Q1: Clinical benefits, harms Q2: Evidence-based guidelines
<b>Study Designs</b>	Health technology assessments, systematic reviews, meta-analyses, evidence-based guidelines

## Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by evidence-based guidelines.

Ten systematic reviews with meta-analyses and one evidence-based guideline were identified regarding vitamin d supplementation for the general population. No relevant health technology assessments were identified.

Additional references of potential interest are provided in the appendix.

## Overall Summary of Findings

Ten systematic reviews with meta-analyses were identified regarding vitamin D supplementation for the general population.<sup>1-10</sup> The systematic reviews with meta-analyses reported a wide range of health outcomes and the conclusions are inconsistent.<sup>1-10</sup> Detailed study characteristics are provided in Table 2.

One evidence-based guideline was identified regarding vitamin D supplementation for the general population.<sup>11,12</sup> The United Kingdom’s National Institute for Health and Care Excellence (NICE) guideline recommends increasing access to vitamin D supplements for pregnant and breastfeeding women, infants and children aged under 4, particularly teenagers and young women, people over 65, people who have low or no exposure to the sun, and people with darker skin.<sup>11</sup> The guideline also recommends raising awareness about the importance of vitamin D supplements and having health professionals recommend vitamin D supplements.<sup>11</sup>

**Table 2: Characteristics of Included Systematic Reviews with Meta-Analyses on Vitamin D Supplementation for the General Population**

First Author, Publication Year, Country	Study Designs, Number of Studies Included and Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes	Conclusions
<b>Martineau, 2017<sup>1</sup></b> <b>Multiple countries</b>	25 RCTs N=11321 Age: 0 to 95 years	Vitamin D3 or vitamin D2 supplement vs. placebo	(i) Risk of acute respiratory tract infection (ii) Safety	“Vitamin D supplementation was safe and it protected against acute respiratory tract infection overall. Patients who were very vitamin D deficient and those not receiving bolus doses experienced the most benefit.” <sup>1</sup>
<b>Mazidi, 2017<sup>2</sup></b> <b>China</b>	12 RCTs N=NR Age NR	Vitamin D supplement vs. placebo	(i) Endothelial function	“Vitamin D supplementation may improve endothelial function.” <sup>2</sup>

First Author, Publication Year, Country	Study Designs, Number of Studies Included and Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes	Conclusions
<b>Yakoob, 2016<sup>3</sup></b> <b>USA</b>	4 RCTs N=3198 Age: children under 5 years	Vitamin D supplement vs. placebo or no intervention	(i) Pneumonia (ii) Diarrhea (iii) Hospitalization (iv) Mean serum vitamin D concentrations	“Evidence from one large trial did not demonstrate benefit of vitamin D supplementation on the incidence of pneumonia or diarrhoea in children under five years.” <sup>3</sup>
<b>Beveridge, 2015<sup>4</sup></b> <b>Scotland</b>	46 RCTs N=3092 Age NR	Vitamin D supplement vs. placebo	(i) Systolic blood pressure (ii) Diastolic BP	“Vitamin D supplementation is ineffective as an agent for lowering BP and thus should not be used as an antihypertensive agent.” <sup>4</sup>
<b>Bjelakovic, 2014<sup>5</sup></b> <b>Serbia</b>	18 RCTs N=50632 Age: aged 47 to 97 years <sup>a</sup>	Vitamin D supplement vs. placebo or no intervention	(i) Cancer occurrence (ii) Cancer mortality (iii) All-cause mortality	“There is currently no firm evidence that vitamin D supplementation decreases or increases cancer occurrence in predominantly elderly community-dwelling women. Vitamin D supplementation decreased cancer mortality and vitamin D supplementation decreased all-cause mortality, but these estimates are at risk of type I errors due to the fact that too few participants were examined, and to risks of attrition bias originating from substantial dropout of participants.” <sup>5</sup>
<b>Keum, 2014<sup>6</sup></b> <b>USA</b>	Number of RCTs NR N=NR Age NR	Vitamin D supplement Comparators NR	(i) Cancer incidence (ii) Cancer mortality	“Over 2-7 years of duration, the benefit of vitamin D supplementation may be limited to cancer mortality.” <sup>6</sup>

First Author, Publication Year, Country	Study Designs, Number of Studies Included and Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes	Conclusions
<b>Newberry, 2014<sup>7</sup></b> <b>USA</b>	154 primary studies (interventional or prospective observational studies) and 2 SRs that incorporated more than 93 additional primary studies  N=NR  Age NR	Vitamin D supplement vs. placebo	(i) Health outcomes <sup>b</sup>	“The majority of the findings concerning vitamin D, alone or in combination with calcium, on the health outcomes of interest were inconsistent... Although a large number of new studies (and longer follow ups to older studies) were identified, particularly for cardiovascular outcomes, all-cause mortality, several types of cancer, and intermediate outcomes for bone health, no firm conclusions can be drawn.” <sup>7</sup>
<b>Pathak, 2014<sup>8</sup></b> <b>Australia</b>	18 RCTs  N=NR  Age NR	Vitamin D supplement vs. placebo	(ii) Body weight (iii) Body mass index (iv) Fat mass (v) Percentage fat mass (vi) Lean body mass	“Meta-regression confirmed that neither the absolute vitamin D status achieved nor its change from baseline influenced the SMD of any obesity measure... Vitamin D supplementation did not decrease measures of adiposity in the absence of caloric restriction.” <sup>8</sup>
<b>Seida, 2014<sup>9</sup></b> <b>Canada</b>	35 RCTs  N=43407  Age: adults	Vitamin D supplement vs. placebo or a non-vitamin D supplement	(i) Insulin resistance (ii) Insulin secretion (iii) Hemoglobin A1C (iv) Safety	“Evidence from available trials shows no effect of vitamin D3 supplementation on glucose homeostasis or diabetes prevention.” <sup>9</sup>
<b>Fortmann, 2013<sup>10</sup></b> <b>USA</b>	26 studies (study type NR)  abstract=NR  Age NR	Vitamin D supplement vs. placebo	(i) Cancer incidence (ii) Cardiovascular disease (iii) All-cause mortality	“There are a limited number of trials examining the effects of dietary supplements on the primary prevention of CVD and cancer; the majority showed no effect in healthy populations. Clinical heterogeneity of included studies limits

First Author, Publication Year, Country	Study Designs, Number of Studies Included and Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes	Conclusions
				generalizability of results to the general primary care population." <sup>10</sup>

BP = blood pressure; CVD = cardiovascular disease; RCT = randomized controlled trial; NR = not reported; SR = systematic reviews; USA = United States of America; vs = versus.

<sup>a</sup> Most trials included elderly community-dwelling women (aged 47 to 97 years).<sup>5</sup>

<sup>b</sup> Included, but not limited to, cardiovascular outcomes, all-cause mortality, several types of cancer, all-cause mortality, hypertension and intermediate outcomes for bone health.<sup>7</sup>

## References Summarized

### Health Technology Assessments

No literature identified

### Systematic Reviews and Meta-analyses

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[PubMed: PM25775274](#)
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10. Fortmann SP, Burda BU, Senger CA, et al. Vitamin, mineral, and multivitamin supplements for the primary prevention of cardiovascular disease and cancer: a systematic evidence review for the U.S. Preventive Services Task Force. (*Evidence synthesis no. 108*). Rockville (MD): Agency for Healthcare Research and Quality; 2013: <https://www.ncbi.nlm.nih.gov/books/NBK173987/>. Accessed 2018 Nov 7.

## Guidelines and Recommendations

11. National Institute for Health and Care Excellence. Vitamin D: supplement use in specific population groups (*Public health guideline PH56*) 2017; <https://www.nice.org.uk/guidance/ph56>. Accessed 2018 Nov 7.

## Appendix — Further Information

### Previous CADTH Reports

12. Calcium and vitamin D supplementation for adults: safety and guidelines. (*CADTH Rapid response report: summary of abstracts*). Ottawa (ON): CADTH; 2018: <https://www.cadth.ca/sites/default/files/pdf/htis/2018/RB1229%20Calcium%20and%20Vitamin%20D%20Final.pdf>. Accessed 2018 Nov 7.

### Systematic Reviews and Meta-Analyses

#### *Alternative Intervention*

13. Zheng YT, Cui QQ, Hong YM, Yao WG. A meta-analysis of high dose, intermittent vitamin D supplementation among older adults. *PLoS One*. 2015;10(1):e0115850. [PubMed: PM25602255](#)

#### *Alternative Outcome*

14. Brett NR, Gharibeh N, Weiler HA. Effect of vitamin D supplementation, food fortification, or bolus injection on vitamin D status in children aged 2-18 years: a meta-analysis. *Adv Nutr*. 2018 Jul 1;9(4):454-464. [PubMed: PM30032221](#)
15. Lamberg-Allardt C, Brustad M, Meyer HE, Steingrimsdottir L. Vitamin D - a systematic literature review for the 5th edition of the Nordic Nutrition Recommendations. *Food Nutr Res*. 2013;57. [PubMed: PM24106457](#)

### Guidelines and Recommendations

#### *Alternative Population*

16. Vitamin D and health. London (UK): Scientific Advisory Committee on Nutrition, Public Health England; 2016: [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/537616/SACN\\_Vitamin\\_D\\_and\\_Health\\_report.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/537616/SACN_Vitamin_D_and_Health_report.pdf). Accessed 2018 Nov 7.

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## Review Articles

24. Mateussi MV, Latorraca COC, Daou JP, et al. What do Cochrane systematic reviews say about interventions for vitamin D supplementation? *Sao Paulo Med J*. 2017 Sep-Oct;135(5):497-507.  
[PubMed: PM29116314](#)
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[PubMed: PM29080644](#)
26. Allan GM, Cranston L, Lindblad A, et al. Vitamin D: a narrative review examining the evidence for ten beliefs. *J Gen Intern Med*. 2016 Jul;31(7):780-791.  
[PubMed: PM26951286](#)
27. Focker M, Antel J, Ring S, et al. Vitamin D and mental health in children and adolescents. *Eur Child Adolesc Psychiatry*. 2017 Sep;26(9):1043-1066.  
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