

BMJ Open Should vitamin B₁₂ tablets be included in more Canadian drug formularies? An economic model of the cost-saving potential from increased utilisation of oral versus intramuscular vitamin B₁₂ maintenance therapy for Alberta seniors

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ABSTRACT

Objective: The aim of this study was to estimate the cost-savings attainable if all patients aged ≥65 years in Alberta, Canada, currently on intramuscular therapy were switched to oral therapy, from the perspective of a provincial ministry of health.

Setting: Primary care setting in Alberta, Canada.

Participants: Seniors of age 65 years and older currently receiving intramuscular vitamin B₁₂ therapy.

Intervention: Oral vitamin B₁₂ therapy at 1000 µg/day versus intramuscular therapy at 1000 µg/month.

Primary and secondary outcome measures: Cost saving from oral therapy over intramuscular therapy, from the perspective of the Alberta Ministry of Health, including drug costs, dispensing fees, injection administration fees, additional laboratory monitoring and physician visit fees.

Results: Over 5 years, if all Albertans aged 65 years and older who currently receive intramuscular B₁₂ are switched to oral therapy, our model found that \$C13 975 883 can be saved. Even if no additional physician visits are billed for among patients receiving intramuscular therapy, \$C8 444 346 could be saved from reduced administration costs alone.

Conclusions: Oral B₁₂ therapy has been shown to be an effective therapeutic option for patients with vitamin B₁₂ deficiency, yet only three provinces and the Non-Insured Health Benefits program include oral tablets on their formulary rather than the parenteral preparation. To ensure judicious use of limited health resources, clinicians and formulary committees are encouraged to adopt oral B₁₂ therapy as a clinically and cost-effective first-line therapy for vitamin B₁₂ deficiency.

BACKGROUND

For over 20 years, oral vitamin B₁₂ has been referred to as ‘medicine’s best kept secret’.¹ Hesitation by clinicians to treat B₁₂ deficiency with oral preparations dates back to a 1959 report by the U.S.P. Anti-Anemia Preparations

Strengths and limitations of this study

- Minimal assumptions built into the model, as exact costs and the exact number of eligible residents comprising the population were available.
- Three randomised controlled trials and two prospective case series support our use of a cost-minimisation analysis approach.
- Comprehensive sensitivity analyses employed using Monte Carlo simulation to incorporate multiple variables.
- Study is from the perspective of the provincial ministry of health (the payer) and does not adopt a societal perspective since much of the additional information required for that is not available.
- Despite being set in one Canadian province, the use of intramuscular B₁₂ therapy is prevalent worldwide. Therefore, these results, while not directly generalisable to other jurisdictions, point to an economic argument for greater uptake of oral B₁₂ therapy which is likely consistent across other jurisdictions.

Advisory Board suggesting inadequate absorption of oral dosage forms.² Despite evidence of the effectiveness of oral B₁₂ therapy,^{3–9} intramuscular administration remains the most commonly prescribed route in North America.¹⁰

Approximately 5% of Canadians are B₁₂ deficient,¹¹ with Framingham data suggesting that B₁₂ deficiency in community-dwelling adults aged 67 years and older may be as high as 12%.¹² Deficiency can occur as a result of gastric atrophy or previous gastric or intestinal surgery, use of antacids and other medications (metformin), inadequate animal product intake, and as a result of deficiency in intrinsic factor, which is required for the absorption of cobalamin from the gut.^{13 14}

While the absorbability of oral B₁₂ has been questioned, a number of studies have reported successful results with oral therapy including treatment in patients with pernicious anaemia or bowel resection.^{5 6 9 15} Since 1% of orally ingested B₁₂ is absorbed via passive diffusion independent of the presence of intrinsic factor,⁸ daily oral doses of 1000 µg or more are considered sufficient to meet daily requirements¹⁶ even in patients with insufficient intrinsic factor.

While oral tablets often cost more to acquire than B₁₂ injection solution, the costs associated with administering the injections in the form of health professionals' time and resources can be significant. A 2001 cost study estimated that between \$C2.9 and \$C17.6 million could be saved over 5 years in the province of Ontario if elderly patients on intramuscular B₁₂ were switched to oral therapy.¹⁷ In addition, a British study estimated that 2000 nursing hours are required to provide 1 year of injections to 492 patients in their homes.¹⁸ Across Canada, only Nova Scotia, Northwest Territories, Yukon and the Non-Insured Health Benefits program for First Nations and Inuit consider oral B₁₂ tablets to be a benefit in their provincial drug formularies, while all provinces and territories cover the injectable product.

The objective of this study was to estimate the cost savings of treatment using daily oral vitamin B₁₂ supplementation at a dosage of 1000 µg daily versus monthly 1000 µg/mL intramuscular injections in Alberta seniors over the age of 65 years who are currently using B₁₂ injection. Such a study is warranted in order to update the 2001 study in Ontario to reflect current costs, and to renew discussion about the best allocation of limited healthcare resources and whether oral B₁₂ should be covered by all Canadian provincial formularies.

METHODS

Study type

A cost-minimisation analysis (CMA) was performed wherein alternatives compared are considered to be equivalent in terms of factors that are relevant to the decision such as efficacy and tolerability, so the lowest cost alternative is selected.¹⁹ While a major assumption, three randomised trials (including a total of 66 participants on oral therapy and 75 patients on intramuscular therapy)^{3–5} and three prospective case series of 151 patients switching from intramuscular to oral therapy^{6 8 9} have concluded that the oral route is as clinically effective as the intramuscular route. Across all case series, no patients switched from intramuscular to oral therapy required a switch back to intramuscular replacement as a result of therapeutic failure. Costs were modelled over a period of 5 years, and the perspective of the Alberta Ministry of Health was adopted for this study.

Setting/patients

The study population consists of individuals aged 65 years or older with an Alberta Health Care number receiving intramuscular B₁₂ therapy. The number of Alberta seniors

dispensed injectable B₁₂ over a 1-year period (January–December 2012) was determined from prescription dispensing records collected by IMS Brogan.²⁰

Primary outcome

Cost savings achievable by the province of Alberta if patients aged ≥65 years and currently receiving intramuscular B₁₂ therapy are switched to oral therapy. Cost savings are estimated in Canadian currency.

Cost determination

All costs are reported in Canadian dollars.

Cost of B₁₂ tablets

The suggested retail price of Swiss Naturals, Jamieson and Nature's Bounty brands of 1000 µg B₁₂ tablets were obtained from the manufacturers and averaged to obtain the cost per tablet. In Alberta, the maximum professional fee allowed for dispensing products with an acquisition cost of ≤\$C74.99 is \$C11.93 (consists of \$C10.22 professional fee and \$C1.71 inventory allowance).²¹

Quantity of B₁₂ tablets and professional fees

It was assumed that patients would receive a 3-month supply with each fill, therefore, amassing four professional fees annually and 365 tablets. Albertans aged 65 years and older are automatically enrolled into a 'Coverage for Seniors' programme, where the patient copay is 30% of the cost to a maximum of \$C25.²² Since this study assumes the perspective of the provincial Ministry of Health, the payer is assumed to cover 70% of the total drug cost. Despite being a non-prescription product, sales tax was not applied since such tablets would be dispensed through the pharmacy as a tax-free product similar to a prescription drug.

Cost of B₁₂ injection

Parenteral B₁₂ in Alberta is available in 10 mL multidose vials at a concentration of 1000 µg/mL. The cost per millilitre for the two products currently available in Alberta (DIN 00521515 and DIN 01987003) was determined from the Alberta Health Drug Benefit List.²³ In Alberta, the total charge allowable for injectable drugs other than insulin is 5/3 of the product's acquisition cost.²¹ Therefore, with an acquisition cost of \$C4.50 per vial of parenteral B₁₂, the total charge allowed—including the drug and professional fee—cannot exceed \$C7.50 or \$C0.75 per dose.

Quantity of B₁₂ injection

At the usual dosage of 1000 µg/month, one vial contains a 10-month supply of drug. Therefore, 1.2 vials would be required for a 1-year supply.

Cost of additional laboratory monitoring

Costs for the laboratory analyses were obtained from Alberta Health Services, laboratory technicians' time to draw and analyse the blood samples were estimated by

consulting with practicing laboratory technicians, and laboratory technician wages were obtained from a Government of Alberta occupational survey²⁴ with a 20% fringe benefit applied.

Quantity of additional laboratory monitoring

To ensure adequate response to therapy, we assumed that patients to be switched from intramuscular to oral B₁₂ would receive a baseline complete blood count and serum B₁₂ prior to the switch, repeated once after the switch to confirm effectiveness. It was assumed that this additional monitoring would occur only upon switch from intramuscular to oral therapy, with long-term monitoring occurring at the same rate as if the patient had remained on intramuscular injections, therefore representing no additional cost of oral therapy over intramuscular therapy following the initial switch.

Cost of injection administration

Currently, physicians, nurses and pharmacists are authorised to administer B₁₂ by intramuscular injection in Alberta. Fees for physician office administration of injections and pharmacist administration of injections are provided in table 1.

Quantity of injection administrations

The proportion of patients on intramuscular B₁₂ therapy receiving their monthly injections from their physician's office or their pharmacy is unknown. For the purpose of the study, based on the experience of the authors including a practicing pharmacist and family physician, it was assumed that 25% of all B₁₂ injections are administered in a community pharmacy with the remainder administered in a medical clinic.

Cost of additional physician visits

The current cost of \$35.91 for a standard family physician consultation visit in Alberta was utilised in the model.

Quantity of additional physician visits.

Based on available administrative data, we were unable to determine the number of additional physician visits received by and billed for patients on intramuscular versus oral B₁₂ supplementation apart from simply the administration of the injection in the medical clinic. For the base case scenario, we assumed that 10% of injections administered in a physician's office also included a billed physician consultation which would not have occurred if the patient were not on intramuscular B₁₂, and have explored other scenarios in sensitivity analyses as described below.

Model assumptions

A number of assumptions were made with the model in addition to those previously described. It was assumed that patients on oral B₁₂ therapy were able to self-administer the medication, and if assistance was required, it was assumed that they already required this assistance for other medications rather than solely for

Table 1 Expected values and distribution parameters for the deterministic model and probabilistic sensitivity analyses

Parameter	Expected value±SE	Distribution
Study population ²⁰	28 252±10%	γ
Cost per B ₁₂ tablet	\$C0.16±0.008	γ
Professional fee for dispensing tablets ²¹	\$C11.93	–
Cost per B ₁₂ injectable dose ^{21–23}	\$C0.75	–
Cost for CBC and serum B ₁₂ analyses*	\$C6.50	–
Laboratory technician time for blood sample draw and analyses (hours)*	0.75 (range 0.25–1)	Triangular
Laboratory technician wage and benefits ^{24*}	\$C44.60 (range \$C35.82–\$C51.41)	Triangular
Fee for administration of intramuscular injection in a physician's office ²⁶	\$C10.30	–
Cost for physician consultation visit ²⁶	\$C35.91	–
Fee for administration of intramuscular injection in a pharmacy ²⁷	\$C20.00	–

Normal distribution sample values probabilistically from a normal curve with specified mean (expected value) and SD. Triangular distribution sample values probabilistically within the range specified, with increasing probability as values near the expected value.

*Indicates parameter only included in year 1 of the model. CBC, complete blood count.

B₁₂ tablets. Since B₁₂ tablets can be taken concurrently with other medications, it was not assumed that additional assistance would be needed if oral B₁₂ were added to their medication regimen. The cost of supplies to administer the intramuscular injection (needle, syringe, alcohol swab, gloves, bandage and sharps disposal) were excluded from the model as these are relatively inexpensive and were not felt to significantly contribute to the overall cost of the injectable product.

Discounting

Consistent with CADTH guidelines for the economic evaluation of health technologies,²⁵ a discount rate of 5% for outcomes occurring after 1 year was applied to the reference case, with sensitivity analyses performed around this value as described below.

Sensitivity analyses

Multiway sensitivity analysis was performed in the form of 10 000 Monte Carlo simulation iterations, adjusting

for a number of variables. Model inputs and the probabilistic distributions used in the sensitivity analyses are presented in table 1. The base case scenario was calculated using the expected value for each variable and assumed a 10% rate of additional physician consultations for patients on intramuscular versus oral therapy.

Sensitivity analysis was also performed for different proportions of additional physician office visits including a billed consultation. While the base scenario assumed a 10% rate of office consultations during injection visits, the analyses were repeated for rates of 0% and 25%. Discounting rates of 0% and 3% were also tested in sensitivity analysis.

RESULTS

Estimated 5-year cost savings associated with switching all Alberta seniors currently receiving injectable B₁₂ to oral therapy is \$C13 975 883. Base scenario and sensitivity analysis results are presented in table 2. Our model found that even if no additional physician visits were billed for among patients receiving intramuscular therapy, over \$C8 million could be saved from reduced administration costs alone.

Owing to the additional laboratory monitoring performed in the year of the change from intramuscular to oral therapy, the model found the switch to be moderately cost effective in the first year, with larger savings realised in years 2–5. For the base scenario, cost savings in year 1 were estimated at \$C48.34 (SD \$C8.58) per patient, increasing to \$C126.55 (SD \$C2.04) in year 2. Over 5 years, average cost savings per patient was estimated at \$C494.69.

DISCUSSION

Over 5 years, the province of Alberta can be expected to free nearly \$C14 million in healthcare costs if all seniors over the age of 65 years currently receiving intramuscular B₁₂ are switched to oral tablets. Despite evidence confirming that sufficient B₁₂ is absorbed by passive diffusion at a dose of 1000 µg daily to be effective even in

patients lacking intrinsic factor or with gastrointestinal disease,¹⁴ the intramuscular route continues to be commonly prescribed. With high health professional workloads and increasingly restricted healthcare budgets, a switch from intramuscular to oral therapy will not only free health professional resources to see patients at greater need, but can also result in cost savings for reinvestment into other needed services.

The option of oral supplementation is well received by patients. A Canadian study by Kwong *et al*⁸ found that 73% of patients receiving B₁₂ injections were willing to try oral B₁₂, and of those who tried the oral therapy, 71% wished to permanently remain on oral therapy. Travel inconveniences were the most common reason for preferring the oral route. The authors concluded that oral therapy would decrease physician burden, increase patient control over therapy and avoid patient discomfort and inconvenience. While willingness-to-pay for avoiding injections is unknown in adult patients, previous research has suggested that patients with diabetes value a reduced injection burden as much as they value disease control.²⁸ Therefore, if a societal perspective including utility were considered, it is likely that the benefit of switching patients from intramuscular to oral therapy would be even greater. Furthermore, the elimination of risk for injection site reactions following a switch to oral therapy represents another potential benefit from the patient perspective.

A number of assumptions employed in the model have the potential to alter the results in either direction. It was assumed that oral tablets were dispensed in 3-month supplies by the pharmacy rather than monthly refills, which would be expected to underestimate the cost-saving potential of oral therapy if not all patients opt for quarterly refills. Underestimation of savings may have also occurred as a result of calculating tablet cost based on non-generic products at higher costs per tablet. Home care costs for the administration of B₁₂ injections in home-bound patients was not included since the proportion of patients receiving in-home injections was unknown, and it was assumed that these

Table 2 Model results over 5 years

Proportion in-office injections including a fee for a physician visit (%)	Discounting rate for years 2–5 (%)	Mean cost saving for payer	Mean cost saving per patient
Reference case			
10	5	\$C13 975 883	\$C494.69
Sensitivity analyses			
0	0	\$C9 564 224	\$C338.53
0	3	\$C8 878 728	\$C314.27
0	5	\$C8 444 346	\$C298.89
10	0	\$C15 677 500	\$C554.92
10	3	\$C14 635 912	\$C518.05
25	0	\$C24 784 224	\$C877.26
25	3	\$C23 212 469	\$C821.62
25	5	\$C22 216 488	\$C786.37

injections would be administered in conjunction with a regular visit rather than as the sole reason for a visit by a nurse. However, if additional home care visits are indeed being performed for B₁₂ injections, then the savings of switching to oral B₁₂ would obviously be greater. Importantly, the model also assumed that all patients making the switch to oral therapy saw clinical benefit and did not require a switch back to intramuscular therapy, therefore representing maximum saving potential. This assumption is consistent with previously published randomised controlled trials and case series reporting treatment success across all patients studied.^{3–9} Additionally, we assumed in the base scenario that additional laboratory monitoring is only required for the first year following the switch to oral therapy, with monitoring as usual for the remaining years. Considering that adherence to self-administered oral therapy may be lower than a healthcare professional-administered injection, even if an additional set of laboratory tests were performed each year for the 5-year term of the model, the estimated cost savings would still amount to \$C12 million.

Direct comparison between our model and the results of the 2001 cost-saving paper cannot be performed due to differing model assumptions and available data. Overall, both models report significant cost-saving potential of the switch from the perspective of a government payer over 5 years. However, due to higher current professional fees for injection administration, our model found overall cost savings even if no additional physician visits occurred for patients receiving B₁₂ injections, whereas the previous study found a break-even point when 16.3% of additional physician visits were avoided.

The use of CMA is controversial as it assumes equal efficacy and tolerability between the two options being compared; however, we feel this assumption is justifiable based on published data comparing the oral and intramuscular routes.^{3–9} However, the total number of patients studied in the randomised trials (total n=141 across 3 studies) and case series (n=151) remains relatively small and doses employed across each study differed. Further research on a larger population, comparing standard-dose intramuscular therapy with standard-dose oral therapy is therefore recommended and is currently being planned. Additionally, payers considering adding oral B₁₂ tablets to their formularies should consider allowing for the coverage of intramuscular therapy in the event of documented treatment failure on oral supplementation, until large-scale studies confirming equivalence are conducted, or allowing for short-term intramuscular therapy for patients with neurological symptoms followed by oral maintenance therapy. Indeed, a planned randomised controlled trial of 320 patients of age ≥65 in Spain will be directly comparing oral with intramuscular B₁₂ and is expected to examine the non-inferiority of oral therapy over 1 year (clinicaltrials.gov NCT01476007).

Overall, our model estimates that \$C8–24 million in cost savings can be realised over 5 years if all Alberta seniors currently receiving intramuscular vitamin B₁₂ are switched to oral therapy. Within closed systems like universal healthcare, this is unlikely to represent true cost savings, but rather room for reallocation of resources to other health system needs. With an ageing population and increasing rates of chronic disease, switching of patients from intramuscular to oral vitamin B₁₂ replacement appears to be not only clinically efficacious but also an effective use of limited healthcare resources.

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REFERENCES

- Lederle FA. Oral cobalamin for pernicious anemia. Medicine's best kept secret. *J Am Med Assoc* 1991;265:94–5.
- Bethell FH, Castle WB, Conley CL. Present status of treatment of pernicious anemia: ninth announcement of the U.S.P. Anti-Anemia Preparations Advisory Board. *J Am Med Assoc* 1959;171:2092–4.
- Kuzminski AM, Del Giacco EJ, Allen RH, *et al*. Effective treatment of cobalamin deficiency with oral cobalamin. *Blood* 1998;92:1191–8.
- Bolaman Z, Kadikoylu G, Yukselen V, *et al*. Oral versus intramuscular cobalamin treatment in megaloblastic anemia: a single-center, prospective, randomized, open-label study. *Clin Ther* 2003;25:3124–34.
- Castelli MC, Friedman K, Sherry J, *et al*. Comparing the efficacy and tolerability of a new daily oral vitamin B12 formulation and intermittent intramuscular vitamin B12 in normalizing low cobalamin levels: a randomized, open-label, parallel-group study. *Clin Ther* 2011;33:358–71.
- Nyholm E, Turpin P, Swain D, *et al*. Oral vitamin B12 can change our practice. *Postgrad Med J* 2003;79:218–20.
- Vidal-Alaball J, Butler C, Cannings-John R, *et al*. Oral vitamin B12 versus intramuscular vitamin B12 for vitamin B12 deficiency. *Cochrane Database Syst Rev* 2005;3:CD004655.
- Kwong JC, Carr D, Dhalla IA, *et al*. Oral vitamin B12 therapy in the primary care setting: a qualitative and quantitative study of patient perspectives. *BMC Fam Pract* 2005;6:8.
- Berlin H, Berlin R, Brante G. Oral treatment of pernicious anemia with high doses of vitamin B12 without intrinsic factor. *Acta Med Scand* 1968;184:247–58.
- Graham ID, Jette N, Tetroe J, *et al*. Oral cobalamin remains medicine's best kept secret. *Arch Gerontol Geriatr* 2007;44:49–59.
- MacFarlane AJ, Greene-Finestone LS, Shi Y. Vitamin B-12 and homocysteine status in a folate-replete population: results from the Canadian Health Measures Survey. *Am J Clin Nutr* 2011;94:1079–87.

12. Lindenbaum J, Rosenberg IH, Wilson PW, *et al.* Prevalence of cobalamin deficiency in the Framingham elderly population. *Am J Clin Nutr* 1994;60:2–11.
13. de Jager J, Kooy A, Lehert P, *et al.* Long term treatment with metformin in patients with type 2 diabetes and risk of vitamin B-12 deficiency: randomized placebo controlled trial. *BMJ* 2010;340:c2181.
14. Andrès E, Vidal-Alaball J, Federici L, *et al.* Clinical aspects of cobalamin deficiency in elderly patients. Epidemiology, causes, clinical manifestations, and treatment with special focus on oral cobalamin therapy. *Eur J Int Med* 2007;18:456–62.
15. Andrès E, Federici L, Affenberger S, *et al.* B12 deficiency: a look beyond pernicious anemia. *J Fam Pract* 2007;56:537–42.
16. Health Canada. Dietary reference intakes: reference values for vitamins. http://www.hc-sc.gc.ca/fnan/nutrition/reference/table/ref_vitam_tbl-eng.php (accessed 17 May 2012).
17. van Walraven CG, Austin P, Naylor CD. Vitamin B12 injections versus oral supplements: how much money could be saved by switching from injections to pills? *Can Med Assoc J* 2001; 47:79–86.
18. Middleton J, Wells W. Vitamin B12 injections: considerable source of work for the district nurse. *BMJ* 1985;270:1254–5.
19. Drummond MF, Sculpher MJ, Torrance G, *et al.* *Methods for the economic evaluation of health care programmes*. 3rd edn. New York: Oxford University Press, 2005.
20. IMS Brogan LRx database, January 2013 and Compuscript audit, January 2013.
21. Alberta Health. Pharmacy fee reimbursement. <http://www.health.alberta.ca/services/pharmacy-fee-reimbursement.html>
22. Alberta Health. Coverage for seniors. <http://www.health.alberta.ca/services/drugs-seniors.html>
23. Alberta Health. Interactive drug benefit list. <https://idbl.ab.bluecross.ca/idbl/load.do>
24. Government of Alberta. 2011 Alberta Wage and Salary Data—Medical Laboratory Technologist. http://alis.alberta.ca/occinfo/content/requestaction.asp?aspaction=gethtmlprofile&format=html&occpro_id=71003140
25. *Guidelines for the economic evaluation of health technologies: Canada*. 3rd edn. Ottawa: Canadian Agency for Drugs and Technologies in Health, 2006. www.cadth.ca/media/pdf/186_EconomicGuidelines_e.pdf
26. Alberta Health Care Insurance Plan. Medical Price List as of 01 April 2012. <http://www.health.alberta.ca/documents/SOMB-Medical-Prices-2012-04.pdf>
27. Alberta Health. Compensation for Pharmacy Services, July 2012. <http://www.health.alberta.ca/documents/Pharmacy-Services-Compensation-2012.pdf>
28. Hauber AB, Johnson FR, Sauriol L, *et al.* Risking health to avoid injections: preferences of Canadians with type 2 diabetes. *Diabetes Care* 2005;28:2243–5.