

Vitamin B12 and Cognitive Function: OHTAC Recommendation

Ontario Health Technology Advisory Committee

November 2013

Suggested Citation

This report should be cited as follows:

Ontario Health Technology Advisory Committee (OHTAC). Vitamin B12 and cognitive function: OHTAC recommendation [Internet]. Toronto: Queen's Printer for Ontario; 2013 November. 11 p. Available from: <http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/ontario-health-technology-assessment-series/B12-cognitive-function>

Permission Requests

All inquiries regarding permission to reproduce any content in Health Quality Ontario reports should be directed to EvidenceInfo@hqontario.ca.

How to Obtain OHTAC Recommendation Reports From Health Quality Ontario

All OHTAC reports are freely available in PDF format at the following URL: <http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/ohtac-recommendations>.

Conflict of Interest Statement

All reports prepared by the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

About Health Quality Ontario

Health Quality Ontario (HQO) is an arms-length agency of the Ontario government. It is a partner and leader in transforming Ontario's health care system so that it can deliver a better experience of care, better outcomes for Ontarians, and better value for money.

Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. The Evidence Development and Standards branch works with advisory panels, clinical experts, developers of health technologies, scientific collaborators, and field evaluation partners to provide evidence about the effectiveness and cost-effectiveness of health interventions in Ontario.

To conduct its systematic reviews of health interventions, the Evidence Development and Standards branch examines the available scientific literature, making every effort to consider all relevant national and international research. If there is insufficient evidence on the safety, effectiveness, and/or cost-effectiveness of a health intervention, HQO may request that its scientific collaborators conduct economic evaluations and field evaluations related to the reviews. Field evaluation partners are research institutes focused on multicentred clinical trials and economic evaluation, as well as institutes engaged in evaluating the safety and usability of health technologies.

About the Ontario Health Technology Advisory Committee

The Ontario Health Technology Advisory Committee (OHTAC) is a standing advisory subcommittee of the Board of Directors of Health Quality Ontario. Based on the evidence provided by Evidence Development and Standards and its partners, OHTAC makes recommendations about the uptake, diffusion, distribution, or removal of health interventions within the provincial health system. When making its recommendations, OHTAC applies a unique decision-determinants framework that takes into account overall clinical benefit, value for money, societal and ethical considerations, and the economic and organizational feasibility of the health care intervention in Ontario.

Publishing Health Quality Ontario Research

When the evidence development process is nearly completed, draft reviews, reports, and OHTAC recommendations are posted on HQO's website for 21 days for public and professional comment. For more information, please visit: <http://www.hqontario.ca/evidence/evidence-process/evidence-review-process/professional-and-public-engagement-and-consultation>.

Once finalized and approved by the Board of Directors of Health Quality Ontario, the research is published as part of the *Ontario Health Technology Assessment Series*, which is indexed in MEDLINE/PubMed, Excerpta Medica/Embase, and the Centre for Reviews and Dissemination database. Corresponding OHTAC recommendations and associated reports are also published on the HQO website. Visit <http://www.hqontario.ca> for more information.

When sufficient data are available, OHTAC tracks the ongoing use of select interventions it has previously reviewed, compiling data by time period and region. The results are published in the Ontario Health Technology Maps Project Report.

Disclaimer

This report was prepared by the Evidence Development and Standards branch at Health Quality Ontario or one of its research partners for the Ontario Health Technology Advisory Committee and was developed from analysis, interpretation, and comparison of scientific research. It also incorporates, when available, Ontario data and information provided by experts and applicants to Health Quality Ontario. It is possible that relevant scientific findings may have been reported since the development of this recommendation. This report may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: <http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations>.

Table of Contents

Background	5
Conclusions.....	6
Decision Determinants.....	7
OHTAC Recommendations	8
Appendices.....	9
Appendix 1: Decision Determinants.....	9

Background

An evidence-based analysis was conducted by Health Quality Ontario to answer the following research questions:

- 1) Is there an association between vitamin B12 deficiency and the onset of dementia or cognitive decline?
- 2) Does treatment with vitamin B12 supplementation improve cognitive function in patients with dementia or cognitive decline and vitamin B12 deficiency?
- 3) What is the effectiveness of oral versus parenteral vitamin B12 supplementation in those with confirmed vitamin B12 deficiency?

During the public consultation phase HQO received feedback from the Ontario Medical Association requesting an evidence review of other conditions for which vitamin B12 levels may be tested. Those conditions were neuropathy, alopecia, dizziness, and fatigue.

Conclusions

Question 1: Is there an association between vitamin B12 deficiency and the onset of dementia or cognitive decline?

- Based on very low quality evidence, there does appear to be an association between homocysteine levels (a by-product of B vitamins) and the onset of dementia.

Question 2: Does treatment with vitamin B12 supplementation improve cognitive function in patients with dementia or cognitive decline and vitamin B12 deficiency?

- Based on moderate quality evidence, treatment with vitamin B12 supplementation does not change cognitive function in patients with or without dementia or cognitive impairment and with or without B12 deficiency.
- Based on low to moderate quality of evidence, treatment with vitamin B12 and folate in patients who have mild cognitive impairment seems to slow the rate of brain atrophy compared with patients who have mild cognitive impairment and are receiving a placebo. Whether this translates into clinical benefit is unknown.

Question 3: What is the effectiveness of oral versus parenteral vitamin B12 supplementation in those with confirmed vitamin B12 deficiency?

- Based on moderate quality evidence, oral vitamin B12 is as effective as parenteral vitamin B12 in patients with confirmed B12 deficiency in the short term.

Rapid Review Question: What is the clinical utility of serum vitamin B12 testing in cases of neuropathy, alopecia, dizziness or fatigue?

- The rapid review found that there was very low quality evidence indicating no association between vitamin B12 levels and neuropathy or alopecia. No studies were identified on the clinical utility of serum vitamin B12 testing in patients with dizziness or fatigue.

Decision Determinants

OHTAC has developed a decision-making framework that consists of 7 guiding principles for decision making and a decision determinants tool. When making a decision, OHTAC considers 4 explicit main criteria: overall clinical benefit, consistency with expected societal and ethical values, value for money, and feasibility of adoption into the health system. For more information on the decision-making framework, please refer to the *Decision Determinants Guidance Document* available at: <http://www.hqontario.ca/evidence/evidence-process/evidence-review-process/decision-making-framework>.

Appendix 1 provides a summary of the decision determinants for this recommendation.

OHTAC Recommendations

- OHTAC recommends that serum vitamin B12 testing be restricted to those with macrocytic anemia or malabsorption.
- OHTAC recommends against serum vitamin B12 testing for the purpose of investigating dementia or cognitive impairment and for vague presentations such as alopecia, dizziness, and fatigue.
- OHTAC recommends oral vitamin B12 be used instead of intramuscular vitamin B12 unless there is evidence of malabsorption.

Appendices

Appendix 1: Decision Determinants

Table A1. Decision Determinants for Vitamin B12 and Cognitive Function

Decision Criteria	Subcriteria	Decision Determinants Considerations
Overall clinical benefit How likely is the health technology/intervention to result in high, moderate, or low overall benefit?	Effectiveness How effective is the health technology/intervention likely to be (taking into account any variability)?	Research questions 1) Is there an association between vitamin B12 deficiency and the onset of dementia or cognitive decline? <ul style="list-style-type: none"> There appears to be an association between low homocysteine levels and the onset of dementia. (GRADE: Very Low–Low) 2) Does treatment with vitamin B12 supplementation improve cognitive function in patients with dementia or cognitive decline and vitamin B12 deficiency? <ul style="list-style-type: none"> Treatment with vitamin B12 in patients with or without cognitive impairment or dementia does not improve cognitive function. (GRADE: Moderate) Treatment with B vitamins in patients with or without cognitive impairment or dementia decreases the rate of brain atrophy. (GRADE: Low–Moderate) 3) What is the effectiveness of oral versus parenteral vitamin B12 supplementation in those with confirmed vitamin B12 deficiency? <ul style="list-style-type: none"> Oral vitamin B12 appears to be as effective as intramuscular vitamin B12 at increasing serum vitamin B12 levels. (GRADE: Moderate)
	Safety How safe is the health technology/intervention likely to be?	No safety concerns were identified.
	Burden of illness What is the likely size of the burden of illness pertaining to this health technology/intervention?	The prevalence of vitamin B12-related anemia is estimated at about 2% in older adults (> 60 years of age).
	Need How large is the need for this health technology/intervention?	The need for vitamin B12 testing and treatment is likely limited because of the inaccuracy of the test, the ease of taking vitamin B12 supplements, and the poor quality of evidence supporting the benefit of B12 supplementation.

<p>Consistency with expected societal and ethical values^a How likely is adoption of the health technology/intervention to be congruent with societal and ethical values?</p>	<p>Societal values How likely is the adoption of the health technology/intervention to be congruent with expected societal values?</p> <p>Ethical values How likely is the adoption of the health technology/intervention to be congruent with expected ethical values?</p>	<p>Testing for vitamin B12 and treating with B12 injections is widespread in patients with confirmed or suspected dementia in Ontario despite the lack of evidence that B12 changes outcomes.</p>
<p>Value for money How efficient is the health technology likely to be?</p>	<p>Economic evaluation How efficient is the health technology/intervention likely to be?</p>	<p>Oral vitamin B12 supplementation is much less expensive than B12 injections because it does not require the frequency of physician visits and because the patient is responsible for the cost of oral B12 (it is not covered by the Ontario Drug Benefit Program).</p>
<p>Feasibility of adoption into health system How feasible is it to adopt the health technology/intervention into the Ontario health care system?</p>	<p>Economic feasibility How economically feasible is the health technology/intervention?</p> <p>Organizational feasibility How organizationally feasible is it to implement the health technology/intervention?</p>	<p>Vitamin B12 testing was removed from the laboratory requisition form in November 2012.</p>

Abbreviations: GRADE, Grading of Recommendations Assessment, Development and Evaluation

Health Quality Ontario
130 Bloor Street West, 10th Floor
Toronto, Ontario
M5S 1N5
Tel: 416-323-6868
Toll Free: 1-866-623-6868
Fax: 416-323-9261
Email: EvidenceInfo@hqontario.ca
www.hqontario.ca

© Queen's Printer for Ontario, 2013