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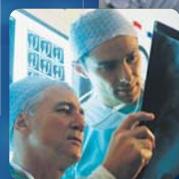
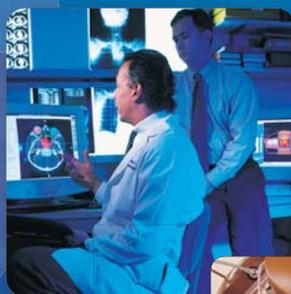
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des médicaments et des  
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## T E C H N O L O G Y   O V E R V I E W

**HTA**

Issue 50  
March 2009

Overview of Intravenous Immunoglobulin  
for Idiopathic Thrombocytopenia Purpura  
and Chronic Inflammatory Demyelinating  
Polyneuropathy



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*Cite as: Overview of Intravenous immunoglobulin for idiopathic thrombocytopenia purpura and chronic inflammatory demyelinating polyneuropathy [Technology Overview number 50].*  
Ottawa: Canadian Agency for Drugs and Technologies in Health; 2009.

Production of this report is made possible by financial contributions from Health Canada and the governments of Alberta, British Columbia, Manitoba, New Brunswick, Newfoundland and Labrador, Northwest Territories, Nova Scotia, Nunavut, Ontario, Prince Edward Island, Saskatchewan, and Yukon. The Canadian Agency for Drugs and Technologies in Health takes sole responsibility for the final form and content of this report. The views expressed herein do not necessarily represent the views of Health Canada or any provincial or territorial government.

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CADTH is funded by Canadian federal, provincial, and territorial governments.

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ISSN: 1203-9012 (print)  
ISSN: 1481-4501 (online)  
O0298 – March 2009

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# Canadian Agency for Drugs and Technologies in Health

## Overview of Intravenous Immunoglobulin for Idiopathic Thrombocytopenia Purpura and Chronic Inflammatory Demyelinating Polyneuropathy

March 2009

We thank Eugenia Palylyk-Colwell for her assistance in creating this overview from three longer reports.

This overview is based on three Technology Reports commissioned by CADTH:

Chen S, Pi D, Ansari M, Puil L, Desjardins B, Banks R. *Polyclonal Intravenous Immunoglobulin in Patients with Immune Thrombocytopenic Purpura: Clinical Systematic Review* [Technology Report No. 108]. Ottawa: Canadian Agency for Drugs and Technologies in Health (CADTH); 2008.

Blackhouse G, Xie F, Campbell K, Assasi N, Gaebel K, Levine M, et al. *Intravenous Immunoglobulin for Treatment of Idiopathic Thrombocytopenic Purpura: Economic and Health Service Impact Analyses* [Technology Report No. 112]. Ottawa: Canadian Agency for Drugs and Technologies in Health (CADTH); 2008.

Gaebel K, Blackhouse G, Campbell K, Robertson D, Xie F, Assasi N, et al. *Intravenous Immunoglobulin for Chronic Inflammatory Demyelinating Polyneuropathy: Clinical and Cost-Effectiveness Analyses* [Technology Report No. 117]. Ottawa: Canadian Agency for Drugs and Technologies in Health (CADTH); 2009.

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# 1 Introduction

Treatment of immune or idiopathic thrombocytopenia purpura (ITP) and chronic inflammatory demyelinating polyneuropathy (CIDP) account for a high use of intravenous immunoglobulin (IVIg) in Canada.<sup>1,2</sup> Increasing demand for the use of IVIg in other indications (many off-label), escalating costs, and a supply shortage have prompted Canadian health care decision-makers to consider new approaches in managing the use of IVIg. Because of the high use and cost of IVIg, the potential availability of alternative therapy, and the uncertainty about a therapeutic advantage when IVIg is compared with less costly alternatives, the assessment of the clinical- and cost-effectiveness and health services impact of IVIg that is used for the treatment of ITP and CIDP in Canada has been identified as a priority.

The incidence of ITP is estimated to be 4.8 per 100,000 children<sup>3</sup> and 2.6 per 100,000 adults.<sup>4</sup> It is caused by an abnormal immune response that destroys platelets and leads to bleeding and a decrease in the number of platelets. Children primarily acquire an acute disease that resolves without treatment in 70% to 90% of cases.<sup>5,6</sup> Ten per cent to 20% of children may develop a chronic form. The most serious complication in acute childhood ITP is life-threatening intracranial hemorrhage (ICH), which is most likely to occur when the platelet count is less than 20,000/ $\mu$ L.<sup>7</sup> Adult ITP usually has an insidious onset and is typically a chronic disease.<sup>8</sup>

The treatment options for acute ITP in children include close observation without treatment, IVIg, anti-D immunoglobulin (in Rh+, non-splenectomized children), corticosteroids, immune globulin and steroids in combination, plasma exchange, and removal of the spleen.<sup>9-11</sup> In general, the treatment options are similar in chronic childhood ITP and adult ITP, although vincristine, platelet transfusions, and factor VIIa have also been used by adults.<sup>5</sup> A platelet count of less than  $20 \times 10^9$ /L if accompanied by bleeding or a platelet count of less than  $10 \times 10^9$ /L without bleeding is usually the threshold for treatment.

CIDP is an acquired immune-mediated inflammatory disorder that destroys the myelin sheaths of nerves in the peripheral nervous system causing motor and sensory symptoms.<sup>12</sup> It typically has a course over months to years, and it may be steadily progressive or relapsing-remitting.<sup>12</sup> CIDP can occur at any age in both sexes, but it is most common in older individuals and males. Canadian CIDP prevalence and incidence rates are not known. As a result, it is assumed that the rate is approximately 1.0 per 100,000 people to 1.9 per 100,000 people, based on countries with similar demographic characteristics such as England<sup>13</sup> and Australia.<sup>14</sup> Although some patients have mild disease, most need treatment to arrest or reverse the disease. Treatment options include corticosteroids<sup>15</sup> or plasma exchange.<sup>16</sup>

IVIg is a human blood product containing pooled IgG immunoglobulins. It is used as a replacement therapy in primary and secondary immune deficiencies and as a therapy in autoimmune diseases and transplantation.<sup>17,18</sup> In Canada, IVIg is approved for primary immunodeficiency, low levels of immunoglobulins in the blood, ITP, pediatric human immunodeficiency virus, bone marrow transplantation, B-cell chronic lymphocytic leukemia, and CIDP.<sup>19,20</sup> IVIg products that are available through Canadian Blood Services are Gamunex 10% (Talecris Biotherapeutics Inc.), IGIVnex 10% (Talecris Biotherapeutics Inc. / Canadian Blood Services), Gammagard-SD, Gammagard Liquid 10%, and Iveegam EN (all Baxter

Bioscience). Privigen (CSL Behring), which is expected to be available in Canada in 2009, will help to maintain a stable supply and reduce the risk of shortages.<sup>21</sup> The cost of IVIg is C\$59.19/g (Mathias Haun, Canadian Blood Services: personal communication, 2008 Apr).

Canada has one of the highest per capita rates of consumption of IVIg in the world.<sup>22</sup> From 1997 to 2008, the average annual increase in IVIg use in Canada was 11.3% (range 6.8% to 20.0%).<sup>23</sup> The high use of IVIg and the other issues led to the undertaking of three Canadian Agency for Drugs and Technologies in Health (CADTH) health technology reports on IVIg use in Canada. This overview summarizes these three reports, which individually investigated the clinical-effectiveness<sup>24</sup> and cost-effectiveness and health services impact<sup>25</sup> of IVIg used in adults and children with ITP, and the clinical- and cost-effectiveness and health services impact of IVIg used in CIDP.<sup>26</sup>

## 2 Objectives

The objectives for assessing the clinical- and cost-effectiveness and health services impact of IVIg used for ITP and CIDP were met by addressing the following research questions:

- Does IVIg have an incremental benefit in treating ITP when compared with alternative standard therapy?
- What place does IVIg have in the management of acute or chronic ITP in children or adults?
- Is there sufficient evidence to identify groups of patients with ITP who may preferentially benefit from IVIg?
- What is the economic evidence regarding the cost-effectiveness of IVIg for ITP?
- What is the cost-effectiveness of the use of IVIg by pediatric patients with ITP in Canada?
- What is the cost-effectiveness of the use of IVIg by adult patients with ITP in Canada?
- What is the impact of IVIg on health services (including an estimated population impact, budget impact, and impact on legal, ethical, and equity issues) when it is used as a treatment of ITP in Canada?
- What is the comparative effectiveness of IVIg versus other standard therapies for short- and long-term CIDP management?
- What is the economic impact (trade-off of resources for health)?
- What is the cost-effectiveness of IVIg for short- and long-term CIDP management?
- What is the cost-effectiveness of IVIg among subgroups of patients with CIDP (progressive or relapsing-remitting; pure motor variant, pure sensory variant, or mixed variant)?
- What are the budgetary implications of adopting optimal treatment strategies?

## 3 Clinical Review

For the clinical reviews of ITP and CIDP, protocols were written beforehand and followed throughout the review process. Detailed searches of the published and grey literature were developed with the help of information specialists. Study selection, data extraction, and quality assessment were performed by two reviewers independently or by one reviewer and subsequently verified by another reviewer. Details of the search strategies and the systematic review process appear in the full reports.<sup>24,26</sup> When the statistical pooling of study data was

appropriate, binary outcomes were represented by relative risks (RR) and 95% confidence intervals. For continuous outcomes, the mean differences between study arms, standard deviation, and 95% confidence intervals were reported. The degree of statistical heterogeneity across studies was assessed using chi-square ( $\chi^2$ ) and  $I^2$  statistics. Pre-planned sensitivity and subgroup analyses were conducted.

## ***Clinical-effectiveness of intravenous immunoglobulin for idiopathic thrombocytopenia purpura***

### **a) Methods**

Study selection criteria were used to include all randomized controlled trials (RCTs) of patients with ITP at any age (other than newborns) receiving any preparation or dosage regimen of IVIg compared with alternative doses or preparations of IVIg, corticosteroids, anti-D immunoglobulin, second-line agents, or removal of the spleen for chronic ITP, placebo, or expectant management. Key clinical outcomes were reduction in bleeding (acute ITP in children), deferred removal of the spleen (chronic childhood ITP and adult ITP), and time to a platelet count of  $20 \times 10^9/L$  or higher or time to a platelet count of  $50 \times 10^9/L$  or higher (all ITP categories). ICH was not a specified outcome in any trial and was not systematically investigated.

### **Results**

A total of 1,577 citations were identified in the original search. From these, 31 publications describing 28 unique RCTs were included. Details about the included and excluded studies appear in the full report.<sup>24</sup> Of the 28 included RCTs, there were 15 RCTs of acute childhood ITP (two RCTs were reported in each of two publications, but only one RCT in each was eligible), four RCTs of chronic childhood ITP, and seven RCTs of adult ITP. In the trials, IVIg was compared with corticosteroids, anti-D immunoglobulin, modified or different doses of IVIg, or close observation. Most of the included trials were of low quality.

For acute childhood ITP, when IVIg (0.8 g to 1 g/kg per day over one to two days) was compared with corticosteroids, five of 11 RCTs suggested that IVIg showed superior efficacy during early recovery when the number of platelets is profoundly decreased. Six trials failed to show a statistically significant result in favour of IVIg or corticosteroids. Meta-analyses could not be done for the primary outcomes of reduction in bleeding or time to platelet counts of  $20 \times 10^9/L$  or higher or  $50 \times 10^9/L$  or higher. Meta-analyses could be performed for the secondary outcomes of children with platelet counts of  $20 \times 10^9/L$  or higher at 24 hours, 48 hours, and 72 hours. At 24 hours, the pooled RR of achieving a platelet count of  $20 \times 10^9/L$  or higher was 1.55 based on five trials with 298 participants. At 48 hours, the RR was 1.34 based on five trials with 288 participants; and at 72 hours, it was 1.17 based on four trials with 246 participants. All the trials were in favour of IVIg compared with corticosteroids. When IVIg was compared with anti-D immunoglobulin, the RR for the patients with platelet counts of  $20 \times 10^9/L$  or higher at 24 hours was 1.52. In patients receiving anti-D immunoglobulin, a reduction in hemoglobin was reported in two trials, but the difference was not statistically significant or not reported. In one trial comparing IVIg and close observation, IVIg resulted in statistically significant earlier improvements in platelet counts.

For chronic childhood ITP, IVIg was compared with corticosteroids in three RCTs. One study with 23 participants concluded that IVIg was superior for a short-term platelet response. The long-term improvement in platelet counts was more favourable with cyclical oral dexamethasone. The other two RCTs concluded that IVIg was not statistically significantly better than corticosteroids in improving platelet counts, reducing the number of severe bleeding episodes and days of severe bleeding, and deferring the removal of the spleen. When IVIg was compared with anti-D immunoglobulin in one trial, the proportion of patients with deferred removal of the spleen was similar in both groups.

Two trials compared IVIg with corticosteroids in adults with ITP. One study found no advantage of IVIg versus oral prednisone in the improvement of platelet counts, time to peak platelet count, and deferral of the removal of the spleen. In the other study, IVIg was superior to intravenous methylprednisolone in the short-term improvement of the decreased number of platelets, but it was associated with more severe adverse events that prolonged hospitalization.

Data of harm to patients could not be analyzed, because of the incomplete or lack of reporting in most of the trials.

### ***Clinical-effectiveness of intravenous immunoglobulin for chronic inflammatory demyelinating polyneuropathy***

#### **a) Methods**

The study selection criteria included all RCTs in patients with probable or definite CIDP of any age receiving any preparation or dosage regimen of IVIg compared with alternative doses or preparations of IVIg, corticosteroids, plasma exchange, extracorporeal immunoadsorption, other immunosuppressants, IVIg in combination with other immunomodulators, or placebo. Key clinical outcomes were change or durability of change in disability or impairment, change in electrophysiologic outcomes, change in quality of life, and adverse events.

#### **b) Results**

From 495 citations that were identified in the original search, 11 reports describing nine unique RCTs were included. Details of the included and excluded studies appear in the full report.<sup>26</sup> Three of the nine RCTs compared IVIg with active treatment (plasma exchange, extracorporeal immunoadsorption, or oral prednisolone). The other six RCTs were placebo-controlled. Most of the trials were of good quality.

In all the included studies, a disability or impairment scale was used to measure a primary outcome. No incremental benefit was observed with IVIg versus the active comparators in any trial. In one trial, a statistically significant improvement in grip strength (a secondary outcome) was seen when IVIg was compared with oral prednisolone at six weeks. Data from four placebo-controlled trials were included in a meta-analysis of change in disability scores. This resulted in a statistically significant treatment effect favouring IVIg. The pooled analysis of the proportion of those who responded to treatment, as defined by the investigators in each trial, resulted in a RR of 2.74, which also favoured IVIg. Among three of the six placebo-controlled trials, there was a statistically significant improvement in an electrophysiological outcome (for example, nerve conduction velocities or action potentials) with IVIg therapy.

## 4 Economic Review

For the economic reviews of ITP and CIDP, protocols were written beforehand and followed throughout the review process. A process similar to that followed for the clinical reviews was used to identify and select relevant economic literature. Details about search strategies and the systematic review process appear in the full reports.<sup>25,26</sup> All included economic studies were summarized qualitatively.

### **Methods**

Study selection criteria included economic evaluations of ITP or CIDP in which IVIg was a treatment comparator, and costs and effectiveness were measured.

### **Results**

From 293 citations on ITP that were identified in the original search, four primary economic evaluations were included. All studies were undertaken from a US perspective. One study compared IVIg with removal of the spleen in children with chronic ITP. Three compared IVIg with alternative treatments (prednisone, prednisolone, anti-D immunoglobulin) in children with acute ITP. No economic evaluations of IVIg for adult ITP were found.

From 330 citations on CIDP that were identified in the original search, one primary economic evaluation that reported patient level results was included. It was based on patients with CIDP who were participating in an international clinical trial and who were randomized to receive IVIg or oral prednisolone according to a crossover design. After adjusting for baseline costs, patients on IVIg had €3,439 higher costs than those on prednisolone. IVIg also resulted in greater utility gain over a six-week period when it was compared with prednisolone. The difference was 0.12, which the study authors claimed to be equivalent to 0.014 quality-adjusted life-years (QALYs). Based on the reported costs and effects, the cost per QALY was €245,643 (C\$388,110).

## 5 Economic Analyses

### ***Cost-effectiveness of intravenous immunoglobulin for idiopathic thrombocytopenia purpura***

#### **a) Methods**

Two primary cost-utility analyses were conducted for ITP. In the first analysis, the incremental cost per QALY was compared between treatments (IVIg, anti-D immunoglobulin, prednisone, methylprednisolone, observation) in hospitalized children (weight 20 kg) with acute ITP and platelet counts less than 20,000/ $\mu$ L. In a secondary analysis, the incremental cost per ICH avoided was examined. The structure of the model was based on that of the model by O'Brien et al.<sup>27</sup> with modifications.

The second analysis compared IVIg and prednisone in a hypothetical cohort of adult patients (age 35 years, weight 70 kg) with ITP and platelet counts of less than 20,000/ $\mu$ L. For both models, the perspective was of a publicly funded health care system, the time horizon was lifetime, and a 5% annual discount was applied to costs and effects. Probabilistic analysis was performed to assess uncertainty, and one-way sensitivity analysis was used to assess variability in the results. Details about the models and the clinical, cost, and utility input variables appear in the full report.<sup>25</sup>

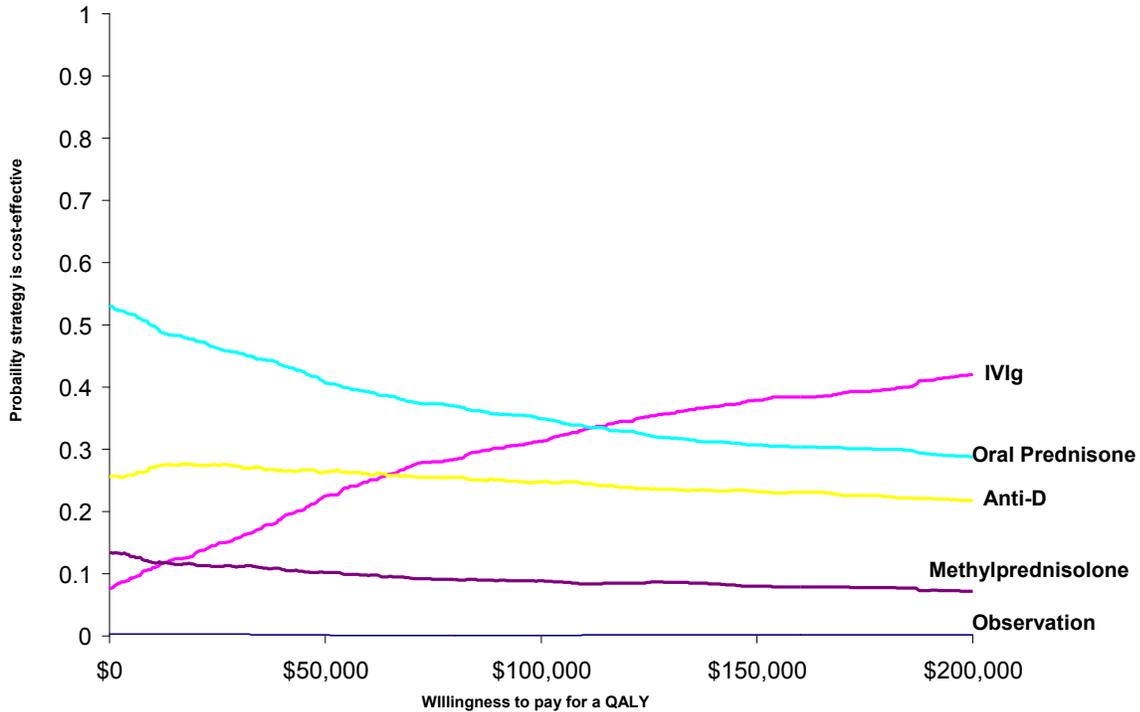
## b) Results

In acute childhood ITP, for the base-case analysis, total costs (treatment, hospital, and ICH costs) ranged from C\$1,844 (prednisone) to C\$2,820 (observation). Compared with anti-D immunoglobulin, IVIg was associated with an additional 0.0025 QALYs and an additional cost of C\$140 per patient, resulting in an incremental cost-effectiveness ratio (ICER) of C\$56,000 per QALY. (see Table 1) In the base-case analysis, it was assumed that there was one IVIg dose of 0.8 g/kg for a 20 kg patient. Among the alternatives (IVIg, anti-D, prednisone, methylprednisolone, observation), IVIg had the highest treatment costs and resulted in the largest number of lifetime QALYs. Compared with alternatives, IVIg has the highest probability of being cost-effective if society is willing to pay more than C\$112,000 per QALY. (see Figure 1) The results were sensitive to the probability of ICH on each day that the children had platelet counts of less than 20,000/ $\mu$ L, IVIg dosing regimen, and patient weight. In the secondary analysis, the number of expected ICHs ranged from 5.02 per 10,000 (IVIg) to 12.51 per 10,000 (observation). The incremental cost per ICH avoided, moving from prednisone to anti-D, was C\$732,789, and moving from anti-D to IVIg, C\$760,778.

Treatment	Treatment Costs	Hospital Costs	ICH Costs	Total Costs	QALYs	Incremental		
						Costs	QALYs	ICUR
Prednisone	\$1	\$1,790	\$53	\$1,844	17.6915	Reference	Reference	Reference
Methylprednisolone	\$189	\$1,729	\$51	\$1,969	17.6919	\$125	0.0004	Dominated
Anti-D	\$375	\$1,521	\$44	\$1,940	17.6933	\$96	0.0018	\$53,333
IVIg	\$947	\$1,100	\$32	\$2,080	17.6958	\$236	0.0043	\$56,000
Observation	\$0	\$2,739	\$81	\$2,820	17.6856	\$976	-0.0059	Dominated

ICH=intracranial hemorrhage; ICUR=incremental cost utility ratio; QALY=quality-adjusted life year.

**Figure 1: Cost-effectiveness acceptability curve**



IVIg=intravenous immunoglobulin; QALY=quality-adjusted life year

In chronic adult ITP, for the base-case analysis, IVIg that was compared with prednisone was associated with an additional 0.003 QALYs and an additional cost of C\$8,070 per patient, resulting in an ICER of C\$2.69 million per QALY. (see Table 2) The clinical literature showed that IVIg and prednisone had similar treatment response and relapse rates, leading to the small long-term difference in QALYs.

	Costs (in 2007 Canadian dollars)			QALY	ICER
	Treatment	Splenectomy	Total		
Prednisone	\$4	\$10,426	\$10,430	11.9385	
IVIg	\$8,287	\$10,213	\$18,500	11.9415	\$2,690,000

ICER=incremental cost-effectiveness ratio; IVIg=intravenous immunoglobulin; QALY=quality-adjusted life year.

**Cost-effectiveness of intravenous immunoglobulin for chronic inflammatory demyelinating polyneuropathy**

**c) Methods**

A cost-utility analysis was conducted comparing IVIg and oral corticosteroids in adult patients (54 years, weight 75 kg) with CIDP. The perspective was that of a publicly funded health care system, a five-year time horizon was assumed, and 5% annual discounts were applied to costs and effects. Probabilistic analysis was performed to assess uncertainty, and one-way sensitivity

analyses were used to assess variability of the results. Details about the model and model inputs appear in the full report.<sup>26</sup>

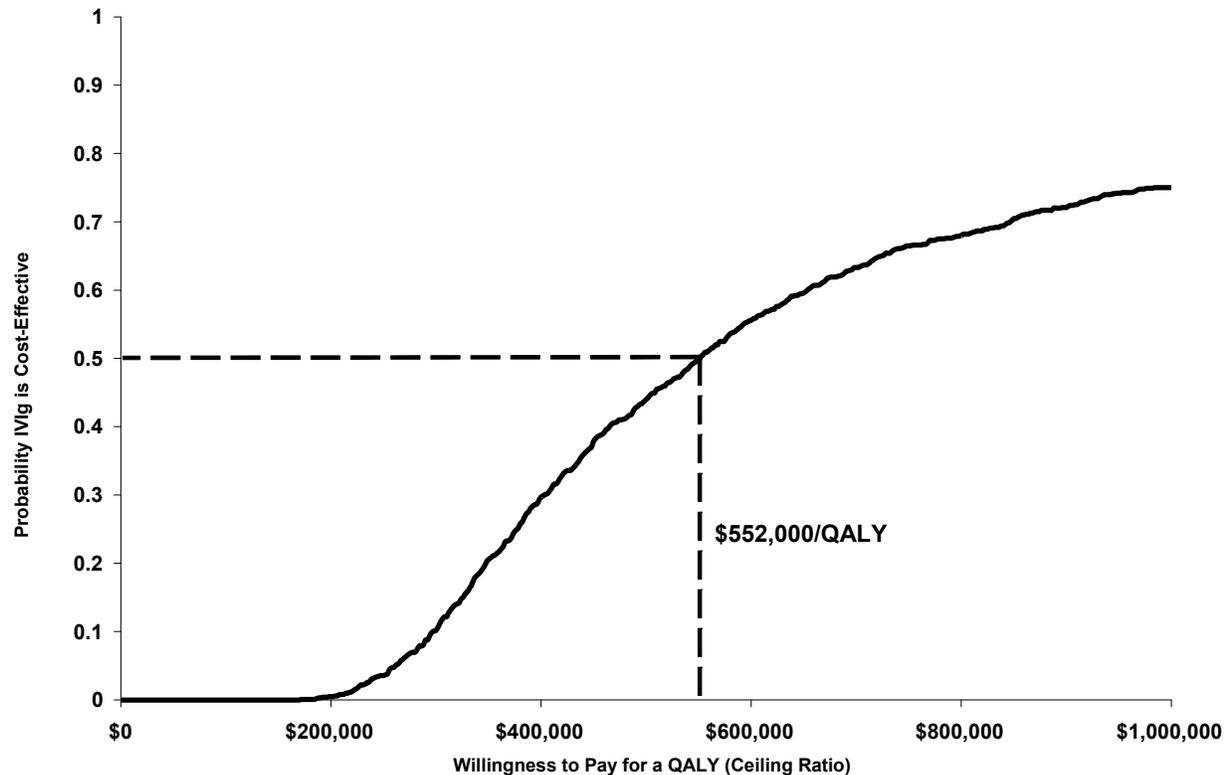
**d) Results**

The primary economic evaluation, taking into account the gain in utility from IVIg treatment and the disutility from adverse events, found that the IVIg arm had 0.187 more QALYs than the corticosteroid arm. The resulting incremental cost-utility ratio (ICUR) of IVIg compared with corticosteroids is C\$549,449 per QALY gained. (Table 3) The ICUR varied with patient weight from C\$262,260 (35 kg) to C\$694,933 (95 kg). The assumption that maintenance treatment with IVIg consists of 0.4 mg/kg doses every eight weeks instead of 1.0 mg/kg doses every three weeks resulted in a cost per QALY estimate of C\$125,241. The probabilistic sensitivity analysis found that at a willingness-to-pay threshold of C\$552,000 per QALY, the probability that IVIg is cost-effective is 50%. (see Figure 2)

<b>Table 3: Base-Case Cost-Effectiveness Analysis</b>					
	<b>Costs (\$)</b>	<b>QALYs</b>	<b>Incremental Costs (\$)</b>	<b>Incremental QALYs</b>	<b>ICUR (\$)</b>
Corticosteroids	2,196	3.783	reference	reference	reference
IVIg	104,943	3.970	102,747	0.187	549,449

ICUR = incremental cost-utility ratio; IVIg = intravenous immunoglobulin; QALYs = quality-adjusted life-years.

**Figure 2: Cost-Effectiveness Acceptability Curve**



IVIg = intravenous immunoglobulin; QALY = quality-adjusted life-year.

## 6 Limitations

Reliability of estimates of effectiveness are limited by small trials, of poor methodologic quality, and of short duration, and reporting IVIg efficacy based on surrogate outcomes with poor predictive value for clinical events.<sup>28</sup> There was also a lack or incomplete reporting of harms data by treatment group.

The economic analyses of ITP and CIDP are based on data from international sources. Therefore, they are limited by the lack of Canadian data. The economic analysis of acute childhood ITP is limited mainly by the lack of direct evidence that treatment with IVIg leads to fewer ICH events when compared with alternative therapies. Another limitation is that some clinicians may prescribe high-dose pulse dexamethasone, which was excluded from the model, instead of prednisone. For adult chronic ITP, the clinical evidence from head-to-head comparisons of IVIg and prednisone is sparse, and the ICERs were sensitive to the utilities that were associated with different health states of chronic ITP. The same utility for each health state was assumed in both treatments because of a lack of empirical evidence.

In the analysis of CIDP, the limitations are related to the assumptions that were made, including the extrapolation of the non-statistically significant utility gain from IVIg<sup>29</sup> over the five-year time horizon of the model and the reliance on this one source of utility gain from IVIg treatment. Other limitations are the reliance on one source to define the corticosteroid adverse events in the model, and because the perspective was that of a public health care payer, indirect costs were not included. Lastly, the analysis did not consider plasma exchange as a treatment comparator.

## 7 Health System Implications

Because of the lack of Canadian prevalence and incidence data, it was necessary to derive the numbers of Canadians with ITP or CIDP using international estimates. The estimated number of chronic adult and child ITP cases was 6,672, and the number of acute ITP cases was 963. The annual per-patient IVIg cost that was used for initial (acute) therapy was estimated to be C\$5,593 (adult) and C\$1,598 (child). The annual per-patient IVIg cost that was used for maintenance (chronic) therapy was C\$26,931 (adult) and C\$1,598 (child). If all patients with ITP in Canada were to receive IVIg therapy, the budgetary impact could be C\$192 million.

The number of prevalent CIDP cases ranged from 145 to 2,434, and the number of incident cases ranged from 13 to 243. The annual per-patient IVIg treatment cost was calculated to be C\$8,287 (acute) and C\$71,679 (chronic), assuming a cost for IVIg of C\$59.19/g for a 70 kg adult. Considering acute and chronic treatment and the number of patients with CIDP based on the similarity in demographic characteristics, the financial impact of IVIg therapy for all patients with CIDP in Canada could range from C\$10.6 million to C\$43.1 million.

Ethical, psychosocial, and legal issues regarding IVIg treatment include adverse events, product safety, standardization of use, costs, supply limitations, and the transmission of infectious agents through blood products.

## 8 Conclusions

The available evidence was systematically reviewed to examine the clinical- and cost-effectiveness of the use of IVIg by patients with ITP or CIDP, compared with other active treatments or observation and placebo. Three primary economic analyses were conducted to assess the cost-effectiveness of IVIg for patients with ITP or CIDP, and the budget impact of funding IVIg for these indications was estimated.

For acute ITP in children, IVIg (0.8 g to 1 g/kg per day over one to two days) was found to be more efficacious than corticosteroids in the early improvement of low platelet counts to counts of  $20 \times 10^9/L$  or higher. The role of IVIg in chronic childhood ITP could not be established because evidence from scant, poorly designed, and poorly reported RCTs could not be synthesized. There were insufficient data to determine if IVIg is superior to other interventions in the long-term management of adult ITP. There was insufficient evidence to identify any groups that may preferentially benefit from IVIg therapy.

In adult patients with profound decreases in platelet counts, the effect of IVIg on clinical outcomes remains indeterminate. Sparse evidence suggests that over the short term, IVIg may be more efficacious than corticosteroids in improving platelet counts, possibly at the risk of more serious adverse events. Until better data become available, the clinical impact of choosing IVIg instead of available alternatives in most situations remains uncertain.

Results from the two primary economic evaluations of the treatment of ITP show that the cost-effectiveness of IVIg may differ according to the patient population. The cost-effectiveness of IVIg was found to be more favourable in the childhood ITP population than in the chronic ITP adult population. The differences between the two cost-effectiveness model results should be considered given the potential impact of IVIg on health services in Canada. Based on published prevalence and incidence studies, the number of chronic adult cases of ITP and the associated maintenance costs were estimated to be larger than the number of acute childhood cases and the associated costs.

The economic evaluations are based on models that synthesize data from various sources. A possible next step that would help answer our research questions would be to conduct Canadian randomized trials that include the collection of patient level health resource utilization and utility data and compare the IVIg treatment options.

For patients with CIDP, IVIg was found to be statistically significantly superior to placebo in reducing impairment and disability. The overall clinical-effectiveness of IVIg was similar to that of corticosteroid and that of plasma exchange therapy. Therefore, in comparison with active comparators, it is unclear whether IVIg has a therapeutic advantage in the management of CIDP. The economic analysis of CIDP found that the ICUR of IVIg compared with corticosteroids (C\$549,449 per QALY gained) is higher than what might be viewed as a cost-effective use of health care resources.

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