Nova Scotia Health

NOVA SCOTIA PROVINCIAL BLOOD COORDINATING PROGRAM

Intravenous Immune Globulin (IVIG) Utilization in the Atlantic Provinces

Fiscal Year 2008/09

Prepared for the Atlantic Collaborative IVIG Utilization Working Group

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Your Health Matters

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1 Executive Summary

This report provides an overview of the distribution and utilization of intravenous immunoglobulin (IVIG) and subcutaneous immunoglobulin (SCIG) in the Atlantic Provinces for the 2008/09 fiscal year.

Canada continues to have the highest per capita IVIG distribution when compared to six other developed countries using IVIG. Over the past eight years IVIG distribution in Canada has increased by 7 to 10% each year, but only increased by 5 % in 2008/09. In the 2008/09 fiscal year, New Brunswick increased per capita distribution of IVIG by 10 g/1,000 population to reach 102 g/1000 population. All other provinces showed decreases with Nova Scotia dropping from 113 g/1000 population in 2007/08 to 111 g/1000 population in 2008/09, and PEI falling from 110 to 100 g/1000 population. Newfoundland and Labrador decreased the most but remained the highest, falling from 141 g/1000 population in 2007/08 to 130 g/1000 population in 2008/09. The overall Atlantic distribution held steady from 2007/08 at 112 g/1000 population.

All Atlantic Provinces, with the exception of Nova Scotia, showed increases in per capita use of IVIG for unlabeled, not indicated (ULN) indications. Newfoundland & Labrador was the highest in 2008/09, having gone from 17 g/1000 population in 2007/08 to 18 g/1000 population. PEI went from 6 g/1000 population in 2007/08 to 14 g/1000 population and New Brunswick increased from 5 to 8 g/1000 population. Nova Scotia decreased its per capita use for ULN, going from 5 to 3 g/1000 population. The overall Atlantic use for ULN indications remained at 8 g/1000 population for 2007/08 and 2008/09. All provinces, with the exception of Nova Scotia, showed increases in the percent of IVIG used for ULN indications. All Atlantic Provinces combined saw 8.2 % of its IVIG used for ULN indications—an increase from 7.6 % in the previous year. The total estimated cost of ULN use in the Atlantic Provinces in 2008/09 was just over $1.1 million. This is up from the estimated $800,000 in 2007/08.

The increase in ULN use that occurred from 2006/07 to 2007/08, especially in Newfoundland and Labrador, is due in part to a change in the appropriateness designation for one indication. Based on recommendations by the National Advisory Committee on Blood and Blood Products, the use of IVIG for bone marrow transplant was converted from “unlabeled, indicated” to “unlabeled, not indicated.”

The proportion of IVIG used in each of the major specialties and the major indications for the use of IVIG remains largely unchanged; however, among the provinces and among the major indications in hematology and neurology, there continues to be wide variation in the number of doses administered higher or more frequent than recommended. For the most common indication in the Atlantic provinces, chronic inflammatory demyelinating polyradiculoneuropathy, New Brunswick had the highest proportion of doses that were higher or more frequent than recommended at 35%., Nova Scotia had 26%. Newfoundland and Labrador 18 % and PEI had all doses within the recommended guidelines. In contrast, all provinces had all doses within recommended guidelines for

multifocal motor neuropathy, except for New Brunswick where 40 percent of doses were too high or too frequent.

In 2008/09 all provinces showed a drop in the proportion of immune deficiency patients having IgG levels monitored. Nova Scotia went from 88 % to 70 %, Newfoundland and Labrador went from 80 % to 69 % and New Brunswick went from 68 % to 46 %. PEI was at 50 % in 2008/09 but this was the first year PEI participated in reporting IgG levels. The decrease seen in the provinces may be related to an actual reduction or confusion over the new confirmation of IgG activity portion of the IVIG utilization data collection tool. Of patients who had IgG levels monitored, there was an improvement in the proportion that had trough IgG levels in the target range of 5–10 g/L. 100 % of patients in Prince Edward Island had their IgG levels in the target range. New Brunswick was most improved, going from 54 % to 62 % of patients in the target range. Nova Scotia showed only slight improvement going from 63 % to 64 %, and Newfoundland and Labrador went from 53 % to 58 %.

All Atlantic Provinces, with the exception of Nova Scotia, showed an increase in reported discards. Nova Scotia reported 78 g of discarded IVIG—down from 225 g in 2007/08. Prince Edward Island reported 23 g of IVIG discarded which is an increase from zero discards in 2007/08. Newfoundland & Labrador increased from 205 g to 288 g and New Brunswick increased from 0 g to 150 g. In New Brunswick, most of the increase derives from an increase in the number of facilities reporting discard information in 2008/09. The total 538 g reported as discarded carries with it an associated cost of $31,000.

In 2008, the Atlantic Collaborative supported the addition of SCIG to its utilization management efforts and utilization data collection began in late 2008. Only 595 g were distributed in the Atlantic Provinces in fiscal year 2008/09. Only three patients were using it (two in Nova Scotia and one in Newfoundland and Labrador) and only began close to the end of the fiscal year. All use was for the treatment of primary immune deficiencies and was within recommended dosing guidelines. No discards of SCIG were reported in any province.

An Atlantic SCIG Working Group was convened to develop guidelines for the implementation of SCIG home infusion programs in hospitals in the Atlantic Provinces. The guidelines were completed in the summer of 2009 and after endorsement by the Atlantic Collaborative IVIG Utilization Working Group, will be disseminated for pilot use for a one year period. Feedback collected during the pilot period will be incorporated into a more formal version for publication in late 2010.

There are several challenges in the current utilization management of IVIG. The use of IVIG for ULN indications continues to increase, some dosing remains outside recommended guidelines for many of the most common indications, IgG levels are not monitored for all patients with immune deficiencies and, if they are, they are not always in the target range. Reported wastage continues to rise although possibly due to an increase in reporting in 2008/09. As well, all provinces continue to have small numbers of cases submitted where the indication is not specific enough to classify into the appropriateness categories and is labeled “insufficient information.”

Next steps for the Atlantic Collaborative are focused on the above mentioned challenges. To address ULN use, a letter will be developed to send to physicians who submit orders for ULN indications, reminding them of the lack of evidence for the use of IVIG. Moving forward on implementing the IVIG request approval process should address issues of dosing in the most common indications. To improve IgG level monitoring, provincial representatives will be given a summary of the cases in which the IgG levels are out of the target range. This, along with monitoring and dose-adjustment information should be used to ensure ordering physicians are aware of the proper protocols for monitoring IgG levels. To improve discards, the NSPBCP will provide each province with a summary of the reasons and locations of all discarded IVIG so representatives can communicate with facilities to discuss discard reduction strategies. To decrease the number of cases classified as "insufficient information" the NSPBCP will provide a guide to data submitters to help them in the acquisition of the additional detail required to prevent cases from being assigned to the "insufficient information" category. SCIG will be monitored closely for any emerging trends that may require utilization management strategies.

2 Introduction

This report is a summary of the utilization of IVIG in the Atlantic Provinces for the fiscal year 2008/09, although most tables and graphs also show the trend over the last 2 or 3 years. The purpose of the report is to illustrate the trends in the amounts of IVIG that are used and to identify areas of utilization that require improvement, especially with respect to appropriateness of indications, dosing, and discards. It also addresses issues of data collection.

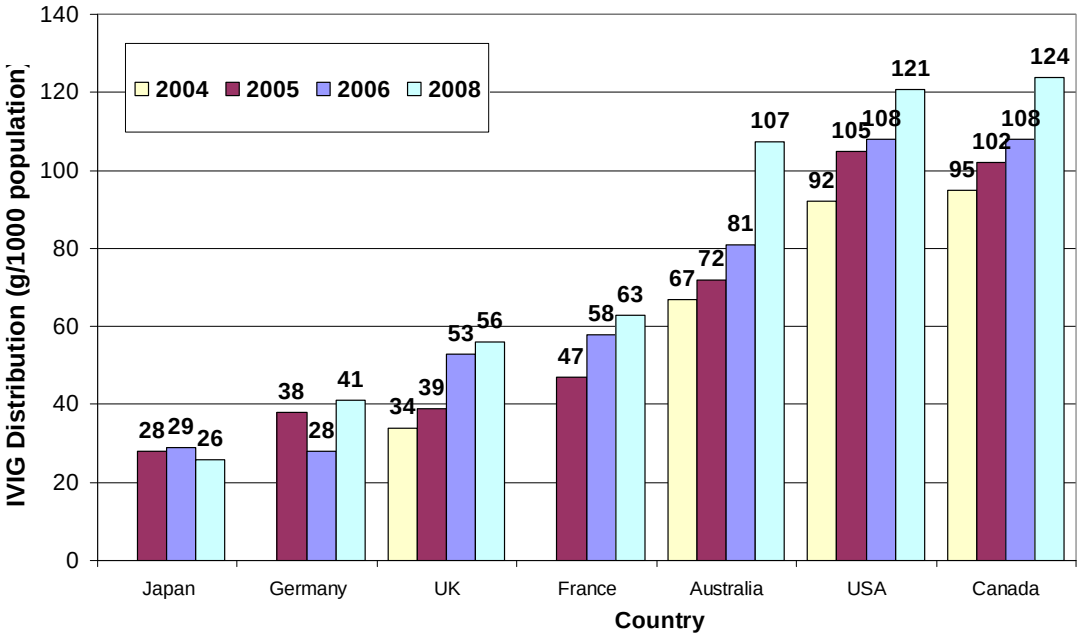
One change from previous reports is the introduction of a comparison with the rest of Canada. Previous reports looked at the Canadian average, but this approach retains the influence of the trends in the Atlantic Provinces. In this report the Atlantic Provinces and the rest of Canada are examined separately.

New to the 2008/09 report is a section on SCIG. The 2008/09 fiscal year is the first time period this new product has been available. Utilization data was collected by adding extra fields to the existing IVIG data collection tools.

3 International and National Perspective

Figure 1 shows an international comparison of yearly per capita IVIG distribution. The graph shows Canada to have the highest use in 2008 and on par with the USA in previous years. The USA and Canada have been using two to three times as much as other countries such as France, the UK, Germany, and Japan.

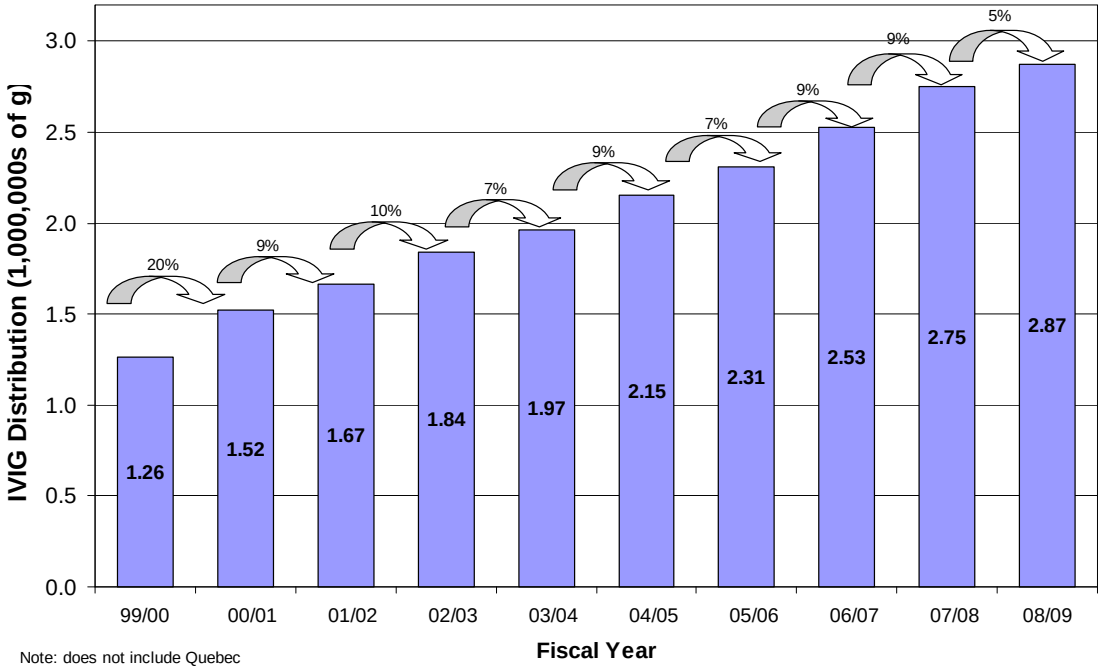
Figure 1: International Comparison of Yearly IVIG Distribution (2004-2008)



Source: International Blood/Plasma News; Australia National Blood Authority; Note: 2007 data not available.

Figure 2 shows the annual distribution of IVIG in Canada since the turn of the millennium. The distribution regularly increases between 7–10 percent each year. The exception is the 2008/09 fiscal year which shows an increase of only 5 percent.

Figure 2: IVIG Distribution in Canada



4 Provincial Distribution Trends

Canadian Blood Services (CBS) distributes IVIG to facilities in all provinces except Quebec. This section summarizes the total amounts of IVIG shipped to facilities in the Atlantic provinces in recent fiscal years. It should be noted that this is not the same as the amount of IVIG that is *utilized*, but it can be used as a very good estimate, especially when monitoring for year-to-year trends.

Table 1 shows the total grams and the cost of IVIG distributed by CBS to each of the Atlantic provinces for fiscal years 2004/05 to 2008/09. In 2008/09 most provinces have shown a decrease in grams and cost from the previous year.

Table 1: Total Grams and Cost* of IVIG Distributed to the Atlantic Provinces by Fiscal Year

Fiscal Year	Newfoundland & Labrador		New Brunswick		Prince Edward Island		Nova Scotia	
	Grams	Dollars	Grams	Dollars	Grams	Dollars	Grams	Dollars
2004/05	59,328	$3,681,747	53,005	$3,263,330	5,650	$344,400	67,338	$4,140,632
2005/06	61,660	$3,639,135	62,828	$3,684,521	7,550	$442,823	65,875	$3,878,469
2006/07	67,800	$3,740,847	64,055	$3,540,739	11,010	$597,763	88,108	$4,867,830
2007/08	71,407	$4,065,703	68,370	$3,819,307	15,235	$821,456	105,479	$5,602,758
2008/09	66,179	$3,782,587	76,001	$4,350,852	13,995	$814,328	104,502	$5,952,086

* Costs shown in this table reflect the actual amounts paid by each province and are not estimates.

Figure 3 shows a per capita comparison of the amount of IVIG distributed in each of the Atlantic provinces as well as the amount distributed throughout all of the Atlantic Provinces and the rest of Canada. In 2008/09, with most Atlantic provinces showing decreases in per capita distribution, the Atlantic provinces combined show no change from the previous year while the rest of Canada shows an increase.

Figure 3: Per Capita IVIG Distribution in the Atlantic Provinces and the Rest of Canada

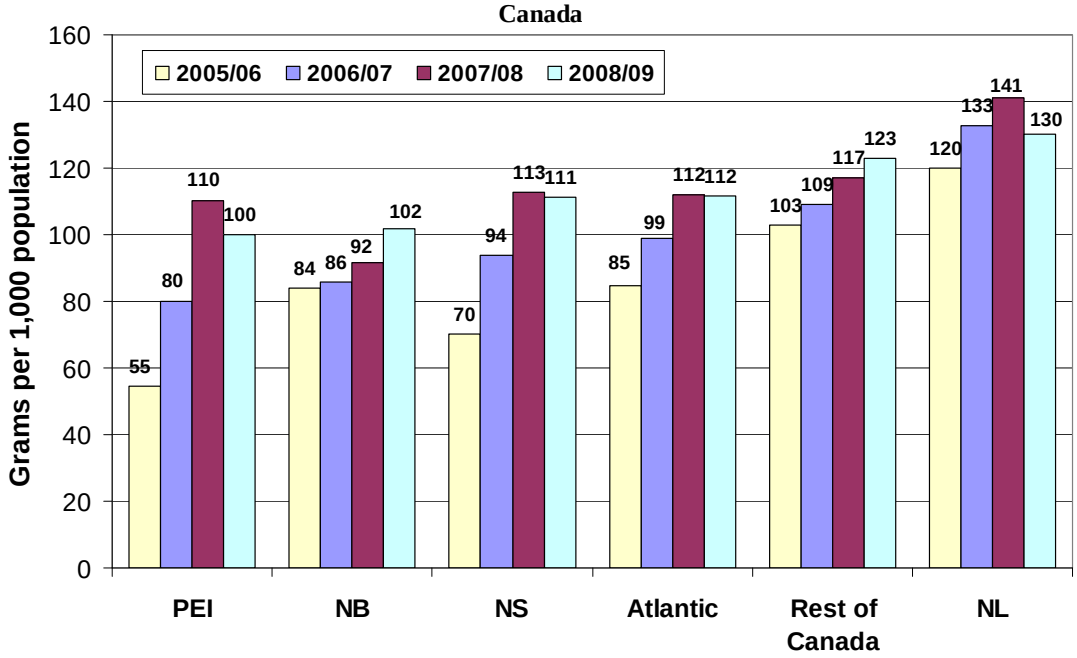
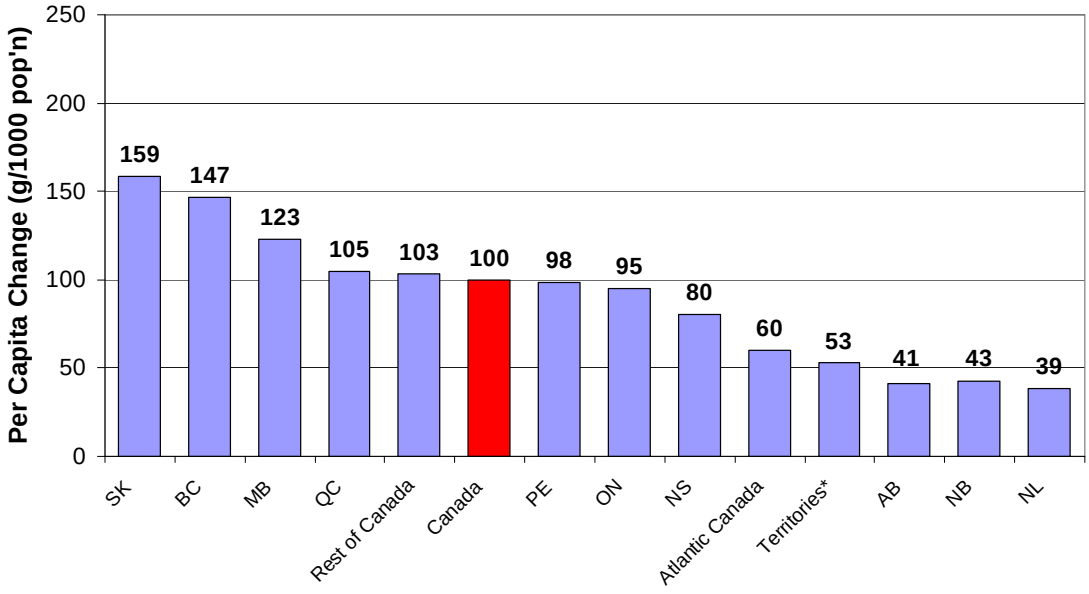


Figure 4 shows a comparison of the provinces and territories in net annual per capita change in IVIG distribution since 2002/03. This is essentially a net summary of all the annual increases and decreases that have occurred over this time period.

Figure 4: Cumulative Annual per Capita IVIG Distribution Changes Between Fiscal Years 2003/04 and 2008/09



* Includes Northwest Territories, Yukon Territories, and Nunavut
Source: Distribution data from CBS; Population data from Institut de la Statistique du Québec and Statistics Canada

5 Utilization Data

The information presented in the remainder of this report is derived from the IVIG utilization database housed at the Nova Scotia Provincial Blood Coordinating Program (NSPBCP). The following sections provide information regarding the data used to create the graphs and tables and should be considered in the interpretation of the utilization information in this report.

5.1 Data Collection

The population of reference for this report is all patients who received doses of IVIG for any indication. Percentage capture of distribution data for the Atlantic Provinces during the time period of this report was 93 percent. This is based on the amount of IVIG reported as *utilized* (242,296 g) compared to the total amount of IVIG *distributed* (261,272 g). This is an improvement from 2007/08 where the percent capture was only 84 percent. The high percent capture numbers indicate the utilization data presented in this report provide a good picture of the actual overall utilization.

Percent capture by province is shown in Table 2. The table also shows the proportion of facilities that currently report IVIG data. 2008/09 was the first year Newfoundland and Labrador had 100 percent of facilities reporting IVIG utilization data. This should be noted when interpreting trends in utilization in that province.

Table 2: Percent Capture for Each Province

Province	Percent Capture	Proportion of Facilities Reporting
Nova Scotia	89.3%	100%
New Brunswick	93.0%	100%
Prince Edward Island	99.1%	100%
Newfoundland and Labrador	97.3%	100%

In previous years, all reporting facilities submitted basic utilization information, but not all facilities submitted all extra data elements such as IgG levels, and discards. In 2008/09 all facilities started reporting all extra data elements. The data coverage for these fields is addressed in the corresponding sections. ITP clinical criteria data was dropped from data collection in 2008/09 as it was not providing sufficient information to assess appropriate use.

5.2 Data Quality

The following list describes relevant data quality activities:

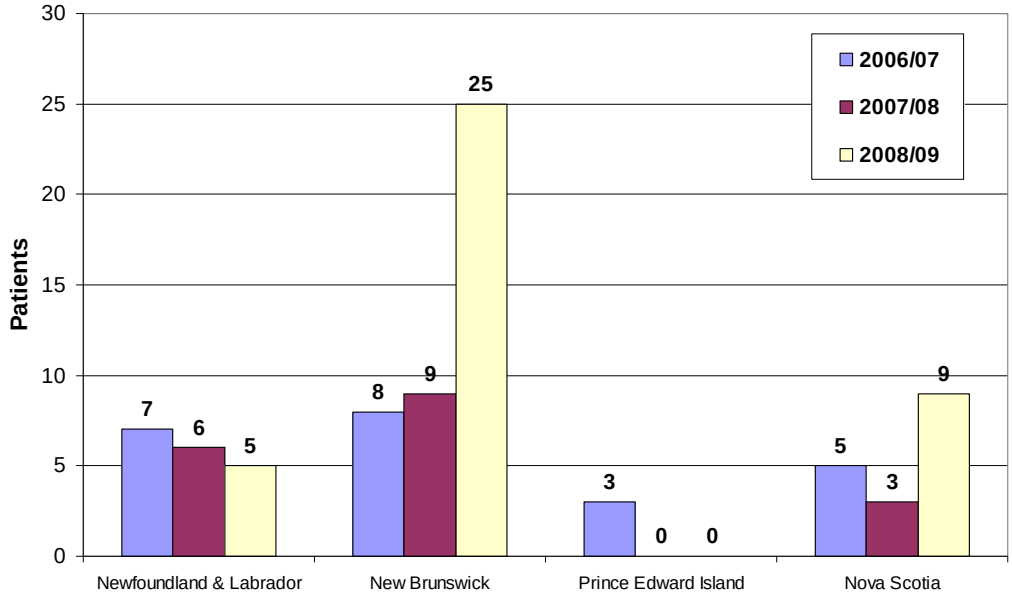
- The NSPBCP reviews all submitted data for questionable fields, inconsistencies, and incompleteness. Most of these checks are now completed using automated integrity queries. Any inconsistencies discovered by the queries are investigated and resolved.
- This report includes data received by the NSPBCP before September 4, 2009. Corrections, revisions, or additions received after this date are added to the database, but are not included as part of this report. A version of the database used in the data analyses for this report has been set aside to allow for reproduction of the information contained in the graphs and figures; however, future data analyses on the same time period using the main database may show minor differences due to the inclusion of these updates.
- New for 2008/09 is the introduction of a confirmation of activity component to the data collection tool. Data submitters are now asked to confirm whether or not there was any activity at their facility during the time period covered in the data submission. This was specific to IVIG and SCIG use and discards and IgG levels. This helps data analysts distinguish between no activity and missing data which would otherwise have the same appearance in the database.

5.3 Insufficient Information

After IVIG utilization data is received by the NSPBCP, each indication is assigned to an appropriateness category. If the names of the submitted indications are not specific enough for categorization (e.g., a symptom rather than a diagnosis or an admitting diagnosis) they are assigned to the "insufficient information" category. As much as possible, staff at the NSPBCP follow up with data submitters to try to obtain more detailed information, but despite these efforts, the required information is not always available.

Figure 5 shows a summary of the numbers of cases that are categorized as “insufficient information” for the 2006/07 to 2008/09 fiscal years. The increase in New Brunswick in fiscal year 2008/09 is largely due to cases reported as “thrombocytopenia.”

Figure 5: Counts of Cases Categorized as "Insufficient Information" in the Atlantic Provinces for Recent Fiscal Years



To present a true picture of the use of IVIG, it is important to minimize the number of cases categorized as “insufficient information.” This will be done by distributing to all data submitters a list of the types of indications that would be considered “insufficient information” accompanied by a guide to the additional detail that is required for each. Data submitters can then use this guide to acquire the required information for each submission.

Recommendation: It is recommended that the NSPBCP provide a guide to data submitters to help them in the acquisition of the additional detail required to prevent cases from being assigned to the “insufficient information” category.

6 Specialties and Indications

When IVIG was first introduced in the early 1980s, it was used exclusively for immune deficiencies. Since that time the number of indications for its use has expanded across a wide range of specialties. Figure 6 shows the relative proportion of IVIG used in each of the major specialties in which IVIG is used. Note in this summary that specialty is based on the categorization of the indications and does not necessarily reflect the specialty of the ordering physicians.

There were no major changes from 2007/08 to 2008/09 with each of the major specialties retaining their overall rank; however, neurology and immunology each saw small increases in utilization, while hematology, rheumatology and dermatology each saw small decreases.

Figure 6: Proportion of IVIG Use by Specialty in the Atlantic Provinces for Recent Fiscal Years

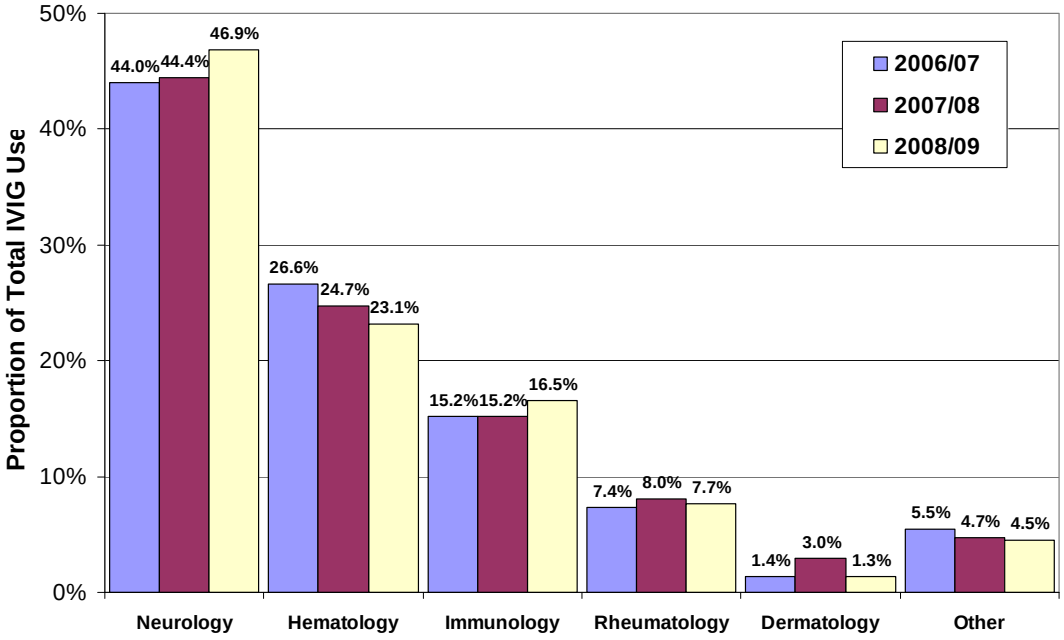
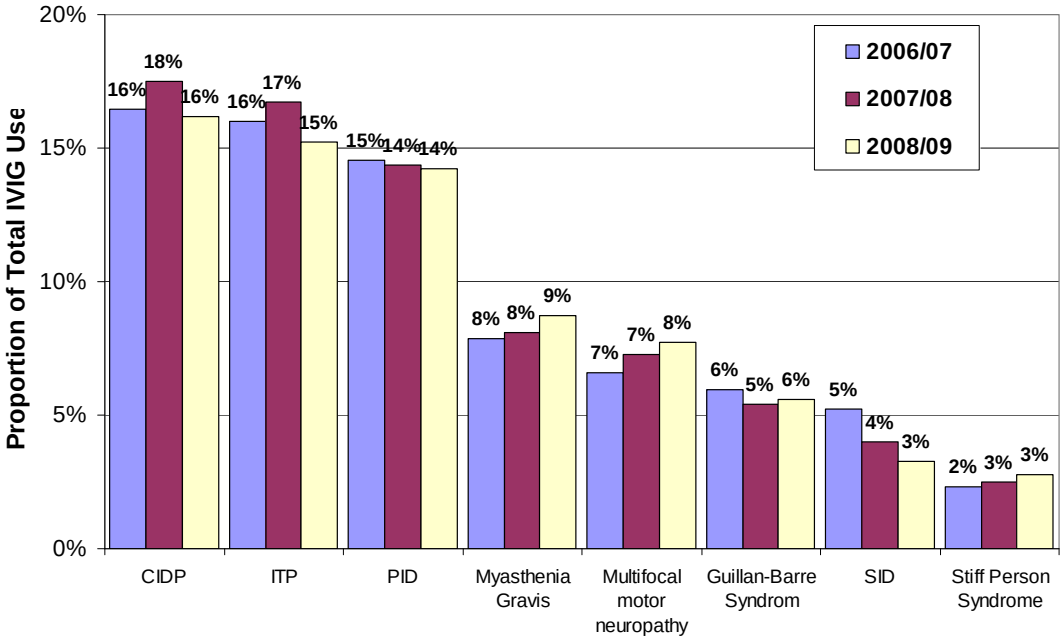


Figure 7 shows the relative proportion of total IVIG used in each of the most common indications. Again, there are only minor fluctuations and each major indication maintained its rank from 2007/08.

Figure 7: Proportion of IVIG Use by Indication in the Atlantic Provinces for Recent Fiscal Years



Graphs showing provincial-level per capita IVIG utilization for each of the indications shown in Figure 7 can be found in Appendix A.

7 Appropriateness of Use

7.1 Appropriateness of Indications

When IVIG utilization data is received by the NSPBCP the indications for the use of IVIG are categorized based on the appropriateness. The following describes the categories used:

- **L** (Labeled): the manufacturer can advertise the use of IVIG for these conditions
- **ULI** (Unlabeled, Indicated): the manufacturer cannot advertise the use of IVIG for these conditions, but there is some evidence to support its use
- **ULN** (Unlabeled, Not Indicated): there is no evidence to support the use of IVIG or evidence exists that shows it to be ineffective
- **Insufficient Information**: the NSPBCP was unable to obtain sufficient information that would lead to a definitive category assignment. In most cases the indication provided is only a symptom or overly general diagnosis rather than the specific indication for the use of IVIG. This category is addressed in the Data Collection section of this report.

Figure 8 shows a summary of the per capita grams of IVIG used for each of the appropriateness categories. This shows all Atlantic Provinces, except Nova Scotia, have increased their per capita use of IVIG for ULN indications from 2007/08 to 2008/09.

Figure 8: Appropriateness of IVIg Use in the Atlantic Provinces

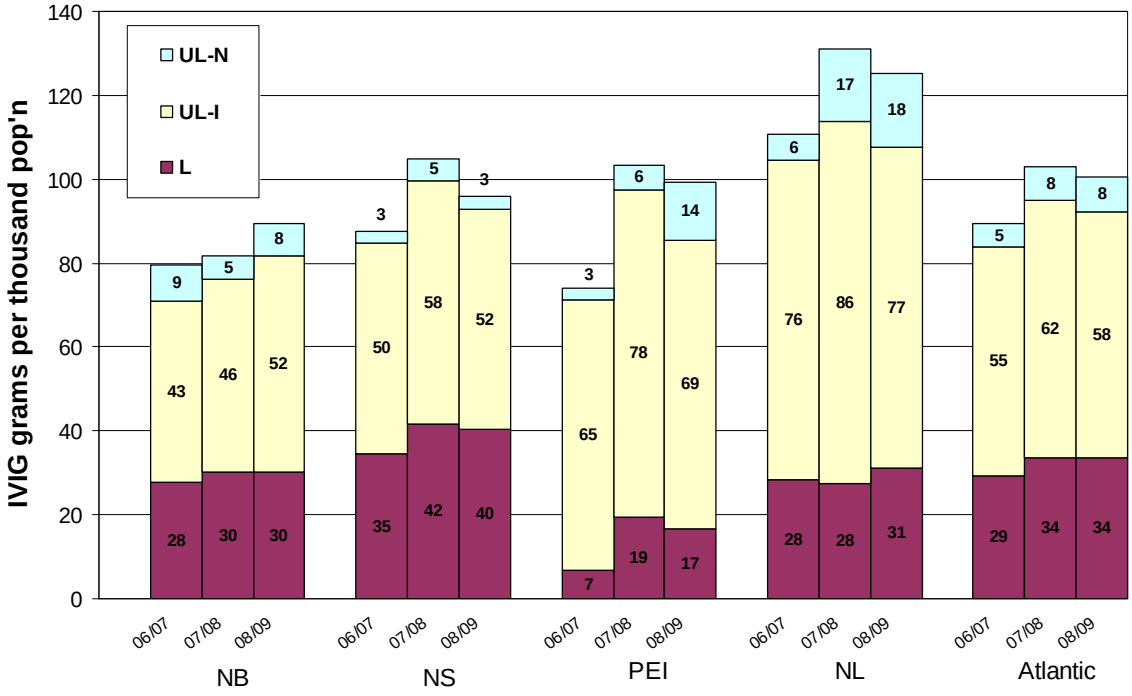
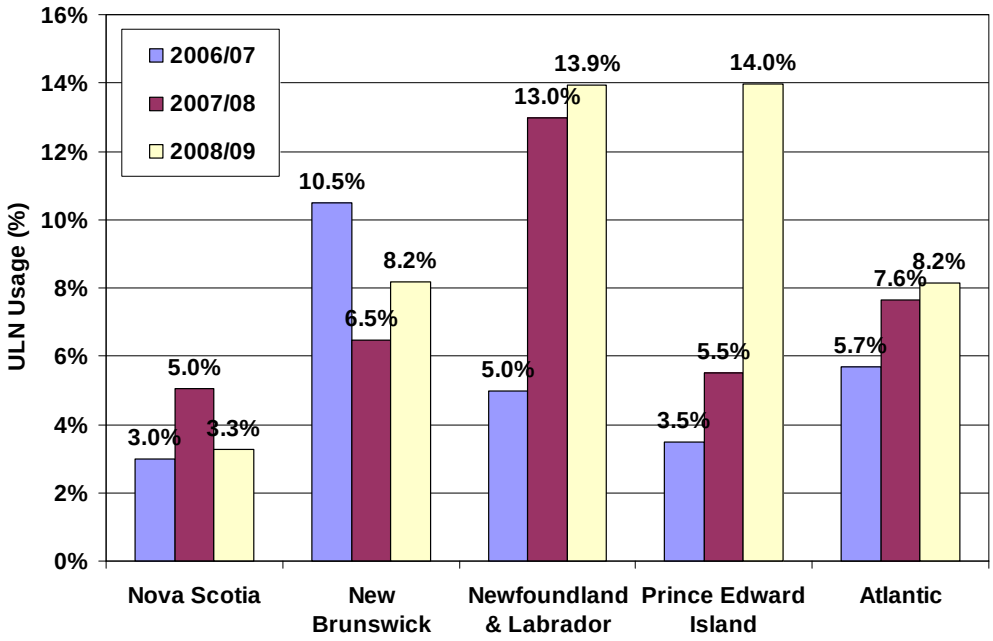


Figure 9 shows the proportion of IVIG for ULN indications in the Atlantic Provinces. The trend is similar to that shown in Figure 8 in that all provinces, with the exception of Nova Scotia, have shown an increase in the proportion of ULN use in 2008/09.

In 2009, the Ontario Regional Blood Coordinating Network released a report on the utilization of IVIG in Ontario, entitled, "Intravenous Immune Globulin (IVIG) Utilization Audit." Based on a three-month audit of IVIG use in 25 facilities in 2007, they found 10.5 % of the total IVIG used was for "unlabeled, not indicated" indications. Assuming this to be comparable to the ULN category used in the present report, the Atlantic region showed a lower rate of 8.2 % in 2008/09.

Figure 9: Proportion of IVIG Use for ULN Indications



The top five ULN indications (with total grams shown in parentheses) in 2008/09 in the Atlantic Provinces combined were:

1. Allogeneic stem cell or bone marrow transplantation (3,075 g)
2. Transverse myelitis (2,405 g)
3. Asthma (2,132 g)
4. Recurrent demyelination of optic nerve (1,650 g)
5. Leukopenia (1,096 g)

In April of 2007, the National Advisory Committee on Blood and Blood Products published guidelines for the use of IVIG in neurological and hematological conditions in the journal, *Transfusion Medicine Reviews*. In these guidelines, IVIG is not recommended for routine use in hematopoietic stem cell transplantation (HSCT).

However, prior to the release of this publication it was considered to be an indication for the use of IVIG. As a result, HSCT (primarily labeled as "allogeneic stem cell or bone marrow transplantation" in the Atlantic IVIG Utilization Database), was included in counts of appropriate indications (as ULI) up to the 2006/07 fiscal year, but was moved to the ULN category for 2007/08 and onward. This explains much of the increase seen in ULN IVIG use after 2006/07, especially in Newfoundland and Labrador.

Table 3 shows a summary of the estimated cost of IVIG used for ULN indications in each of the Atlantic Provinces. In 2008/09, all provinces, with the exception of Nova Scotia, have shown increases. In the 2008/09 fiscal year, the estimated total cost of ULN IVIG use in all Atlantic Provinces combined was just over $1.1 million. This is up from $800,000 in 2007/08.

Table 3: Estimated Cost* of ULN IVIG Use in the Atlantic Provinces in Recent Fiscal Years

Fiscal Year	Newfoundland and Labrador	New Brunswick	Prince Edward Island	Nova Scotia
2005/06	$128,324	$235,471	$14,862	$61,161
2006/07	$167,765	$365,795	$21,149	$140,842
2007/08	$500,093	$230,355	$44,871	$284,542
2008/09	$513,097	$329,699	$110,890	$174,950

* Estimated cost is calculated by multiplying the total grams by an average price per gram of $57.16

It is important to minimize the use of IVIG for ULN indications. One way to do this is through written communications with prescribing physicians. It is recommended that each time a blood bank receives an order for IVIG for a ULN indication, staff in the blood bank will send a letter to the ordering physician. The letter will state the absence of literature supporting the use of IVIG for the given indication, will ask if the ordering physician has evidence to support the use if IVIG, and will ask about patient outcome. All orders will still be filled. The NSPBCP will develop a form letter that may be used in this communication. A list of ULN indications will be approved by clinical experts in the relevant specialties and will be provided to blood banks.

Recommendation: it is recommended that a letter be sent to ordering physicians when an order for a ULN indication is received by the blood bank.

7.2 Dosing

Even if an indication is classified as "labeled" or "unlabelled, indicated" there are other factors to consider such as clinical criteria and proper dosing. Data on clinical criteria are not collected, but enough information is collected on patient doses to make an assessment as to whether or not the dosing guidelines are being followed.

Table 4 provides an overview of the percent of doses that were either too high or too frequent for some of the top indications. The assessment was based on the guidelines

adopted for the common request approval process in the Atlantic Provinces. The source for these was the 2007 National Advisory Committee on Blood and Blood Products guidelines for hematology and neurology. In completing the analysis, it could be seen that many variations in dosing exist. For consistency, a dosing pattern was considered appropriate if the total amount used in a given time period (usually four weeks) was within the recommended amount, even if the actual frequency of administration differed somewhat from the guidelines. In other words, weekly, biweekly, and monthly dosing regimes were all considered appropriate if the total amount in a four-week period was in line with the guidelines. Keep in mind that this review does not take into account any clinical criteria—it only compares the reported dosing to dosing guidelines.

Table 4: Percent of Doses Administered Higher or More Frequent than Recommended for Selected Indications

Indication	NL			NB			PE			NS		
	06/07	07/08	08/09	06/07	07/08	08/09	06/07	07/08	08/09	06/07	07/08	08/09
CIDP*	0	1	18	6	11	35	16	0	0	19	33	26
Myasthenia Gravis	0	0	4	10	7	7	0	0	**	7	2	19
Guillain-Barré Syndrome	16	0	41	23	36	57	65	69	63	10	10	12
Multifocal Motor Neuropathy	0	9	0	48	50	40	58	0	0	0	0	0
Multiple Sclerosis	33	0	0	0	29	0	56	**	**	68	54	31
Stiff Person Syndrome	0	13	0	**	0	78	**	**	**	0	2	0
ITP	35	17	7	18	15	24	39	25	14	26	33	14
Secondary Immuno-Deficiency	13	19	20	6	9	6	0	0	0	49	11	32
Primary Immuno-Deficiency	14	16	11	7	11	15	**	0	0	36	24	28

* chronic inflammatory demyelinating polyradiculoneuropathy
** IVIG was not used for this indication in the given time period.

From Table 4 it can be seen that in some cases there were many doses that varied from what is recommended in the guidelines and there are wide variations among the provinces.

Further investigation was done with regard to dosing regimens for the treatment of ITP in the 2007/08 fiscal year. This showed a large proportion of the doses that were too high or too frequent were associated with chronic treatment regimens (56 % in Newfoundland & Labrador, 86 % in New Brunswick, 63 % in PEI, and 93 % in Nova Scotia). Details of this analysis can be found in Appendix B.

Efforts should be made to reduce the amount of improper dosing. The IVIG request approval process already planned for implementation should address this by providing dosing guidelines at the time of ordering (provided on the back of the pre-printed IVIG order form) and through a request review by local blood banks. A repeat of this analysis after the request approval process has been implemented will provide an indication of its effectiveness in reducing inappropriate dosing.

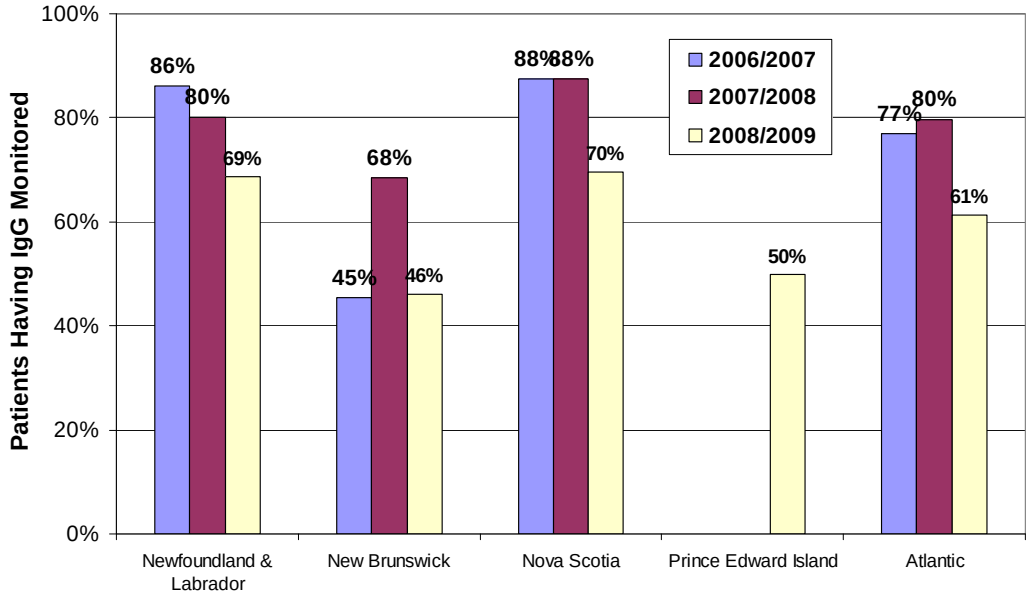
A pilot request approval process has been implemented in a single facility long enough to complete a preliminary assessment of its effectiveness. Doses for the indications shown in Table 4 that were higher or more frequent than recommended were counted for eight-month periods prior to and following the implementation. In the period prior to the implementation, seven percent of doses were found to be higher or more frequent than recommended. In the period following the implementation, *all* doses were found to be within the recommended guidelines. This is a strong indication that broader implementation of the request approval process will have a very positive impact on appropriateness of dosing for the most common indications.

Recommendation: Provinces should proceed with plans to implement the IVIG request approval process.

7.3 IgG Levels for Immune Deficiencies

When patients are receiving IVIG for the treatment of immune deficiencies it is recommended serum IgG levels be measured on a regular basis and the dose of IVIG be adjusted to keep the IgG level above 5 g/L. Figure 10 shows the proportion of patients who were on IVIG for immune deficiencies who had their IgG levels monitored. The frequency of monitoring cannot be inferred from this graph.

Figure 10: Proportion of Patients with Primary or Secondary Immune Deficiency who had IgG Levels Monitored



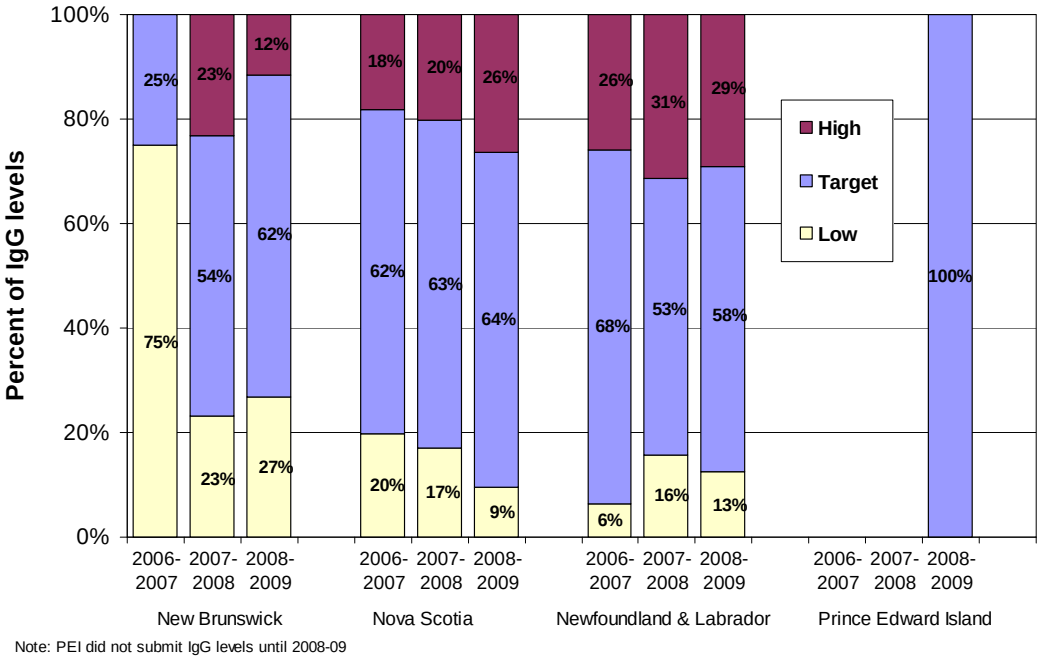
Note: PEI did not report IgG levels until 08/09

From Figure 10, it can be seen that a high proportion of patients with immune deficiencies were having their IgG levels monitored, but there was quite a drop in 2008/09. This may be related to data submitters incorrect use of the new IgG confirmation of activity portion of the data collection tool (checking off that there was no IgG level activity when actually IgG levels were being done but not reported) or it may actually be due to fewer patients having IgG levels done or a combination of the two.

Figure 11 illustrates the proportions of patients whose most recent IgG levels were within the target range of between 5 and 10 g/L. This is indicated by the size of the middle section of each bar. The top and bottom sections indicate the proportions of patients whose most recent IgG levels were above and below the target range respectively. This graph only includes the most recent IgG level within each given time period. This is to reduce the influence of initially high or low IgG levels that may have since been brought into the target range using dose adjustments.

It can be seen that a large proportion of IgG levels are within the desired range and in 2008/09 there are more IgG levels in the desired range than in 2007/08. But in all provinces with the exception of New Brunswick, there are still patients with IgG levels above the target range. Further analysis shows that in Newfoundland & Labrador and New Brunswick patients aged greater than 16 years account for all instances of IgG levels above the target range. In Nova Scotia, about half of the patients with IgG levels above the target range are less than or equal to 16 years old. Appendix C shows a breakdown of IgG level ranges by age group (pediatrics vs. adults).

Figure 11: IgG Level Ranges



Note: PEI did not submit IgG levels until 2008-09

Efforts should be made to increase the proportion of IgG levels in the target range. This can be done by providing provincial representatives with a summary of the cases in which the IgG levels are out of the target range. This will include facility, anonymous

physician code, and the specific IgG levels. Each province can then use the information to follow up with the physicians. To assist with this, the NSPBCP will provide guidelines IgG level monitoring based on the National Advisory Committee on Blood and Blood Products guidelines for the use of IVIG in immunology—expected to be published in early 2010.

Recommendation: It is recommended that provincial representatives be given a summary of the cases in which the IgG levels are out of the target range. This, along with guidelines should be used to ensure ordering physicians are aware of the proper protocols.

8 Discards

It is important IVIG be prescribed appropriately, but sometimes, for a variety of reasons, it is discarded even before it is used. Figure 12 shows a summary of the amount of IVIG reported as discarded in the Atlantic Provinces in recent fiscal years. Fiscal year 2008/09 was the first time all facilities were reporting discards. New Brunswick showed a large increase from 2007/08 to 2008/09, but most of this increase can be accounted for by discards reported by facilities that were not reporting discard data prior to 2008/09. In PEI and Newfoundland & Labrador, facilities starting to report discards in 2008/09 did not contribute significantly to the increases shown. Nova Scotia showed a decrease in reported discards even with the increase in facilities reporting. Table 5 shows the estimated costs associated with IVIG discards in recent fiscal years.

Figure 12: IVIG Discards in the Atlantic Provinces for Recent Fiscal Years

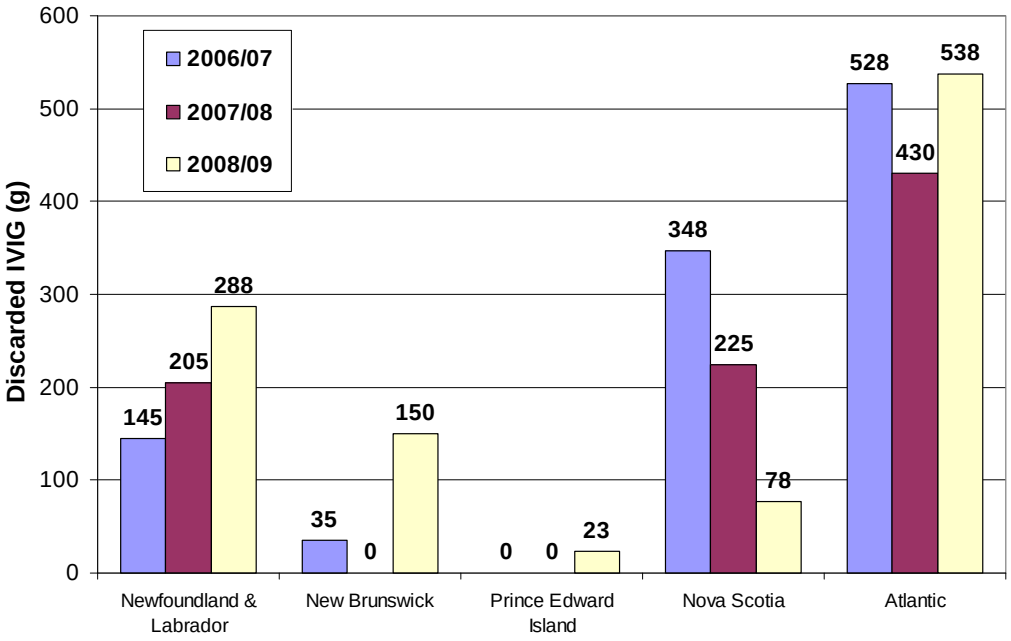


Table 5: Estimated Cost* of Reported IVIG Discards in the Atlantic Provinces in Recent Fiscal Years

Fiscal Year	Newfoundland and Labrador	New Brunswick	Prince Edward Island	Nova Scotia	Atlantic
2006/07	$7,782	$1,878	$0	$18,677	**$28,337**
2007/08	$11,261	$0	$0	$12,359	**$23,620**
2008/09	$16,434	$8,574	$1,315	$4,430	**$30,752**

* Estimated cost was calculated by multiplying the total grams by an average price per gram for that year.

To reduce the amount of discards, representatives from each province will be provided with a breakdown of the facilities that have discarded IVIG, the amounts, and the specific reasons for the discards. This will allow representatives to communicate with facilities to assist in formulating strategies to reduce the chance of further discards.

In Nova Scotia, a large proportion of the improvement seen in 2008/09 can be attributed to one facility having changed its policy for returning unused plasma proteins to the fridge. After consultation with manufacturers, they changed the blanket policy of discarding plasma protein products after being out of the fridge for 30 minutes to allowing IVIG products to be returned to the fridge after being out for 24 hours, as long as the vials are completely intact. Vials returned to the fridge after being out for less than 24 hours are, however, short dated to a six-month expiry date from the date of return to the fridge.

Recommendation: It is recommended that provincial representatives use a province-specific discards summary to target and communicate with facilities that have reported IVIG discards to discuss specific strategies to reduce the amount of IVIG that is discarded.

9 Subcutaneous Immunoglobulin

In 2008, SCIG became a regular product within Canadian Blood Services' plasma protein products portfolio and the Atlantic Collaborative supported the addition of SCIG to its utilization management endeavors. Utilization data collection began in late 2008 by building it into the existing IVIG data collection tools. Distribution data is provided by Canadian Blood Services. This section provides an overview of distribution and utilization.

9.1 Distribution

Figure 13 shows the amount of SCIG distributed to each of the Atlantic Provinces in the 2008/09 fiscal year.

Figure 13: SCIG Distributed to Atlantic Provinces in Fiscal Year 2008/09

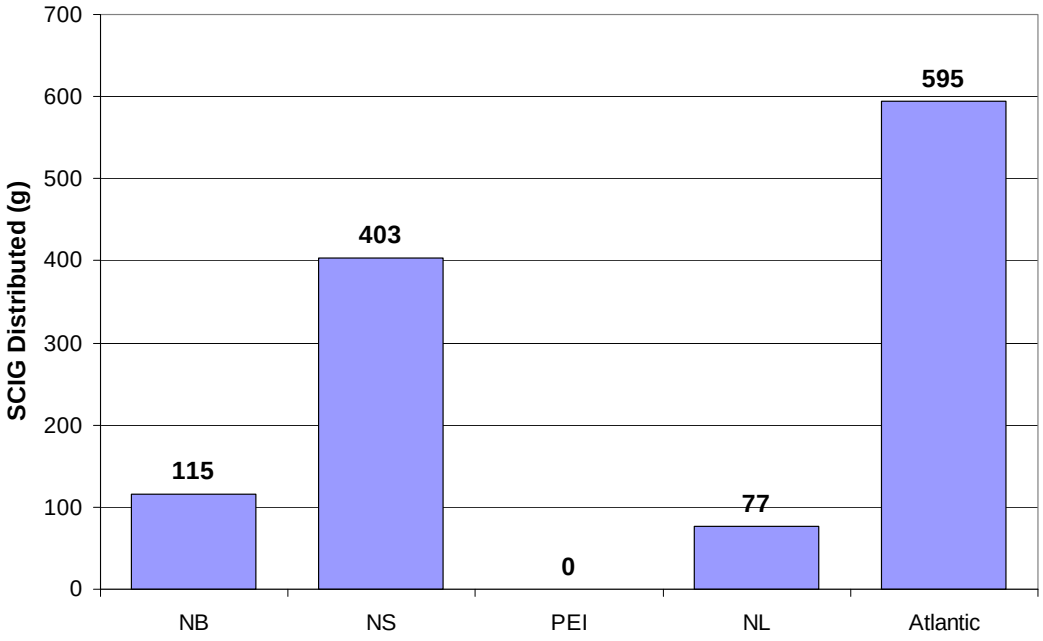


Table 6 shows the actual cost of SCIG for each of the Atlantic Provinces. The average price of SCIG in 2008/09 was $60.03 per gram. This is slightly higher than the average price of IVIG for the same time period which was $57.16 per gram.

Table 6: Amount Distributed and Total Cost of SCIG for Fiscal Year 2008/09

Province	SCIG (g)	Cost of SCIG
New Brunswick	115	$6,913
Nova Scotia	403	$24,194
Prince Edward Island	0	$0
Newfoundland & Labrador	77	$4,608
Atlantic Total	**595**	**$35,715**

9.2 Utilization

In fiscal year 2008/09, there was reported use of SCIG for three patients with primary immune deficiencies. Two of them were in Nova Scotia and the third was in Newfoundland and Labrador. The patients in Nova Scotia used a combined total of 42 grams and the patient in Newfoundland and Labrador used 29 grams. The low amounts are explained by the fact that the patients just started SCIG use near the end of the 2008/09 fiscal year. Dosing for all patients was according to the recommended 0.1 to 0.2 g/kg per week.

9.3 Discards

No SCIG discards were reported in the 2008/09 fiscal year.

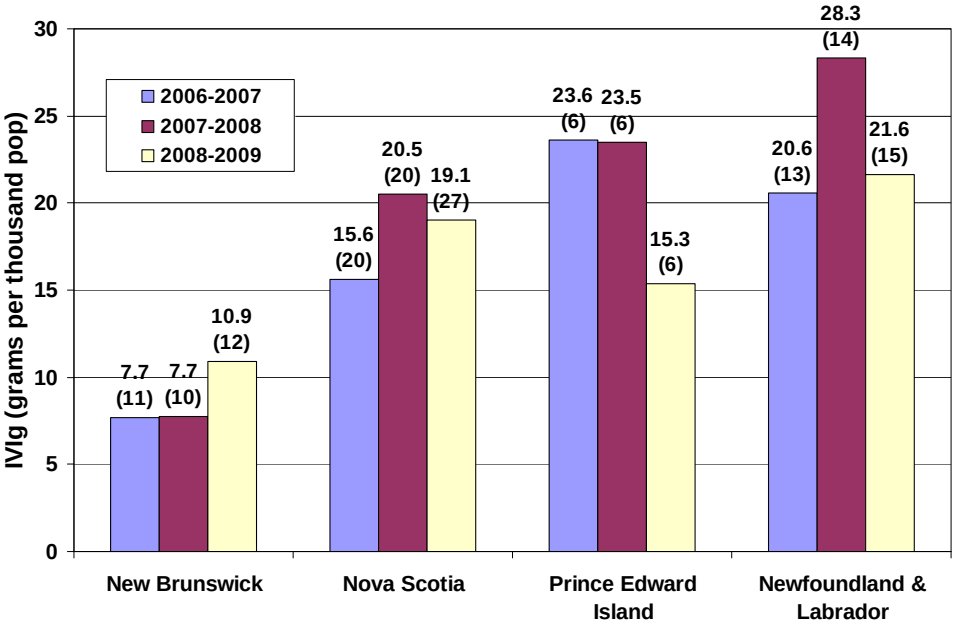
9.4 Atlantic Guidelines

In an effort to ensure SCIG continues to be used according to the recommended guidelines, and in response to recommendations made in 2008 by the National Advisory Committee on Blood and Blood Products, an Atlantic SCIG Working Group was convened to develop guidelines to be used for the implementation of SCIG home infusion programs in hospitals in the Atlantic provinces. The guidelines were completed in the summer of 2009 and after endorsement by the Atlantic Collaborative IVIG Utilization Working Group, will be disseminated for pilot use for a one year period. Feedback collected during the pilot period will be incorporated into a formal version for publication in 2010.

Appendices

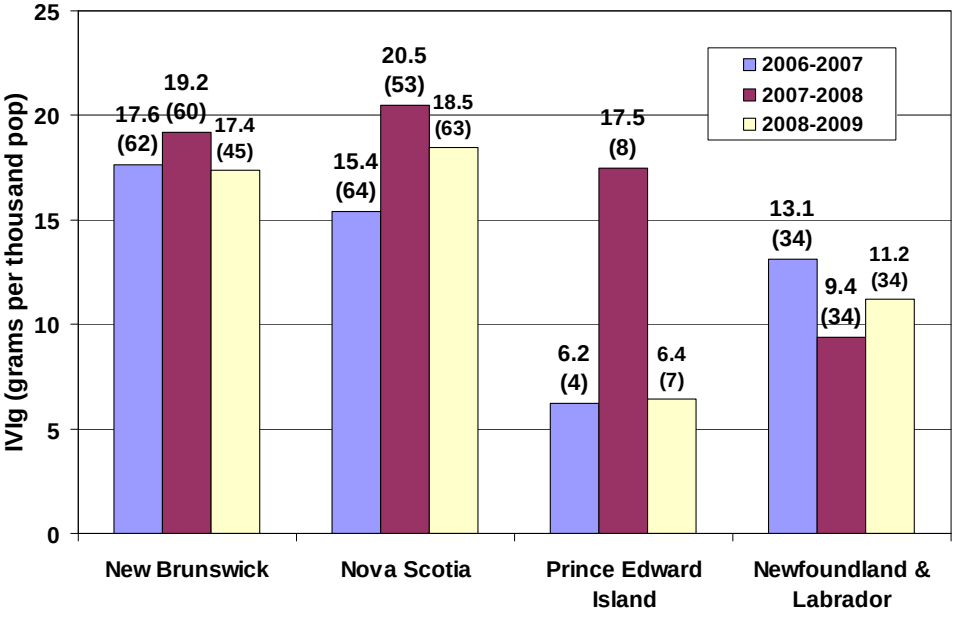
Appendix A: Per Capita Utilization of IVIG for the Top Indications

Figure A1: Per Capita Utilization of IVIG for CIDP



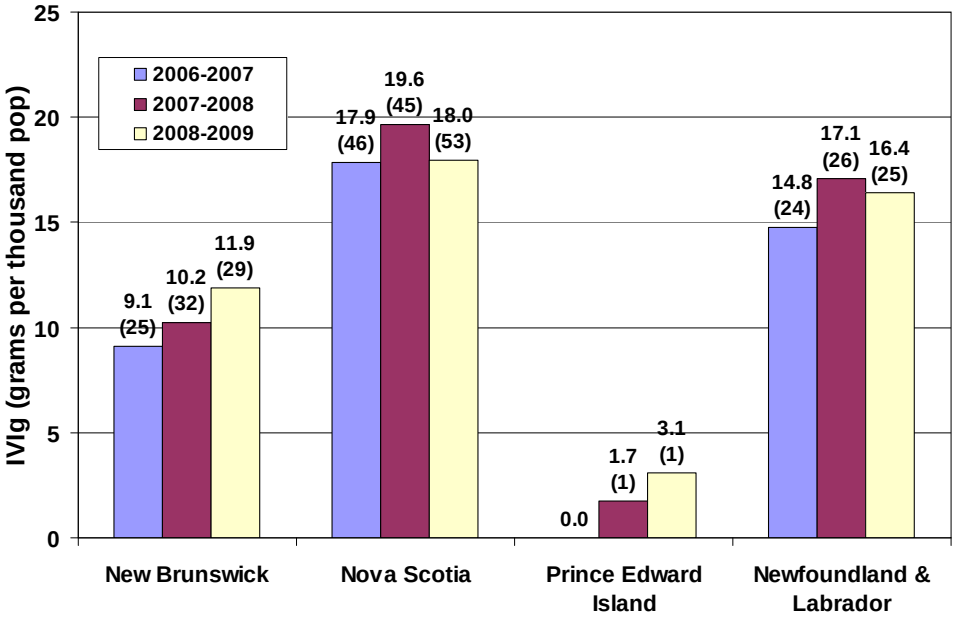
Parentheses indicate total number of patients

Figure A2: Per Capita Utilization of IVIG for Idiopathic Thrombocytopenic Purpura



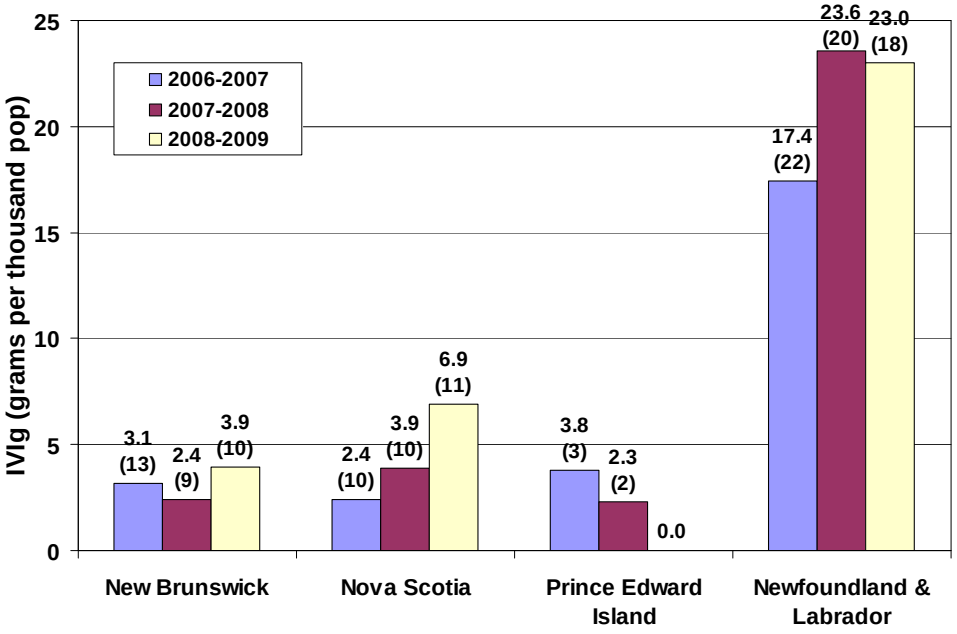
Parentheses indicate total number of patients

Figure A3: Per Capita Utilization of IVIG for Primary Immune Deficiencies



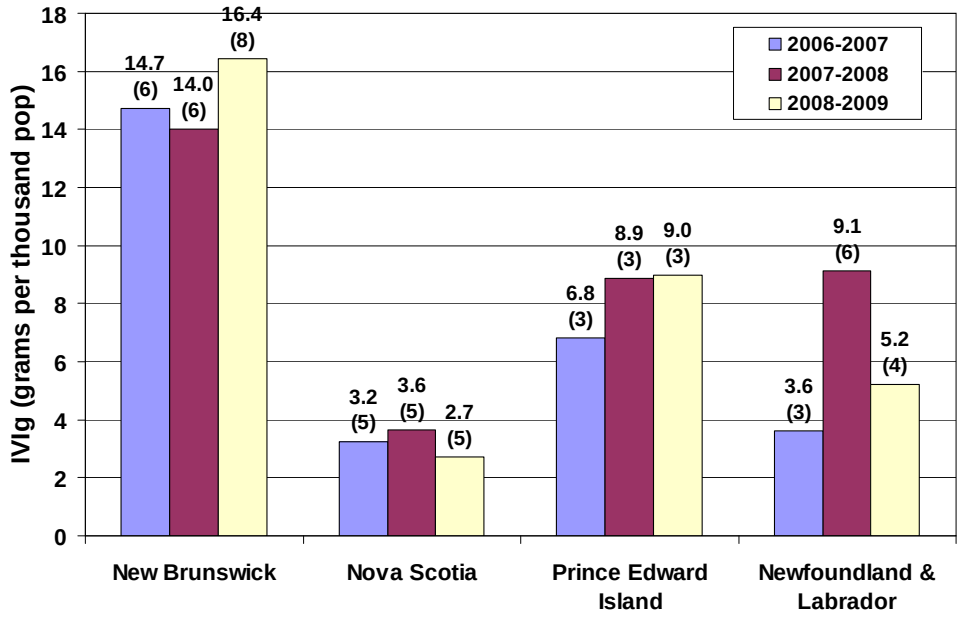
Parentheses indicate total number of patients

Figure A4: Per Capita Utilization of IVIG for Myasthenia Gravis



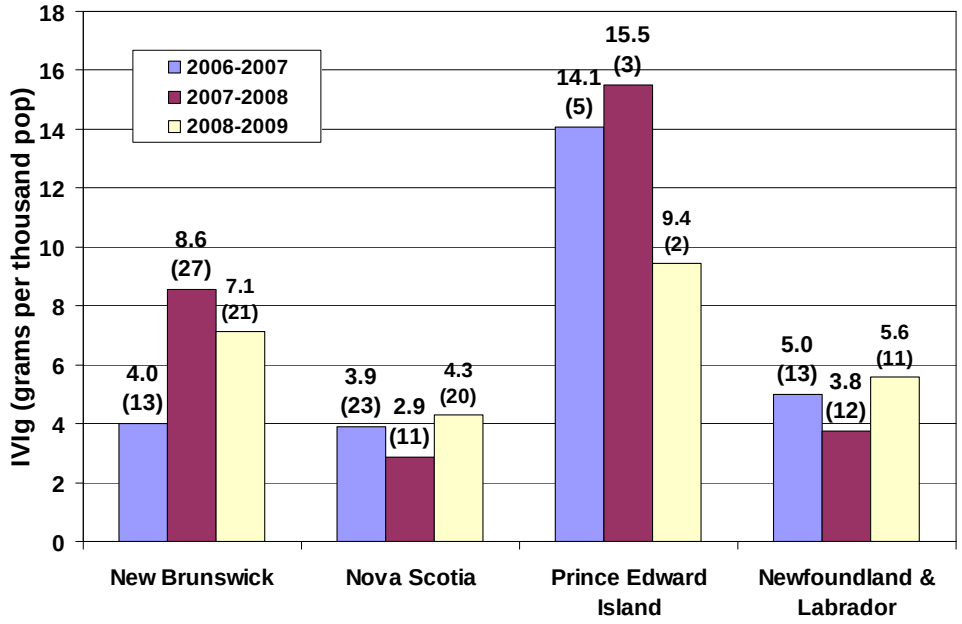
Parentheses indicate total number of patients

Figure A5: Per Capita Utilization of IVIG for Multifocal Motor Neuropathy



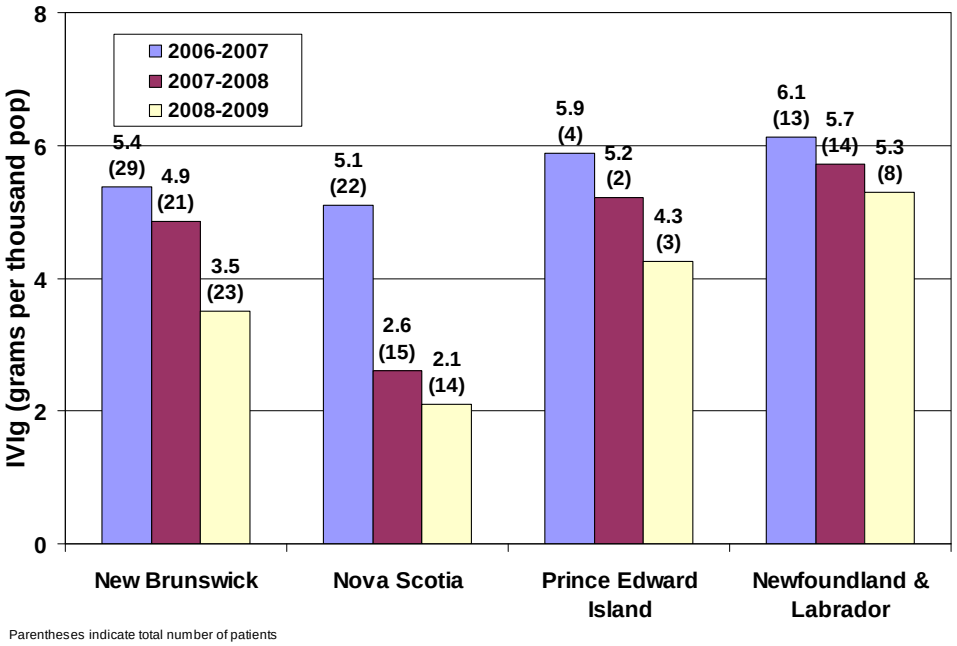
Parentheses indicate total number of patients

Figure A6: Per Capita Utilization of IVIG for Guillain-Barré Syndrome



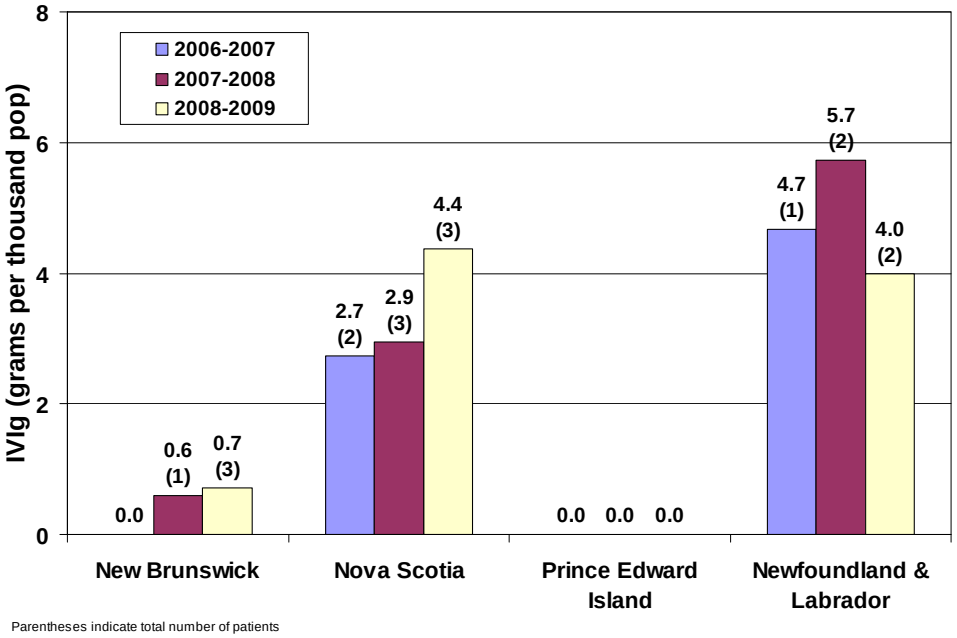
Parentheses indicate total number of patients

Figure A7: Per Capita Utilization of IVIG for Secondary Immune Deficiency



Parentheses indicate total number of patients

Figure A8: Per Capita Utilization of IVIG for Stiff Person Syndrome



Parentheses indicate total number of patients

Appendix B: Analysis of ITP Dosing Regimens

Table B1: ITP Acute vs Chronic use for Fiscal Year 2007-08

Province	% of Acute Patients	% of Acute Doses	% of Doses Outside Guidelines	% of Doses Outside Guidelines that were for Chronic Use
NL	86%	68%	17%	56% (of 9)
NB	77%	46%	15%	86% (of 36)
PEI	75%	78%	25%	63% (of 8)
NS	82%	39%	40%	93% (of 112)

Definitions for Table B1:

% of Acute Patients – the proportion of *patients* who received IVIG for the treatment of ITP who were on an acute dosing regimen

% of Acute doses – the proportion of *doses* administered to patients for the treatment of ITP that were part of acute treatment regimens

% of Doses Outside Guidelines – the proportion of *all doses* administered for the treatment of ITP that were either higher or more frequent than recommended (according to Atlantic guidelines)

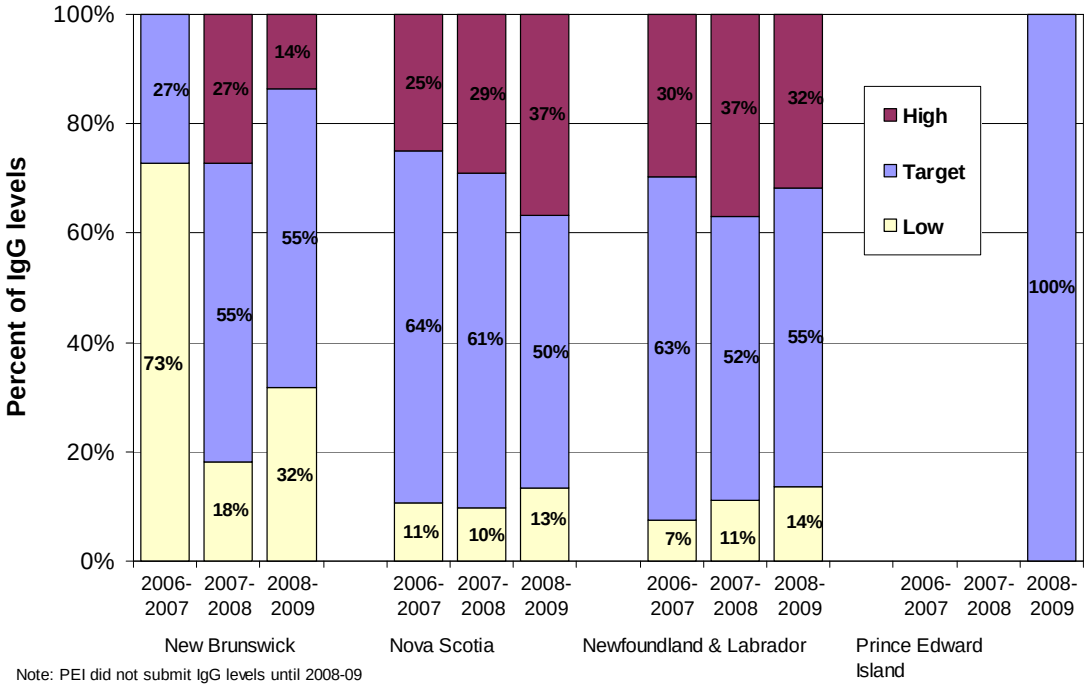
% of Doses Outside Guidelines that were for Chronic Use – the proportion of doses administered higher or more frequent than recommended (according to Atlantic guidelines) that were administered as part of a chronic treatment regimen. The parentheses indicate the total doses that were higher or more frequent than recommended, including both acute and chronic regimens.

Table B2: Acute and Chronic ITP Patient Counts for Fiscal Year 2007-08

Province	Acute Patients	Chronic Patients	Total
NL	24	10	34
NB	47	13	60
PEI	6	2	8
NS	44	9	53

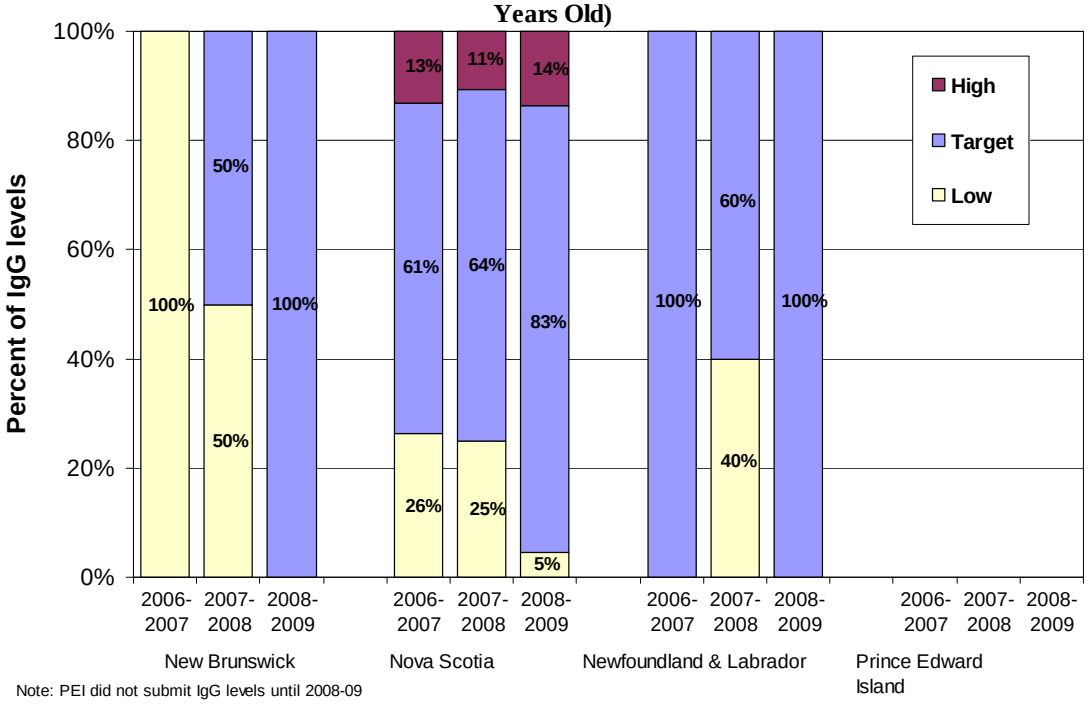
Appendix C: IgG Level Ranges by Age Group

Figure C1: IgG Level Ranges Adult Patients (Greater Than 16 Years Old)



Note: PEI did not submit IgG levels until 2008-09

Figure C2: IgG Level Ranges for Pediatric Patients (Less Than or Equal to 16 Years Old)



Note: PEI did not submit IgG levels until 2008-09

Appendix D: Year to Year Carry-Through Patients

At the 2008 ACIUWG Meeting, the question arose as to how much chronic use was due to patients who carry through from year to year on long term treatment. Figure C1 shows the results of the analysis. It can be seen that there are many patients who do carry through from year to year. Below Figure D1, Tables D1 to D3 provide a more precise breakdown of the 319 patients who carried through from the various years and their indications.

Figure D1: IVIG Patient Counts Flowchart

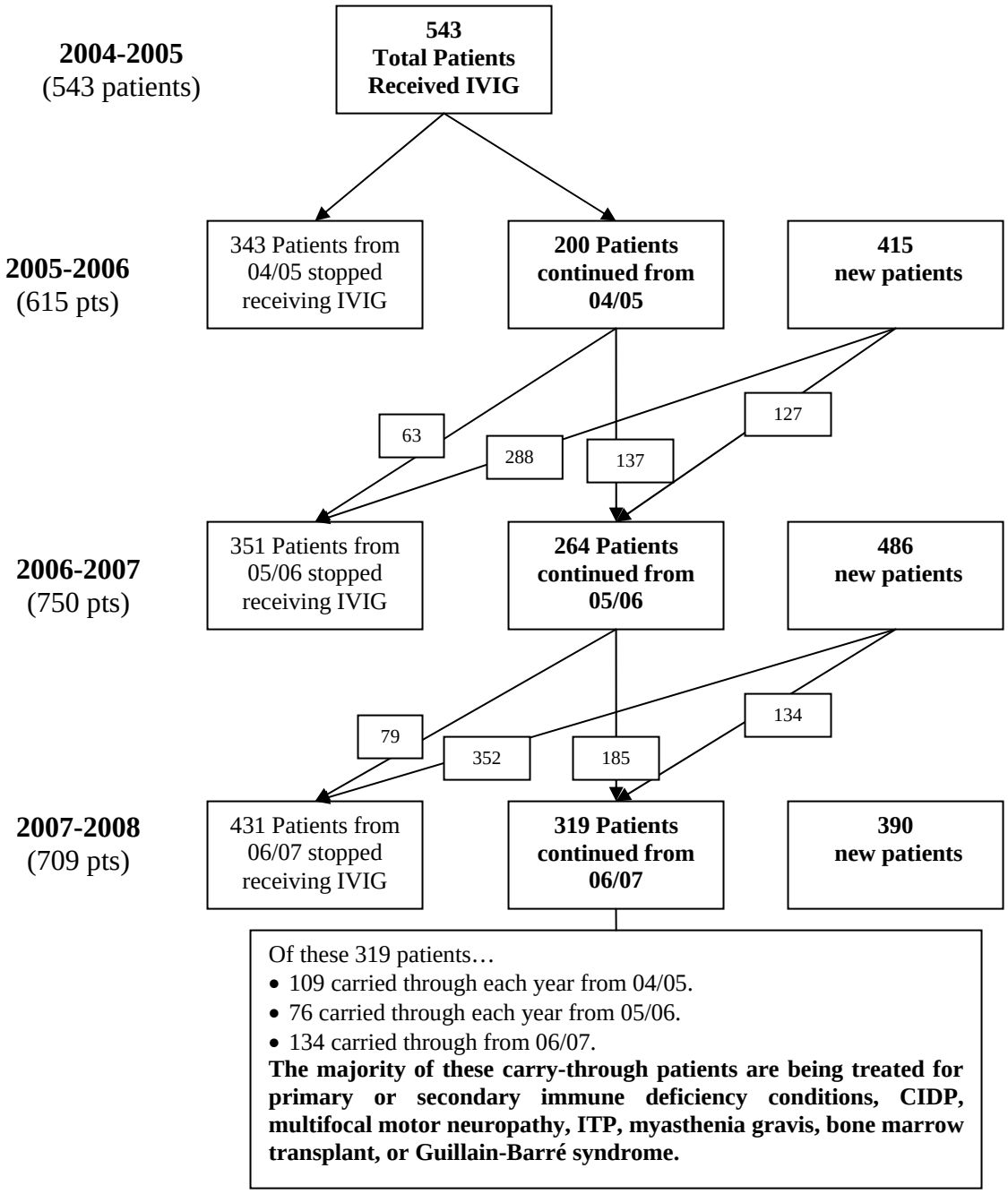


Table D1: Overview of the Patients Carried Through From 2004/05

Indication	# of Patients
Primary immune deficiency conditions	49
Chronic inflammatory demyelinating polyradiculoneuropathy, including MADSAM variant	17
Secondary immune deficiency conditions	8
Multifocal motor neuropathy	7
Allogeneic stem cell or bone marrow transplantation	6
Idiopathic thrombocytopenic purpura	4
Asthma	2
Guillain-Barre Syndrome including Miller-Fisher syndrome, Pan autonomic polyneuropathy	2
Amyotrophic Lateral Sclerosis	1
Chronic Lymphocytic Leukemia	1
Cicatricial Pemphigoid	1
Dermatomyositis	1
Epileptic Encephalopathy	1
Juvenile Rheumatoid Arthritis	1
Multiple Miscarriages	1
Multiple Sclerosis	1
Myasthenia gravis, including Lambert-Eaton myasthenic syndrome	1
Polyarthritis/polychondritis/lytic bone lesions	1
Rheumatoid Arthritis	1
Stiff Person Syndrome	1
Systemic rheumatoid juvenile arthritis with exacerbation	1
Transverse Myelitis	1
Total	**109**

Table D2: Overview of the Patients Carried Through From 2005/06

Indication	# of Patients
Primary immune deficiency conditions	15
Idiopathic thrombocytopenic purpura	12
Myasthenia gravis, including Lambert-Eaton myasthenic syndrome	10
Secondary immune deficiency conditions	7
Chronic inflammatory demyelinating polyradiculoneuropathy, including MADSAM variant	6
Allogeneic stem cell or bone marrow transplantation	3
Multifocal motor neuropathy	3
Polymyositis	3
Chronic Lymphocytic Leukemia	2
Acute Disseminated Encephalomyelitis	1
Auto Immune Lumbosacral Plexitis	1
Bronchial infections	1
Cerebellar Ataxia	1
Cerebral Vasculitis	1
Dermatomyositis	1
Goodpasture's Syndrome	1
Hypogammaglobulinemia	1
Juvenile Dermatomyositis	1
Lymphoma	1
Monoclonal gammopathy with demyelinating neuropathy	1
Multiple Myeloma	1
Multiple Sclerosis	1
Rheumatoid Arthritis	1
Stiff Person Syndrome	1
Total	**76**

Table D3: Overview of the Patients Carried Through From 2006/07

Indication	# of Patients
Idiopathic thrombocytopenic purpura	21
Primary immune deficiency conditions	19
Secondary immune deficiency conditions	16
Myasthenia gravis, including Lambert-Eaton myasthenic syndrome	15
Chronic inflammatory demyelinating polyradiculoneuropathy, including MADSAM variant	12
Guillain-Barre Syndrome including Miller-Fisher syndrome, Pan autonomic polyneuropathy	6
Allogeneic stem cell or bone marrow transplantation	4
Multifocal motor neuropathy	3
Polymyositis	3
Asthma	2
Dermatomyositis	2
Multiple Myeloma	2
Multiple Sclerosis	2
Acute Lymphocytic Leukemia	1
Amyotrophic lateral sclerosis	1
Auto Immune Hemolytic Anemia	1
Axonal Polyneuropathy	1
Cellulitis	1
Crohn's disease	1
Erythema Multiforme Major	1
Febrile Neutropenia	1
Fetal-Neonatal Alloimmune Thrombocytopenia	1
Hypogammaglobulinemia	1
IgM are low	1
Juvenile dermatomyositis	1
Juvenile Rheumatoid Arthritis	1
Kawasaki disease	1
Leukemia	1
Monoclonal gammopathy	1
Motor Neuron Disease	1
Nerve impairment similar to MS	1
Opsoclonus-Myoclonus	1
Paraneoplastic Subacute Cerebellar Degeneration	1
Pemphigus Vulgaris	1
Post AML	1
Pure Red Cell Aplasia	1
Recurrent demyelinating of optic nerve	1
Scleroderma	1
Stiff Person Syndrome	1
Waldenstroms macroglobulinemia	1
Total	**134**

Appendix E: Indications Showing Increasing Grams and Doses per Patient

The following are indications for which there is a trend of both increasing total grams and total doses per patient (based on 05/06 to 07/08 Data):

- ITP
- Primary Immune Deficiency Conditions
- CIDP
- Myasthenia Gravis
- Polymyositis
- Dermatomyositis