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Vitamin B12 Intramuscular Injections Versus Oral Supplements: A Budget Impact Analysis

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Health Quality Ontario 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 expert advisory panels, clinical experts, scientific collaborators, and field evaluation partners to conduct evidence-based reviews that evaluate the effectiveness and cost-effectiveness of health interventions in Ontario.

Based on the evidence provided by Evidence Development and Standards and its partners, the Ontario Health Technology Advisory Committee—a standing advisory subcommittee of the Health Quality Ontario Board—makes recommendations about the uptake, diffusion, distribution, or removal of health interventions to Ontario's Ministry of Health and Long-Term Care, clinicians, health system leaders, and policy-makers.

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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. This report is current as of the date of the literature search specified in the Research Methods section. Health Quality Ontario makes no representation that the literature search captured every publication that was or could be applicable to the subject matter of the report. It is possible that relevant scientific findings may have been reported since the completion of the review. This analysis may be superseded by an updated publication on the same topic.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.

Abstract

Background

Vitamin B12 deficiency can lead to adverse health effects such as anemia and, in some cases, permanent neurologic damage. In Canada, patients with vitamin B12 deficiency are typically given intramuscular injections, which incur considerable cost and inconvenience. The clinical evidence-based analysis has found that oral supplementation is as effective as intramuscular injections.

Objectives

This economic analysis aimed to estimate the cost savings of switching from intramuscular injections to high-dose oral supplements for patients aged 18 years and older with confirmed vitamin B12 deficiency.

Data Sources

Population-based administrative databases for Ontario were used to identify patients receiving vitamin B12 intramuscular injections in any fiscal year between 2006 and 2011. The Ontario Drug Benefit (ODB) database was used to identify patients who were prescribed vitamin B12 injections, and the Ontario Health Insurance Plan database was used to identify all physician claims for intramuscular injections as well as laboratory tests assessing vitamin B12 levels. The Registered Physicians Database was used to identify the type of physician; the analysis was restricted to family physicians and internists.

Review Methods

Two cohorts of patients were identified. For cohort 1, the ODB database was used to identify patients who were prescribed vitamin B12 injections. Those covered under the ODB are 65 years of age or older and are economically deprived. A second cohort was created to capture those 18 to 64 years of age receiving injections. Cohort 2 consisted of patients (not in cohort 1) who received 6 or more intramuscular injections within 1 year and had a laboratory test 2 months before the intramuscular injection claim. Physician experts were consulted to estimate the resources and costs of converting patients to oral supplements. The Ministry of Health and Long-Term Care perspective was taken, and all costs are expressed in 2013 Canadian dollars.

Results

The budget impact analysis demonstrated costs of $2.8 million to the Ministry of Health and Long-Term Care in the first year of conversion; however, in subsequent years there are savings of $4.2 million per year. The cumulative 5-year budget impact demonstrates savings of $14.2 million to the health care system.

Limitations

This analysis represents the cost of conversion for those currently receiving intramuscular injections. There are no conversion costs for those who are prescribed oral supplements as an initial therapy, and so the savings could be even greater than reported. As well, an underlying assumption of this analysis is that patients will comply with oral supplementation.

Conclusions

Over 5 years, there are savings of $14.2 million to the health care system from switching to vitamin B12 oral supplements.

Plain Language Summary

Vitamin B12 deficiency has long been thought to be associated with dementia and other neurocognitive disorders. In a separate report, Health Quality Ontario (HQO) reviewed the published research on this issue and found only weak evidence that vitamin B12 deficiency is associated with the onset of dementia. That review also found moderate evidence that treatment with vitamin B12 does not improve dementia and that oral supplements are as effective as injections of vitamin B12.

In 2010, more than 2.9 million serum vitamin B12 tests were performed in Ontario at a cost of $40 million. Each year, approximately 110,000 residents receive vitamin B12 injections to boost their levels of vitamin B12. HQO commissioned an economic analysis to estimate the cost savings of switching from vitamin B12 injections to high-dose oral supplements for patients aged 18 years and older with confirmed B12 deficiency. This study concluded that the Ontario health care system could save $14.5 million in 5 years by switching to oral supplements, assuming that patients took the oral supplements as required.

Table of Contents

List of Tables

List of Figures

List of Abbreviations

CINAHL	EBSCO Cumulative Index to Nursing and Allied Health Literature
HQO	Health Quality Ontario
ODB	Ontario Drug Benefit
OHIP	Ontario Health Insurance Plan
OHTAC	Ontario Health Technology Advisory Committee
OSB	Ontario Schedule of Benefits

Economic Analysis

The Programs for the Assessment of Technology in Health (PATH) was commissioned by Health Quality Ontario to evaluate the budget impact of switching from intramuscular injections of vitamin B12 to high-dose oral supplements for patients aged 18 years and older with confirmed B12 deficiency. Published economic evaluations are reviewed, and the budget impact of switching from intramuscular injections to oral supplements is estimated.

Health Quality Ontario conducts full evidence-based analyses, including economic analyses, of health technologies being considered for use in Ontario. These analyses are then presented to the Ontario Health Technology Advisory Committee, whose mandate is to examine proposed health technologies in the context of available evidence and existing clinical practice, and to provide advice and recommendations to Ontario health care practitioners, the broader health care system, and the Ontario Ministry of Health and Long-Term Care.

DISCLAIMER: Health Quality Ontario uses a standardized costing method for its economic analyses. The main cost categories and associated methods of retrieval from the province's perspective are described below.

Hospital costs: Ontario Case Costing Initiative cost data are used for in-hospital stay, emergency department visit, and day procedure costs for the designated International Classification of Diseases diagnosis codes and Canadian Classification of Health Interventions procedure codes. Adjustments may be required to reflect accuracy in the estimated costs of the diagnoses and procedures under consideration. Due to difficulties in estimating indirect costs in hospitals associated with a particular diagnosis or procedure, Health Quality Ontario normally defaults to a consideration of direct treatment costs only.

Non-hospital costs: These include physician services costs obtained from the Ontario Schedule of Physician Benefits, laboratory fees from the Ontario Schedule of Laboratory Fees, drug costs from the Ontario Drug Benefit Formulary, and device costs from the perspective of local health care institutions whenever possible, or from the device manufacturer.

Discounting: For cost-effectiveness analyses, a discount rate of 5% is applied (to both costs and effects/QALYs), as recommended by economic guidelines.

Downstream costs: All reported downstream costs are based on assumptions of population trends (i.e., incidence, prevalence, and mortality rates), time horizon, resource utilization, patient compliance, health care patterns, market trends (i.e., rates of intervention uptake or trends in current programs in place in the province), and estimates of funding and prices. These may or may not be realized by the Ontario health care system or individual institutions and are often based on evidence from the medical literature, standard listing references, and educated hypotheses from expert panels. In cases where a deviation from this standard is used, an explanation is offered as to the reasons, the assumptions, and the revised approach.

The economic analysis represents ***an estimate only***, based on the assumptions and costing methods explicitly stated above. These estimates will change if different assumptions and costing methods are applied to the analysis.

NOTE: Numbers may be rounded to the nearest decimal point, as they may be reported from an Excel spreadsheet.

Background

Vitamin B12 (cobalamin) is essential for normal red blood cell formation, certain enzyme reactions, and neurologic function. (1) This vitamin can be found in foods of animal origin (i.e., meat, fish, eggs) as well as in some fortified substitutes. Vitamin B12 deficiency is defined as a serum vitamin B12 level of less than 150 pmol/L. This deficiency can cause anemia and in some cases, permanent neurologic damage. People who consume diets free of animal products as well as those who have pernicious anemia (i.e., malabsorption) are at a greater risk of developing vitamin B12 deficiency. (1;2)

For those with deficiency, the dose of vitamin B12 required varies by severity; however, on average 1,000 µg/day is recommended. (3) In Canada, this vitamin is often administered through intramuscular injections in a physician's office, which results in substantial costs and inconvenience. (4) In the clinical evidence-based analysis, 3 randomized controlled studies reported that oral vitamin B12 supplementation

was as effective as vitamin B12 intramuscular injections in treating patients with vitamin B12 deficiency. Despite the first publication of this finding by Kuzminski in 1998, (5) a survey of Canadian physicians in 2007 revealed that 5.6% used oral vitamin B12 as an alternative to intramuscular injections and that only 25% of physicians were aware of the published trial. (4)

Objective

This economic analysis aims to determine the cost of switching from intramuscular injections to high-dose oral supplements for patients with confirmed vitamin B12 deficiency.

Economic Literature Review

An economic literature search was first conducted on October 9, 2012, and a second search was conducted on June 3, 2013, to update the literature. The following databases were searched: Ovid MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, Ovid Embase, Wiley Cochrane, EBSCO Cumulative Index to Nursing & Allied Health Literature (CINAHL), and Centre for Reviews and Dissemination/International Agency for Health Technology Assessment. Studies published from January 1, 2002, until June 3, 2013 were included. The following criteria were considered:

- Full economic evaluations: cost-utility analysis, cost-effectiveness analysis, cost-benefit analysis
- Economic evaluations reporting incremental cost-effectiveness ratios (i.e., cost per quality-adjusted life year/life years gained or cost per event avoided)
- Studies in patients with confirmed vitamin B12 deficiency
- Studies in English

Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search. Appendix 1 describes the literature search strategy.

Of 121 citations, 4 were identified as potentially relevant. After full-text review, 1 article was found that examined the costs of switching patients from vitamin B12 intramuscular injections to oral supplements. By examining the reference list of this article, another economic article was identified and included. Therefore the economic literature search identified 2 relevant articles.

One Canadian study used a third-party payer perspective to estimate the savings of switching all elderly patients (65 years of age or older) receiving vitamin B12 (cobalamin) injections to oral supplements. (3) The estimated savings over 5 years was between $2.8 million and $17.6 million (Cdn). These savings were mostly attributed to avoidable physician visits for injections. In another study conducted in the United Kingdom, the potential savings were estimated from a health care system perspective. (6) The results suggest that conversion to oral supplements in the first year was considerably more expensive than intramuscular injections as a result of closer monitoring of those on oral supplements during the first year. However, once the conversion period ended, the oral regimen was cheaper (£35.55 [GBP] per patient for oral supplements compared with £55.99–99.99 per patient for intramuscular injections). These savings were mainly attributed to nursing time avoided.

Primary Economic Evaluation

Published economic evaluations demonstrated the budget impact of switching from intramuscular injections to oral supplements. However, the Canadian study included only patients aged 65 years and older, and the other study was conducted in the United Kingdom. Because of these limitations, a budget impact analysis of switching patients aged 18 years and older to oral supplements was conducted.

Target Population

The target population of this economic analysis was patients aged 18 years and older with confirmed vitamin B12 deficiency.

Perspective

The primary analytic perspective was that of the Ministry of Health and Long-Term Care.

Economic Analysis Method

Patients and Databases

Population-based administrative databases for Ontario were used to identify patients receiving vitamin B12 (cobalamin) intramuscular injections in any fiscal year between 2006 and 2011. Two cohorts of patients were identified. For cohort 1, the Ontario Drug Benefit (ODB) database was used to identify patients who were prescribed vitamin B12 injections. The ODB covers the cost of select prescriptions for those 65 years of age and older or those who are economically deprived. To measure resource use for administering vitamin B12 injections to patients, all physician claims for intramuscular injections (fee codes G372 and G373) were identified from the Ontario Health Insurance Plan (OHIP) database for 1 year following the vitamin B12 prescription claim. Because those younger than 65 years of age would not be captured by the ODB database, another cohort was created. Cohort 2 consisted of patients 18 to 64 years of age who received 6 or more intramuscular injections (fee codes G372 and G373) within 1 year and had a vitamin B12 level laboratory test (fee code L345) 2 months before the intramuscular injection claim.

To avoid intramuscular injections for other indications, only those injections performed by family physicians and internists (identified through the Registered Physicians Database) were included in the analysis. Because vaccinations are claimed using a separate code, the intramuscular injections should primarily represent vitamin B12 injections.

Resources and Costs

To estimate the resources needed to switch all patients from vitamin B12 intramuscular injections to high-dose oral B12 supplements, physician experts were consulted. The resources and costs are reported in Table 1. We assumed that a physician visit to explain to patients the benefits of oral therapy and instructions for use would take place on the day they came in to receive their intramuscular injection, and so this visit was not added to the conversion cost. To convert patients to oral therapy, we assumed there would be a physician visit (intermediate assessment fee code A007) at 6 months in order to test the patient's vitamin B12 level and complete blood count. A blood sample collection fee was also added to the conversion cost.

The annual cost of vitamin B12 injections was determined by multiplying the total number of ODB prescription claims and OHIP intramuscular injection claims by their unit cost. The ODB database was

used to collect the number of ODB claims and the unit cost. It was assumed that one prescription claim would last the whole year. A cost of $6.74 was applied to each vitamin B12 prescription claim, as this was the mean cost of a vitamin B12 prescription among our sample. This cost was obtained from the ODB database and included the drug cost and a pharmacist dispensing fee. The number of claims for intramuscular injections, separated by fee code, was obtained from the OHIP database. The cost of the intramuscular injection was taken from the Schedule of Benefits for Physician Services and was $6.75 for the first injection (fee code G373) and $3.89 for each additional injection or billed with a visit (fee code G372). All costs are expressed in 2013 Canadian dollars.

Table 1: Resource Items and Costs of Oral Therapy and Intramuscular Injections

Item	Unit Cost ($)	Source
Physician conversion costs (first year of conversion only)		
Physician visit	33.70	OSB fee code A007, intermediate assessment
Complete blood count	8.27	OSB fee code L393
Vitamin B12 level	14.48	OSB fee code L345
Blood sample collection	7.76	OSB fee code L700
Intramuscular injection		
Vitamin B12 prescription: 1,000 µg/mL injection (10-mL pack)	6.74	Reported mean cost obtained from the ODB database
Intramuscular injection (with visit)	3.89	OSB fee code G372
Intramuscular injection (sole reason)	6.75	OSB fee code G373

Abbreviations: ODB; Ontario Drug Benefit, OSB; Ontario Schedule of Benefits.

Variability and Uncertainty

A sensitivity analysis was conducted on the criteria for identifying cohort 2. The timing of the vitamin B12 laboratory test varied from 2 months to 4 months before the first intramuscular injection. As well, the number of intramuscular injections a patient needed to receive to be included in the cohort varied from 6 or more injections to 4 or more injections within 1 year.

Generalizability

The findings of this economic analysis cannot be generalized to all patients with vitamin B12 deficiency. They can, however, be used to guide decision-making about the specific patient populations addressed in the trials.

Results of Budget Impact Analysis

Figure 1 demonstrates the volume of patients in each cohort per fiscal year. In 2006/2007 there was a steep increase in the volume of patients receiving vitamin B12 intramuscular injections; however, over the remaining 4 years the volume of patients remained stable. As a result, we have based our estimates on the volume of patients in the most recent fiscal year available (2010/2011).

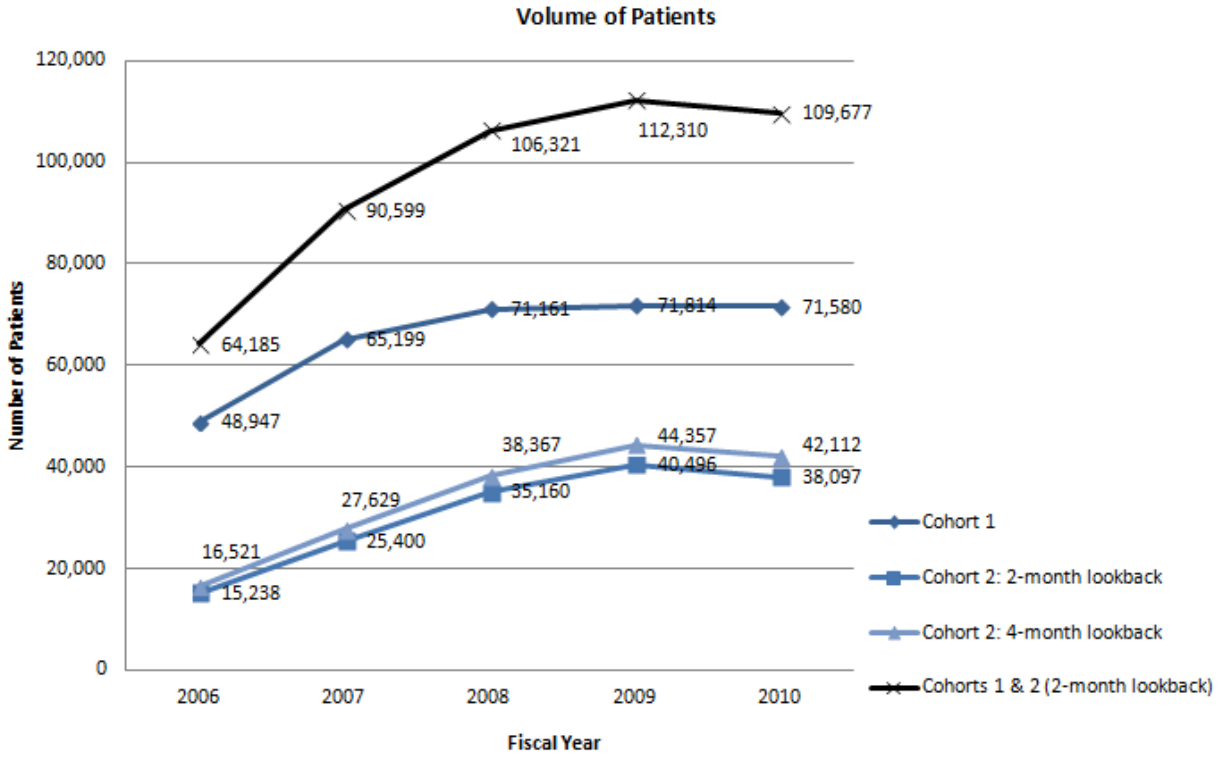

Figure 1: Volume of Patients in Each Cohort per Fiscal Year

Patient Characteristics

Most patients in cohort 1 were female (62.2%), and the mean age was 70.4 years (standard deviation [SD],13.2). In cohort 2, most patients were also female (68.1%), and the mean age was 50.6 (SD, 14.4).

Budget Impact

Figure 2 demonstrates that the number of intramuscular injection has remained stable over the past 3 years. In fiscal year 2010/2011 the number of intramuscular injection claims was 302,156 and 137,839 for fee codes G372 and G373, respectively. For a volume of 71,580 patients, the mean number of intramuscular injections per patient was 6.15 per year.

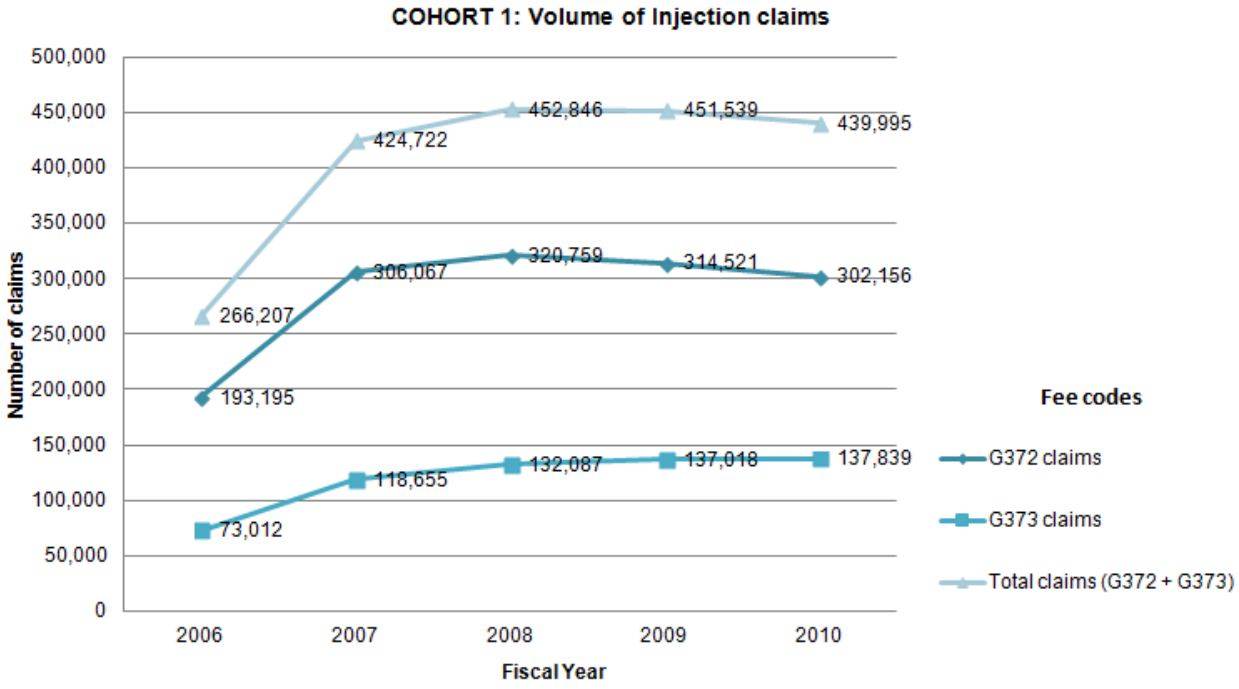

Figure 2: Number of Intramuscular Injection Claims for Cohort 1

The total annual cost for cohort 1 was $482,449 for the ODB vitamin B12 prescription claims and $2.1 million for the intramuscular injection claims (Table 2). Therefore, the total cost to the Ministry of Health and Long-Term Care is $2.6 million. The cost to the ministry for converting 71,580 patients to oral therapy is $4.6 million in the first year; however, in subsequent years there are no conversion costs. The incremental cost in year 1 is $2 million; however in each subsequent year there are savings of $2.6 million.

Table 2: Cohort 1 (n = 71,580) Costs of Oral Supplements and Intramuscular Injections

Item	Total Annual (N)	Unit Cost ($)	Total Annual Cost ($)
A. Physician conversion costs (first year of conversion only)			
Physician visit	71,580	33.70	2,412,246
Complete blood count	71,580	8.27	591,967
Vitamin B12 level	71,580	14.48	1,036,478
Blood sample collection	71,580	7.76	555,461
Total cost to Ministry (year 1)			4,596,152
Total cost to Ministry (subsequent years)			0
B. Intramuscular injections			
Vitamin B12 prescription: 1,000-µg/mL injection (10-mL pack)	71,580	6.74	482,449
Intramuscular injection (with visit)	302,156	3.89	1,175,387
Intramuscular injection (sole reason)	137,839	6.75	930,413
Total cost to Ministry			2,588,249
Incremental cost year 1 (A–B)			2,007,903
Incremental cost subsequent years (A–B)			-2,588,249

Figure 3 demonstrates the number of intramuscular injection claims per fiscal year for cohort 2. The total number of intramuscular injection claims in fiscal year 2010/2011 was 335,729. Among 38,097 patients the mean number of intramuscular injections per patient was 8.81 per year.

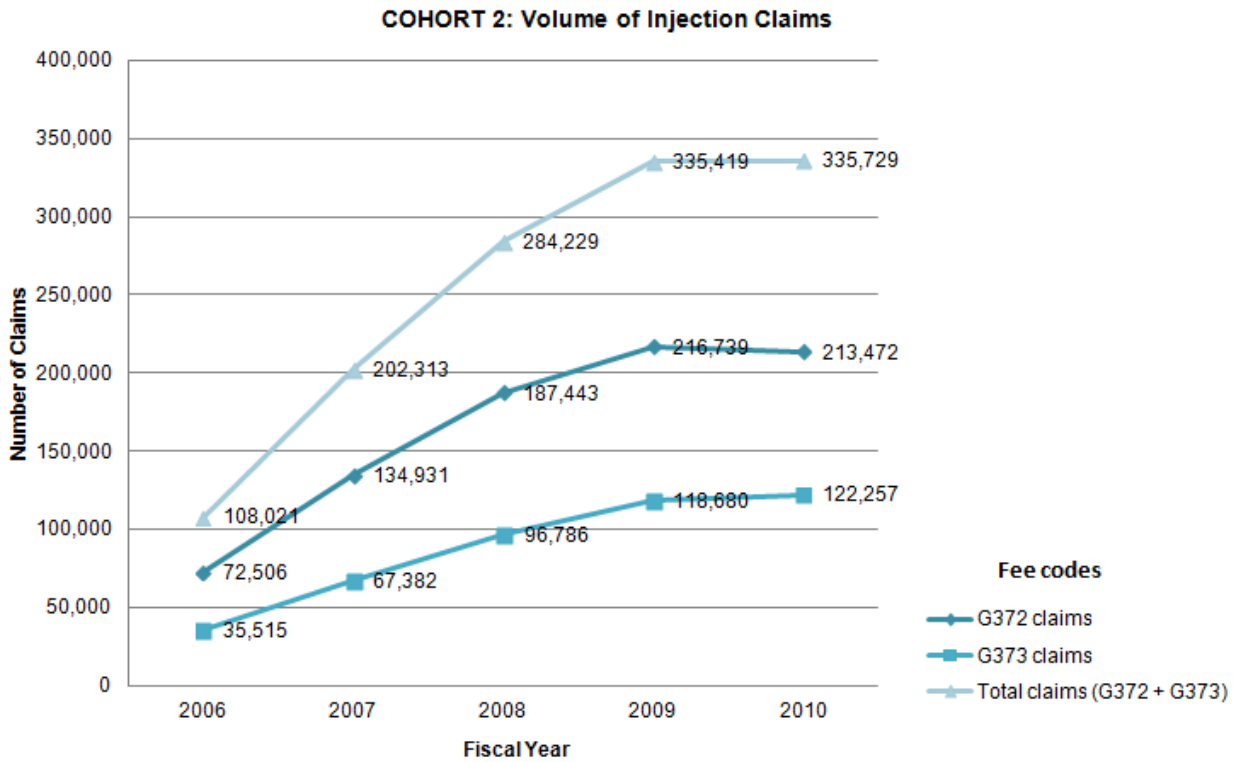

Figure 3: Number of Intramuscular Injection Claims for Cohort 2

The total annual cost for intramuscular injections for cohort 2 was $1.6 million (Table 3). The cost to the ministry for converting patients to oral therapy is $2.5 million in the first year and zero in subsequent years. Therefore, there is an incremental cost of $790,567 in the first year of converting patients to oral vitamin B12; however, there are savings of $1.6 million in each subsequent year.

Table 3: Cohort 2 (n = 38,097) Costs of Oral Supplements and Intramuscular Injections

Item	Total Annual (N)	Unit Cost ($)	Total Annual Cost ($)
C. Physician conversion costs (first year of conversion only)			
Physician visit	38,097	33.70	1,283,868
Complete blood count	38,097	8.27	315,062
Vitamin B12 level	38,097	14.48	551,645
Blood sample collection	38,097	7.76	295,633
Total cost to Ministry (year 1)			2,446,208
Total cost to Ministry (subsequent years)			0
D. Intramuscular injections			
Intramuscular injection (with visit)	213,472	3.89	830,406
Intramuscular injection (sole reason)	122,257	6.75	825,235
Total cost to Ministry			1,655,641
Incremental cost year 1 (C–D)			790,567
Incremental cost subsequent years (C–D)			-1,655,641

The annual and 5-year budget impact of converting patients in both cohorts to oral supplement therapy is presented in Table 4. Over 5 years the savings to the ministry are $14.2 million.

Table 4: Annual and 5-Year Budget Impact

	Year 1 ($)	Year 2 ($)	Year 3 ($)	Year 4 ($)	Year 5 ($)	Total ($)
Cohort 1	2,007,902	-2,588,249	-2,588,249	-2,588,249	-2,588,249	-8,345,094
Cohort 2	790,567	-1,655,640	-1,655,640	-1,655,640	-1,655,640	-5,831,993
Total yearly budget impact	2,798,469	-4,243,889	-4,243,889	-4,243,889	-4,243,889	**-14,177,087**

Sensitivity analysis

The results were insensitive to variations in the identification of cohort 2 (Table 5). If the review period for a vitamin B12 test is 4 months instead of 2 months, the savings increase to $14.6 million. If the review period increases to 4 months and patients receive 4 or more injections within 1 year, instead of 6 or more, the savings are $15 million.

Table 5: Sensitivity Analysis

Scenarios	Cumulative 5-year savings ($)
Base case: Cohort 1 and 2 (2-month review, 6 or more injections)	-14,177,087
Cohort 2 (2-month review, 4 or more injections)	-14,499,675
Cohort 2 (4-month review, 6 or more injections)	-14,645,028
Cohort 2 (4 month review, 4 or more injections)	-15,035,823

Conclusions

Approximately 110,000 patients receive vitamin B12 intramuscular injections in Ontario annually. Of these, approximately 65% are 65 years of age or older and most are female. This analysis demonstrated that converting this treatment to oral supplements would save the Ministry of Health and Long-Term Care the costs of the vitamin B12 drug and injections; however, there would be conversion costs in the first year. The net budget impact in the first year is $2.8 million, but there are savings of $4.2 million per year thereafter. The cumulative 5-year budget impact demonstrates savings of $14.2 million to the health care system. These savings could be greater, as there are no conversion costs for newly identified cases of vitamin B12 deficiency. However, an underlying assumption in this analysis is that patients will comply with oral therapy.

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Clinical Expert Advisory Panel: Appropriate Utilization of Vitamin B12 Testing for Neurocognitive-Based Indications

Panel Members	Affiliation(s)	Appointment(s)
Chair		
Dr. Joel Ray	St. Michael's Hospital/University of Toronto	Scientist/ Assistant Professor, Department of Medicine
Family Medicine		
Dr. Andrea Moser	**Baycrest Health Services**	Associate Medical Director
Geriatric Medicine		
Dr. Angeles Garcia	Queen's University	Professor, Department of Medicine
Neurology		
Dr. Stephen H. Pasternak	University of Western Ontario	Director, Cognitive Neurology & Alzheimer's Disease Research
Elizabeth Finger	University of Western Ontario	Assistant Professor, Clinical Neurological Sciences
Medial Biochemistry & Medical Genetics		
Dr. David E. C. Cole	University of Toronto	Professor, Laboratory Medicine & Pathobiology
Health Care System Representation		
Laurie Sweeting	Ministry of Health & Long Term Care	Senior Program Consultant

Appendices

Appendix 1: Literature Search Strategies

Literature Search - Vitamin B12 Economic Evidence-Based Analysis
Search date: June 3, 2013
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE; All EBM Reviews; CINAHL;
Limits: 2002-present; English
Filters: Economic
Questions:

1. Is there an association between vitamin B12 deficiency and the onset of dementia?
2. What is the effect of treatment of vitamin B12 in patients with dementia who are vitamin B12 deficient?
3. Is treatment with oral vitamin B12 supplements as effective as treatment with intramuscular vitamin B12 in patients with confirmed B12 deficiency? (this doesn't need to be specifically within a population with dementia—this is for all people with confirmed vitamin B12 deficiency)

Database: EBM Reviews - Cochrane Database of Systematic Reviews 2005 to April 2013, EBM Reviews - ACP Journal Club 1991 to May 2013, EBM Reviews - Database of Abstracts of Reviews of Effects 2nd Quarter 2013, EBM Reviews - Cochrane Central Register of Controlled Trials April 2013, EBM Reviews - Cochrane Methodology Register 3rd Quarter 2012, EBM Reviews - Health Technology Assessment 2nd Quarter 2013, EBM Reviews - NHS Economic Evaluation Database 2nd Quarter 2013, Embase 1980 to 2013 Week 22, Ovid MEDLINE(R) 1946 to May Week 4 2013, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations June 03, 2013
Search Strategy:

#	Query	Results
1	exp Vitamin B 12 Deficiency/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	9463
2	exp Vitamin B 12/df use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	18
3	Transcobalamins/df use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	113
4	exp Cyanocobalamin Deficiency/ use emez	6345
5	((b12 or b 12 or cyanocobalamin or cobalamin* or transcobalamin* or cobamide? or hydroxocobalamin or hydroxo-cobalamin or hydroxycobalamin) adj3 (deficien* or inadequa* or insufficien* or low blood level* or low serum level* or low plasma level* or suboptimal or sub-optimal or subnormal or sub-normal)).ti,ab.	9274
6	(an?emia* adj2 (addison* or pernicious* or megaloblastic)).ti,ab.	11200
7	or/1-6	25941
8	exp Vitamin B 12/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	18642
9	Transcobalamins/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	952
10	Transcobalamin/ use emez	613
11	Cyanocobalamin/ use emez	28702
12	(b12 or b 12 or cyanocobalamin or cobalamin* or transcobalamin* or cobamide? or hydroxocobalamin or hydroxo-cobalamin or hydroxycobalamin).ti,ab.	50629
13	or/8-12	67748
14	7 or 13	77991
15	exp Parenteral Nutrition/	56461

16	exp injections, intramuscular/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp intramuscular drug administration/ use emez	85543
17	exp injections, subcutaneous/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp subcutaneous drug administration/ use emez	120840
18	(((parenteral or intravenous) adj (feeding* or nutrition* or alimentation* or supplement*)) or ((intramuscular or subcutaneous) adj injection*)).ti,ab.	95436
19	or/15-18	302737
20	14 and 19	1530
21	exp Economics/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Models, Economic/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp Resource Allocation/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp "Value of Life"/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed or exp "Quality of Life"/ use mesz,acp,cctr,coch,clcmr,dare,clhta,cleed	607787
22	exp "Health Care Cost"/ use emez or exp Health Economics/ use emez or exp Resource Management/ use emez or exp Economic Aspect/ use emez or exp Economics/ use emez or exp Quality Adjusted Life Year/ use emez or exp Socioeconomics/ use emez or exp Statistical Model/ use emez or exp "Quality of Life"/ use emez	1323230
23	(econom* or cost* or budget* or pharmacoeconomic* or pharmaco-economic* or valu*).ti.	525746
24	((cost$ adj benefit$) or costbenefit$ or (cost adj effective$) or costeffective$ or econometric$ or life value or quality-adjusted life year$ or quality adjusted life year$ or quality-adjusted life expectanc$ or quality adjusted life expectanc$ or sensitivity analys$ or "value of life" or "willingness to pay").ti,ab.	220684
25	ec.fs.	3581989
26	or/21-25	5575546
27	20 and 26	287
28	limit 27 to english language [Limit not valid in CDSR,ACP Journal Club,DARE,CCTR,CLCMR; records were retained]	242
29	limit 28 to yr="2002 -Current" [Limit not valid in DARE; records were retained]	120
30	remove duplicates from 29	114

Database: CINAHL

#	Query	Results
S1	(MH "Vitamin B12 Deficiency+")	638
S2	((b12 or b 12 or cyanocobalamin or cobalamin* or transcobalamin* or cobamide? or hydroxocobalamin or hydroxo-cobalamin or hydroxycobalamin) N3 (deficien* or inadequa* or insufficien* or low blood level* or low serum level* or low plasma level* or suboptimal or sub-optimal or subnormal or sub-normal))	860
S3	(an?emia* N2 (addison* or pernicious* or megaloblastic))	282
S4	S1 OR S2 OR S3	1,062
S5	(MH "Vitamin B12")	2,059
S6	(b12 or b 12 or cyanocobalamin or cobalamin* or transcobalamin* or cobamide? or hydroxocobalamin or hydroxo-cobalamin or hydroxycobalamin)	3,641
S7	S5 OR S6	3,641
S8	S4 OR S7	3,778
S9	(MH "Parenteral Nutrition+")	3,740
S10	(MH "Injections, Intramuscular+")	2,453
S11	(MH "Injections, Subcutaneous+")	2,377
S12	(((parenteral or intravenous) N1 (feeding* or nutrition* or alimentation* or supplement*)) or ((intramuscular or subcutaneous) N1 injection*))	10,277
S13	S9 OR S10 OR S11 OR S12	10,343
S14	S8 AND S13	68
S15	(MH "Economics+") or (MH "Resource Allocation+") or MW ec or (MH "Quality of Life+") or (econom* or cost* or budget* or pharmacoeconomic* or pharmaco-economic* or valu*) or ((cost* N1 benefit*) or costbenefit* or (cost N1 effective*) or costeffective* or econometric* or life value or quality-adjusted life year* or quality adjusted life year* or quality-adjusted life expectanc* or quality adjusted life expectanc* or sensitivity analys* or "value of life" or "willingness to pay")	758,377
S16	S14 AND S15	16
S17	S14 AND S15 Limiters - Published Date from: 20020101-20131231; English Language	14

References

(1) Health Canada. Food and Nutrition: Vitamin B12. 2012 Mar. 22 [cited 2013 Apr 4]. Available from: http://www.hc-sc.gc.ca/fn-an/surveill/nutrition/measures-mesures/vit_b12-eng.php

(2) Food and Agriculture Organization of the United Nations. Vitamin B12. Rome: world Health Organization, Food and Agriculture Organization of the United Nations: 2013 Apr 4 [cited 2013 Apr 4]. Chapter 5, Human Vitamin and Mineral Requirements: report of a joint FAO/WHO expert consultation, Bankok, Thailand. Available from: http://www.fao.org/docrep/004/Y2809E/y2809e0b.htm

(3) van Walraven C, Austin P, Naylor CD. Vitamin B12 injections versus oral supplements. How much money could be saved by switching from injections to pills? Can Fam Physician. 2001;47:79-86.

(4) Graham ID, Jette N, Tetroe J, Robinson N, Milne S, Mitchell SL. Oral cobalamin remains medicine's best kept secret. Arch Gerontol Geriatr. 2007:44(1):49-59.

(5) Kuzminski AM, Del Giacco EJ, Allen RH, Stabler SP, Lindenbaum J. Effective treatment of cobalamin deficiency with oral cobalamin. Blood. 1998;92(4):1191-8.

(6) Vidal-Alaball J, Butler CC, Potter CC. Comparing costs of intramuscular and oral vitamin B12 administration in primary care: a cost-minimization analysis. Eur J Gen Pract. 2006;12(4):169-73.

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