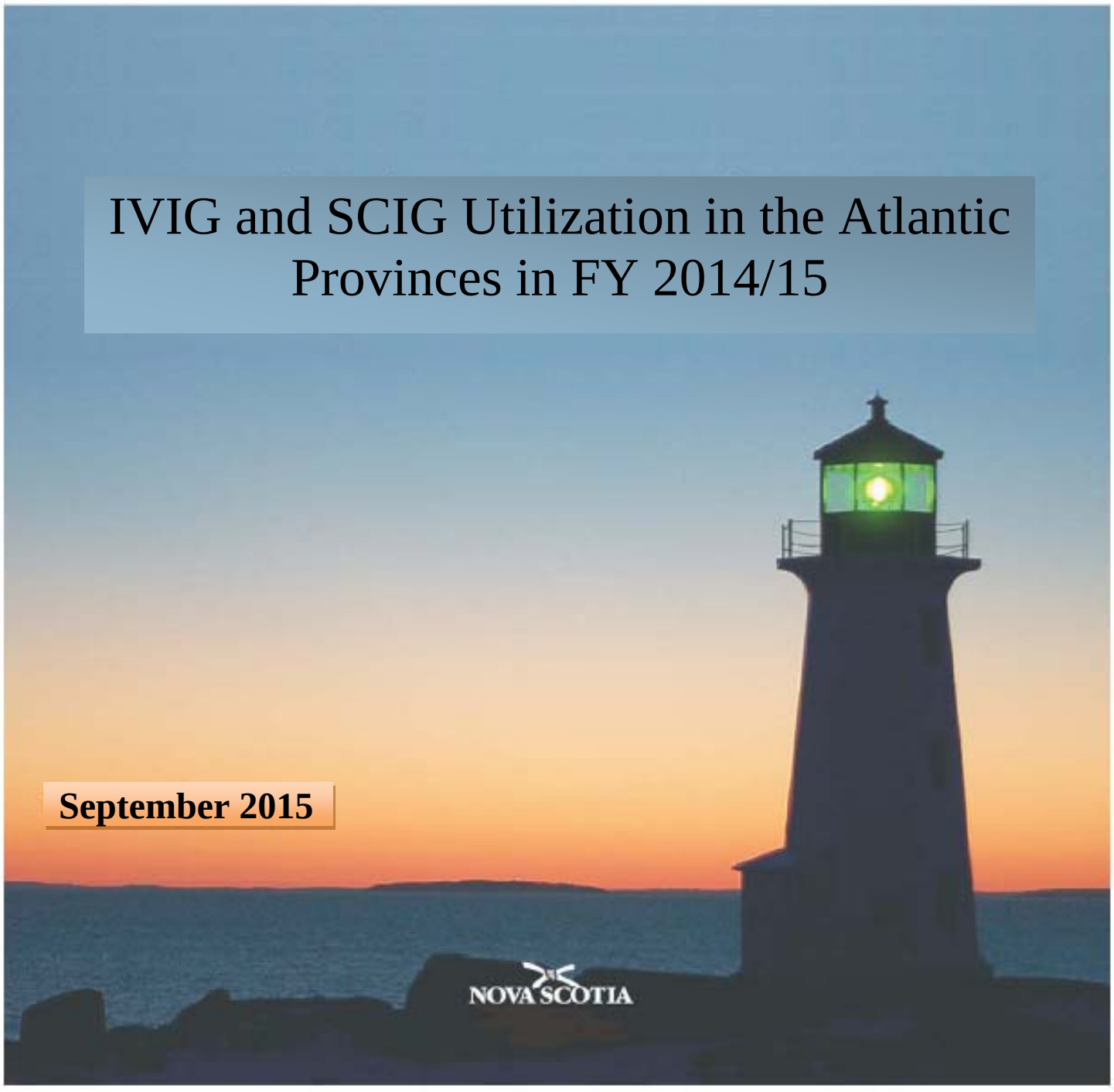
NOVA SCOTIA PROVINCIAL
BLOOD COORDINATING PROGRAM

IVIG and SCIG Utilization in the Atlantic Provinces in FY 2014/15



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Report Prepared by:
Tabassum Quraishi, Utilization Management Coordinator

Data Analysis by:
Tanja Keselj, Senior System Analyst
Erica Paolone, Data Analyst
Mark Daine, Database Coordinator
Graham Wile, Senior System Analyst

Nova Scotia Provincial Blood Coordinating Program
Room 2123
1673 Bedford Row
Halifax, Nova Scotia B3J 1T1
Phone: (902) 487-0506

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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 2014/15 fiscal year.

When compared with many other developed countries, Canada has the highest per capita consumption of IVIG and SCIG; the distribution of these immune globulins in Canada has continued to rise over the last ten years by 5 to 10% each year. In the 2014/15 fiscal year, Canada had a rise in the distribution by 6% from what it was in the previous year. Atlantic Canada demonstrated a 5% increase in the distribution of IVIG and SCIG in 2014/15 from what it was in 2013/14. New Brunswick was the only Atlantic Province showing a distribution decrease (-7.3%). Growth rate of the IVIG and SCIG distribution during 2014/15 in Nova Scotia and Newfoundland and Labrador were contained at 7%. This was better than last year's growth rate of 12.3% in Nova Scotia and 19% in Newfoundland and Labrador respectively. Prince Edward Island exhibited a growth rate of 30.5% in its distribution of IVIG and SCIG for 2014/15. This large growth rate is a reflection of a relatively small change in the distribution of IVIG/SCIG in Prince Edward Island. The distribution of IVIG and SCIG in Prince Edward Island were 19013 grams in 2013-14 and increased by 5808 grams to 24821 grams in 2014-15.

During 2014/15 the use of IVIG/ SCIG increased in Neurology, Immunology, Rheumatology and Dermatology; it decreased in Hematology compared to last year. The top three uses of IVIG and SCIG in Atlantic Canada are for the treatment of Primary Immune Deficiency (PID), Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP), and Immune Thrombocytopenia Purpura (ITP). The Atlantic use of IVIG decreased for Immune Thrombocytopenia Purpura (ITP) and Multifocal Motor Neuropathy (MMN); while it increased for Primary Immune Deficiency (PID), Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP), Myasthenia Gravis (MG), Secondary immune deficiency (SID), Stiff Person syndrome and Guillian Barré Syndrome (GBS) in Atlantic Canada.

In Atlantic Canada this year, 2.9% of the total IVIG administered, was given for Unlabeled conditions (UL-N) for which there is no evidence to support the use of IVIG; where as 97% of the use was for appropriate indications.

Monitoring patient serum IgG levels every 3-6 months is recommended for PID to ensure that patients using IVIG and SCIG are being dosed appropriately. This fiscal year, 79% of patients in Atlantic Canada had their serum IgG levels monitored. This is an improvement from last year when 71% of patients in Atlantic Canada had their serum IgG levels monitored and reported. The target range for IgG levels is between 7 and 10 g/L. For those PID patients whose IgG levels are 10g/L or above, there is the potential to reduce the amount of product they are receiving while still experiencing clinically beneficial outcomes. These patients are identified in all Atlantic provinces and their information is shared in their respective province specific report to explore the opportunity for dose adjustment.

The dosing of IVIG, based on dosing body weight rather than actual body weight, was introduced by the Nova Scotia Provincial Blood Coordinating Program (NSPBCP) in 2010/11. It is applicable to all patients excluding patients with Guillian Barré Syndrome, solid organ transplant and those who are shorter than 5 feet in height. In 2014/15, the analysis of 1008 Atlantic patients revealed that 62% of them were dosed according to their dosing body weight. There was an estimated cost avoidance of $3,406,968 for 71,201grams, an increase from last year's estimated savings of $1,252,861.70 for 25,705grams of IVIG and SCIG.

The combined total of IVIG discards in the Atlantic Provinces increased to 1098 grams in 2014/15 which is 240 grams more than 858grams of 2013/14. This year's discards are 0.28% of the total distributed IVIG and SCIG.

In conclusion, The Atlantic distribution of 162 g/1000 population of IVIG is less than the Canadian distribution of 177g/1000 population in 2014/15. IVIG and SCIG distribution increased in the Atlantic Provinces by 5% during the 2014/15 fiscal year, which is less than the 6% growth rate of distribution in Canada. Among Canadian Provinces New Brunswick at 126g/1000 population is ranked second best in her per capita distribution of IVIG/SCIG after the Territories, while Nova Scotia and Newfoundland and Labrador have contained the growth rate of IVIG/SCIG distribution at 7% each. While the majority of the IVIG and SCIG transfused in Atlantic Canada have been appropriate, 2.9% was utilized in patients with conditions for which there are little evidence to support its use. The NSPBCP continues to be effective in monitoring the use of IVIG and determining the indications and appropriateness of its use. The data generated through the Atlantic Collaborative allows the development of strategies for optimizing the use of IVIG with the end goal being to ensure that patients are dosed appropriately, clinical benefit is achieved, adverse reactions are avoided, and product wastage is minimized. In 2014/15, the initiative of dosing body weight prevented over 71,000 grams of IVIG from being transfused into 624 patients in Atlantic Canada, resulting in a cost avoidance of $3,406,968.

It is recommended that all eligible future patients of IVIG and SCIG be dosed based on the dosing body weight. It is also recommended that all primary immune deficiency patients be consulted with immunologists. And for patients with the serum IgG levels that are above the target range, the Blood Transfusion Medical Directors should have a discussion with the respective prescribing physicians for dose adjustment.

2 Introduction

This report is a summary of the utilization of IVIG and SCIG in the Atlantic Provinces for the fiscal year 2014/15. The purpose of this report is to describe the use of IVIG and SCIG in the Atlantic Provinces, to identify recommendations for improvement in data quality, and to identify strategies for optimizing appropriate use of these products to minimize product wastage.

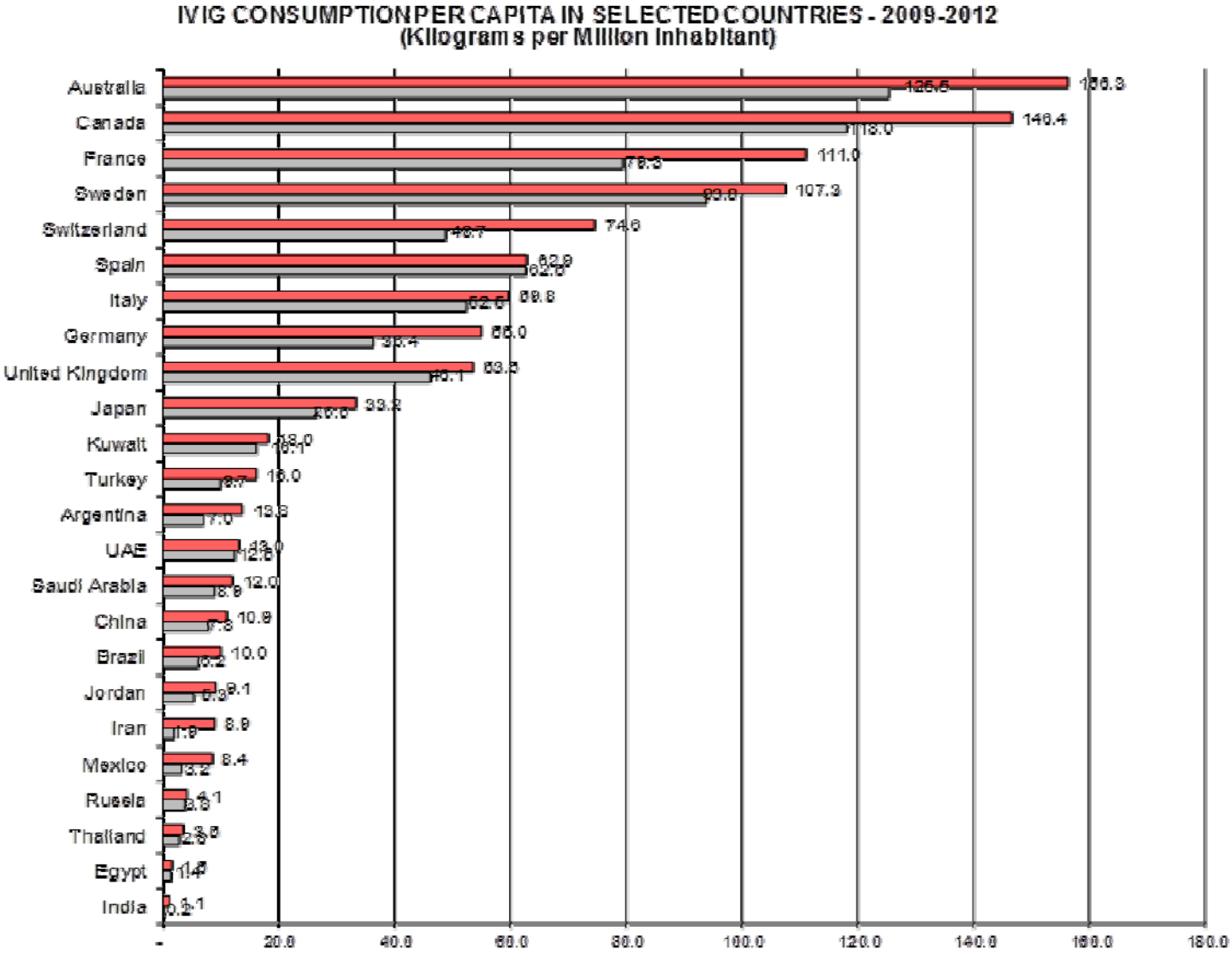
In this report the NSPBCP continues to publish the comparison of IVIG and SCIG distribution data with the rest of Canada, as this serves as a benchmark for the Atlantic Provinces. The Atlantic Provinces and the rest of Canada are examined separately in this report.

The data analysis for this report was conducted on a subset of the data that was reported to NSPBCP on or before May 8, 2015. Any data submitted after this date is not included in this report's analysis but will impact on next year's analysis.

3 International and National Perspective

Figure 1 shows an international comparison of per capita IVIG and SCIG consumption for 2009 and 2012 in select countries of the world. Canada was the second highest user of IVIG and SCIG in 2009 and 2012. The IVIG and SCIG consumption was 118g/1000 population in Canada for 2009 which increased to 146.4g/1000 population in 2012. Australia and Canada are using two to three times more than other countries such as United Kingdom, Germany and Japan.

Figure 1



Source: Market Research Bureau (via Canadian Blood Services)

Figure 2 shows the annual combined distribution of IVIG and SCIG across Canada (including Quebec) for the last five fiscal years. Since 2010, Canada's IVIG and SCIG distribution rates have consistently increased by 6 to 9%, with a 6% increase in 2014/15.

Figure 2

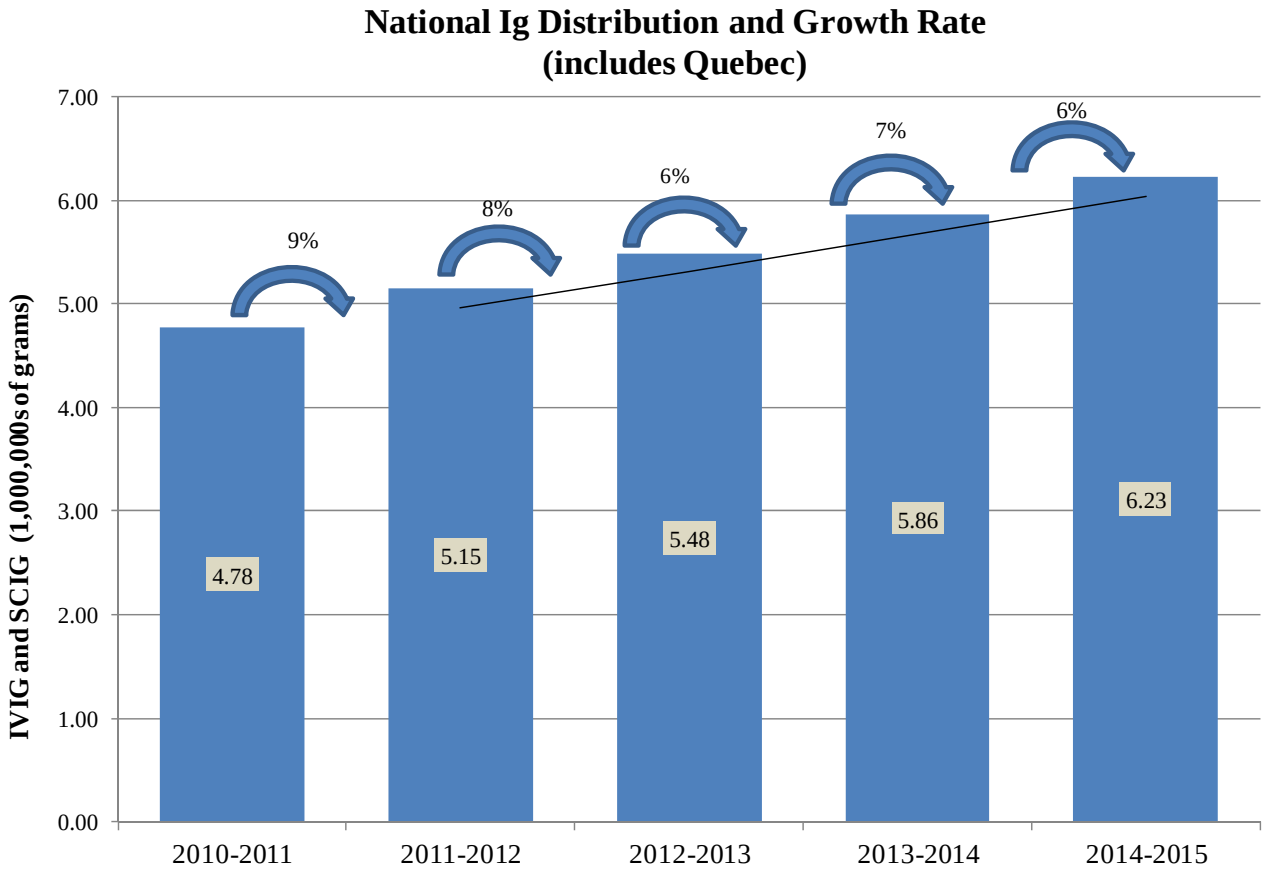


Figure 3

IVIG and SCIG Distribution and Growth Rate in Atlantic Canada

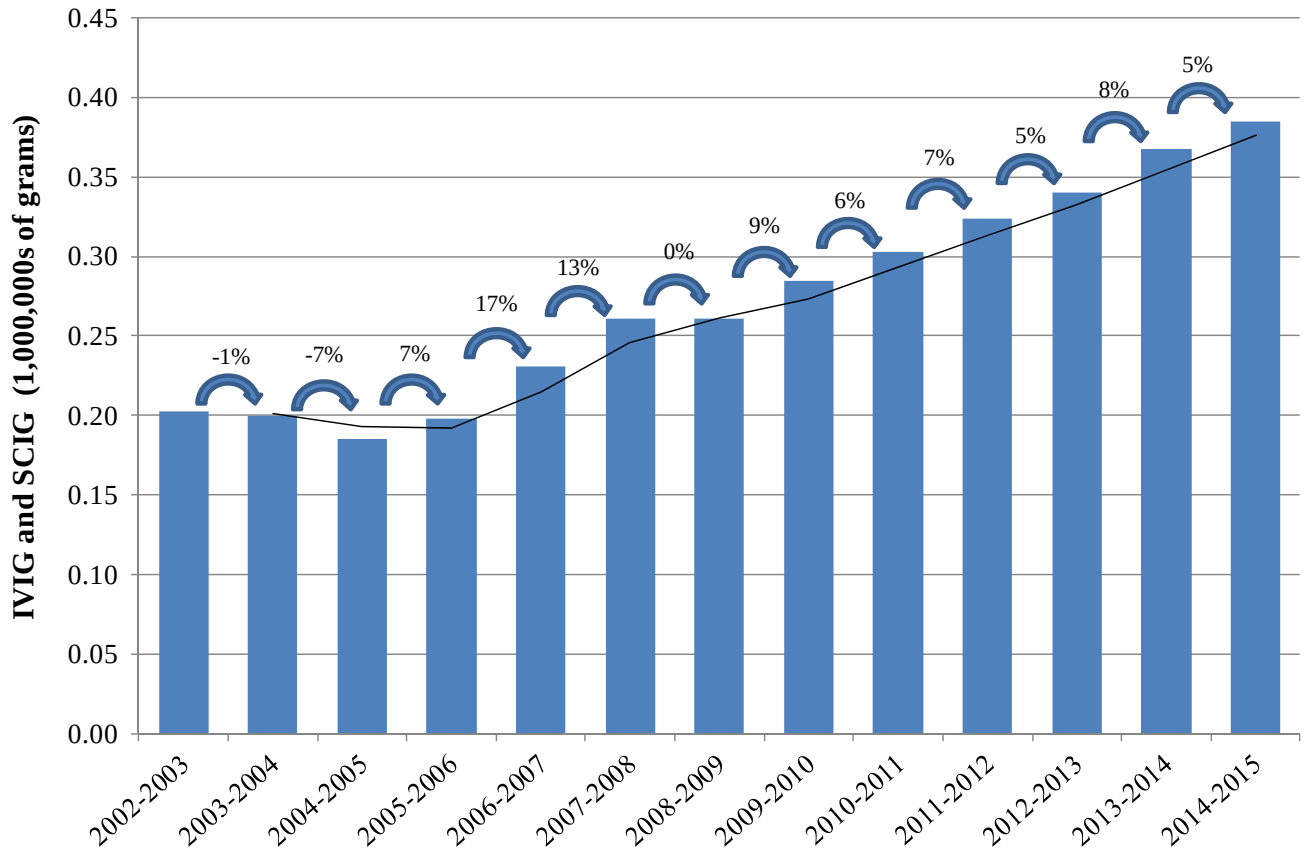


Figure 3 shows Atlantic Canada's combined annual distribution of IVIG and SCIG for the last thirteen years. Distribution rates were relatively unchanged from 2002 through to 2006, as demonstrated by this graph; the last eight fiscal years show steady increases to the distribution rate. Atlantic Canada saw an 5% distribution increase in 2014/15 from the previous fiscal year.

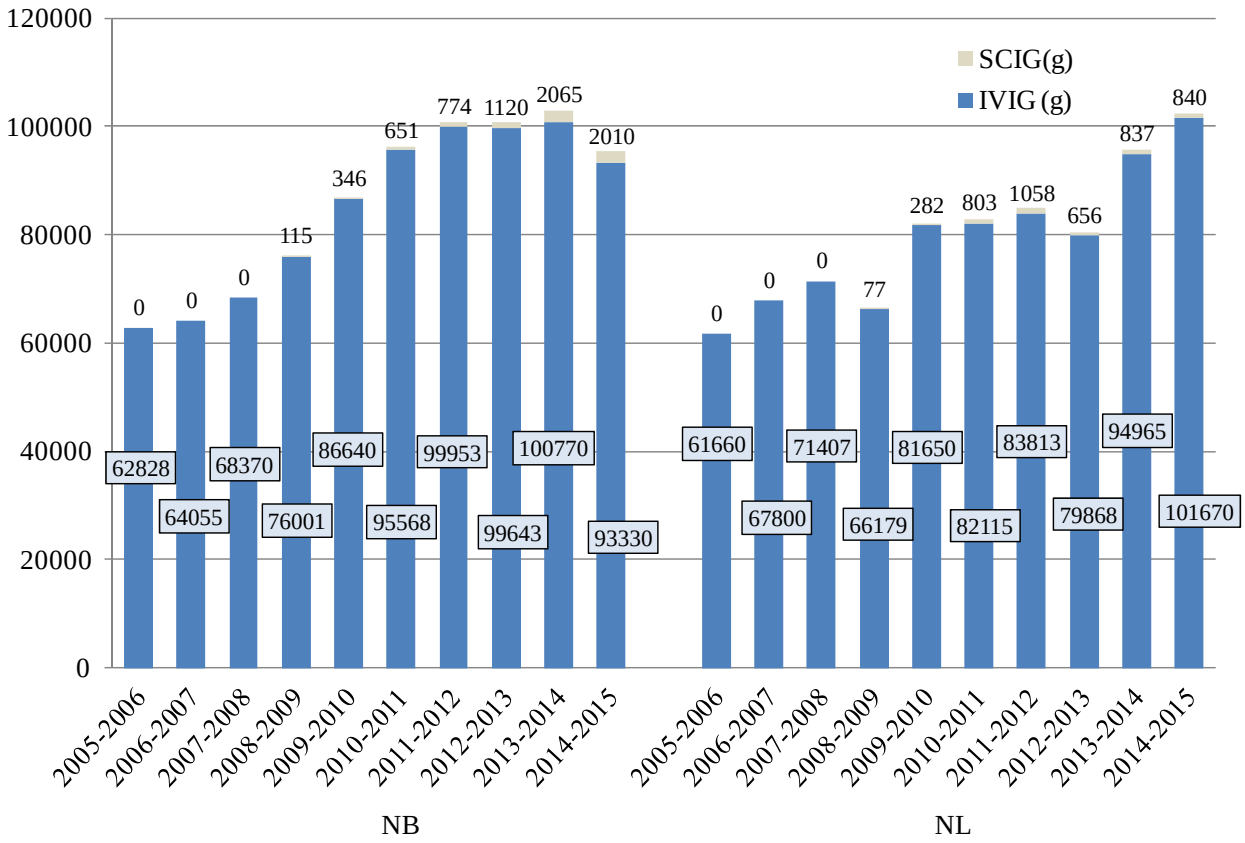
4 Provincial Distribution Trends

This section summarizes the total amounts of IVIG and SCIG *distributed* to facilities in the Atlantic Provinces in recent fiscal years. While different from the amount of IVIG and SCIG *utilized*, it provides a reference for monitoring year-to-year trends.

Figure 4 demonstrates the total grams of IVIG and SCIG distributed by CBS to New Brunswick and Newfoundland and Labrador from the 2005/06 fiscal year until 2014/15.

Figure 4

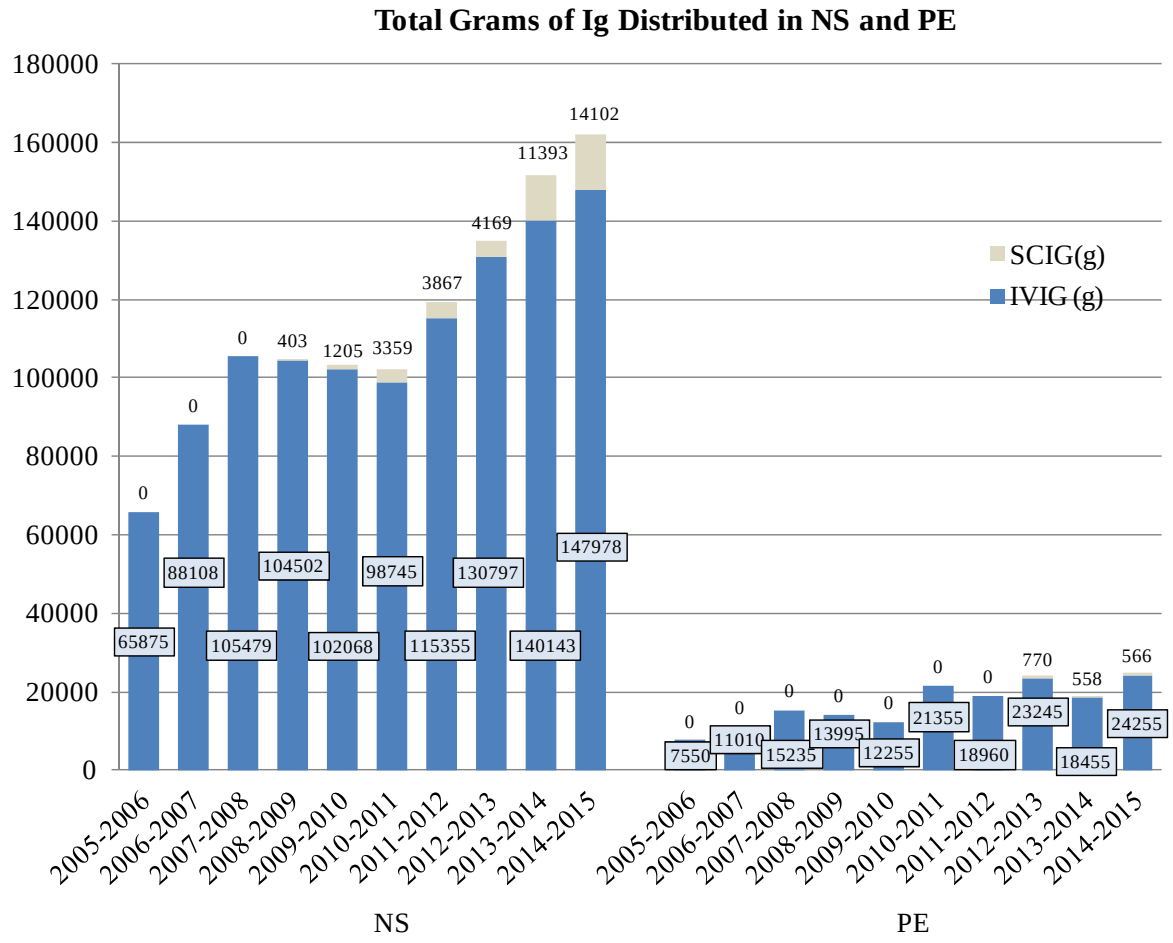
Total Grams of Ig Distributed in NB and NL



New Brunswick was the only Atlantic province to exhibit a decrease in the distribution of IVIG and SCIG in 2014/15 by 7.3%. The growth rate in distribution for Newfoundland and Labrador (Figure 4) and Nova Scotia (Figure 5) were contained at 7% each. Newfoundland and Labrador demonstrated a great increase at 19% in 2013/14, after showing a 6% distribution decline in 2012/13. The increase in Newfoundland and Labrador in 2014/15 is in part due to an increase in the use of IVIG for the treatment of Myasthenia Gravis, Chronic Inflammatory Demyelinating Polyradiculoneuropathy, Gullian Bare Syndrome, immune mediated thrombocytopenic Purpura and Multifocal Motor Neuropathy.

Figure 5 demonstrates the total grams of IVIG and SCIG distributed by CBS to Nova Scotia and Prince Edward Island from the 2005/06 fiscal year until 2013/14.

Figure 5



Nova Scotia has shown an increasing trend in IVIG and SCIG distribution in the past four years. In 2013/14, the high growth rate of 12.3% was attributable to a higher number of cases (63) treated with IVIG/SCIG than previous year (2012/13); where as in 2014/15, the growth rate in distribution was by 7%, with an increase in distribution to 162,080 grams. This is 10,544 grams higher than what it was last year.

Prince Edward Island demonstrated a 30.5% increase in the distribution of IVIG and SCIG in 2014/15 after a decline by 20.8 in the previous year. This increase may be attributed to a rise in the new cases treated with IVIG/SCIG in PEI. There were 23 new cases in 2013/14 and 30 new cases in 2014/15. The use of IVIG/SCIG increased in Primary Immune Deficiency, CIDP, Immune Throbocytopenic Purpura (ITP), and SPS in PEI during 2014/15.

Table 1 highlights the actual cost of IVIG that has been in Atlantic Canada; both in the current and for the past 5 fiscal years.

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

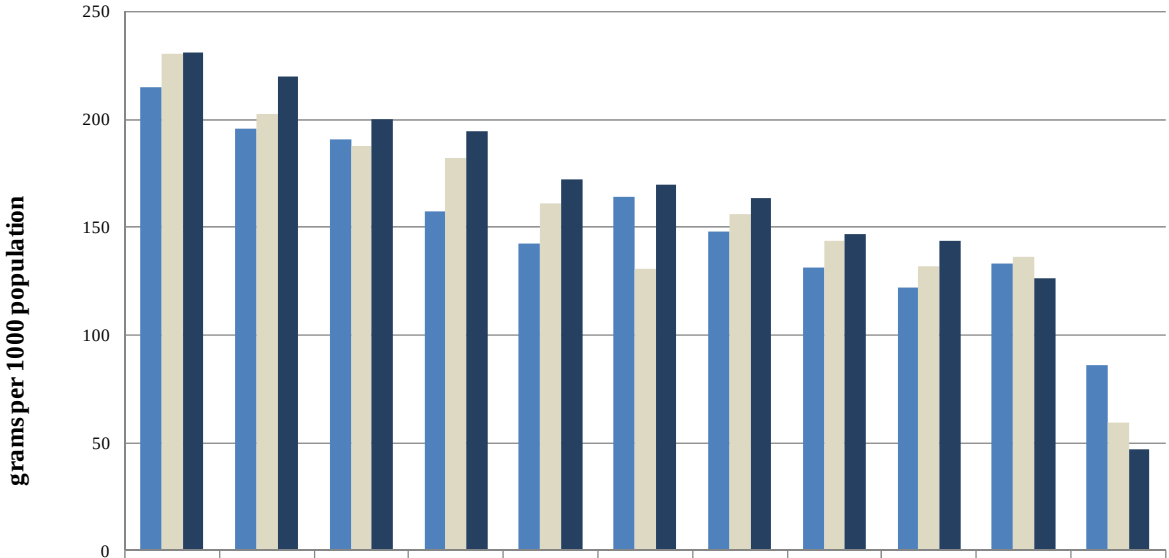
Fiscal Year	Avg. Price per gram	New Brunswick		Nova Scotia		Prince Edward Island		Newfoundland & Labrador	
		Grams	Cost	Grams	Cost	Grams	Cost	Grams	Cost
2009-2010	$66.72	86986	$5,792,106	103352	$6,905,712	12255	$817,074	81932	$5,469,634
2010-2011	$62.90	96219	$6,052,345	102104	$6,422,546	21355	$1,343,266	82918	$5,215,717
2011-2012	$58.97	100727	$5,940,309	119222	$7,031,042	18960	$1,118,155	84870	$5,005,162
2012-2013	$55.29	100763	$5,571,253	134967	$7,462,434	24015	$1,327,812	80524	$4,452,220
2013-2014	$48.74	102835	$5,011,807	151536	$7,385,297	19013	$926,626	95802	$4,669,051
2014-2015	$47.85	95340	$4,561,917	162080	$7,755,341	24821	$1,187,659	102510	$4,904,995

The price of per gram IVIG/SCIG declined by 89 cents in 2014/15. New Brunswick was the only Atlantic Province in 2014/15 to exhibit decline in the total amount paid for the IVIG /SCIG due to their decline in the use. While all the other three provinces saw the overall cost of Ig *increase* from last fiscal year due to rise in the amount distributed. The variation and impact of the IVIG costs per gram demonstrates how continued appropriate utilization is essential to ensuring that this expensive product is available to those who most need it.

Figure 6 below compares the amount of IVIG and SCIG distributed, per thousand population, among the Canadian provinces and territories for the last three fiscal years.

Figure 6

National IVIG and SCIG Distribution per 1000 Population



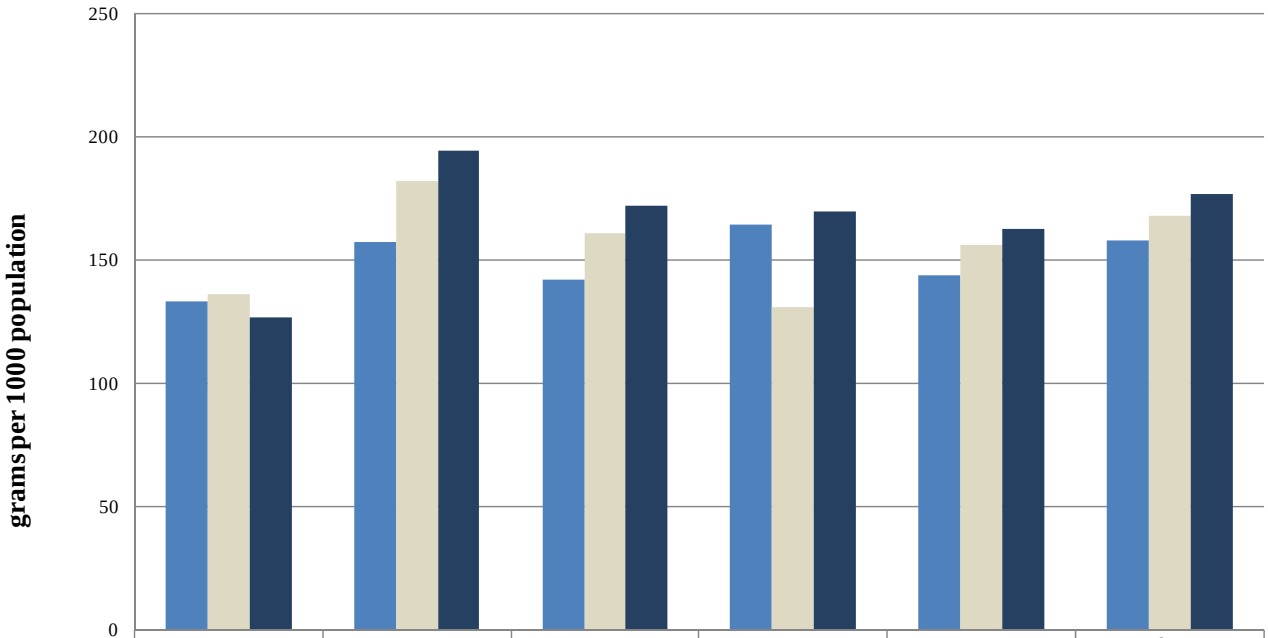
	QC	MN	AB	NL	NS	PEI	SK	BC	ON	NB	YT/NT/ NU
2012-2013	215	196	191	157	142	164	148	132	122	133	86
2013-2014	230	202	188	182	161	131	156	143	132	136	59
2014-2015	231	220	200	195	172	170	163	147	144	126	47

All Canadian Provinces exhibited a rise in the per capita distribution of IVIG/SCIG except New Brunswick. The three territories, collectively, also show a decrease in distribution per thousand population. At the distribution of 126 per thousand population this year, New Brunswick is the lowest in distribution (per 1000 population) in the country, behind the territories.

Figure 7 below compares the amount of IVIG and SCIG distributed, per thousand population, among the Atlantic provinces, Atlantic region and rest of Canadian provinces and territories excluding Atlantic Canada for the last three fiscal years.

Figure 7

Atlantic IVIG and SCIG Distribution per 1000 Population



	NB	NL	NS	PEI	Atlantic	Rest of Canada
2012-2013	133	157	142	164	144	158
2013-2014	136	182	161	131	156	168
2014-2015	126	195	172	170	162	177

All Atlantic Provinces exhibited a rise in the per capita distribution of IVIG/SCIG except New Brunswick. At the distribution of 126 per thousand population this year, New Brunswick is the lowest in distribution (per 1000 population) among Atlantic Provinces.

All Atlantic provinces, collectively, also show an increase in distribution per thousand population. At the distribution of 162 per thousand population this year, Atlantic Region continues to be lower than Rest of the country in distribution per 1000 population.

5 Utilization Data

The information presented in the remainder of this report is derived from the Intravenous Immunoglobulin Network (IVIN) database housed at the 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 NSPBCP introduced a new data network at the end of the fourth quarter in 2013/14 titled Intravenous Immunoglobulin Network (IVIN). IVIN was developed over several months with stakeholder participation from Nova Scotia, New Brunswick, and Prince Edward Island. The key objectives of IVIN were to replace its predecessor DaISI with an updated, user friendly interface that would reduce the amount of time spent inputting data and reduce the number of potential errors in data submissions. The use of IVIN for the utilization data reporting during 2014/15 had been a successful experience for the NSPBCP as well as the data submitters.

By gathering and storing data for this report through the IVIN system, we are ensuring that it remains current and reproducible. On occasion, revisions, corrections and additions may be identified following the publication of the annual report. In the event that this occurs, the data in the database is adjusted and the amendments are documented. When conducting analyses on past years the amended data is used. This is a consideration when noting differences in numbers between previous reports and the current report.

The NSPBCP continues to successfully liaise with one of the DHAs in Nova Scotia and the Lab Information System manager to obtain a quarterly data extract from the District's Laboratory Information System (LIS). This approach has decreased human resource dependence as well as eliminated manual data entry errors. It is recommended that in order to minimize the human error, jurisdictions consider the option of exploring extracts of data from Laboratory Information System (LIS) into IVIN.

The NSPBCP implemented a new strategy for SCIG log sheets that resulted in marked improvement in the reporting and monitoring of SCIG data during 2014/15. Until last fiscal year the clinics received the log sheets from the patients, verified content and then forward it to the Blood Transfusion Laboratory. A slight lack of compliance at any step resulted in a poor capture of the utilization data. In order to improve this, NSPBCP implemented the strategy where the log sheets (or their copy) are required to be returned to the dispensing BTS by the patient in order to receive more product. The BTS then enter the information into IVIN. In case of non compliance, the product dispense is limited to a week's supply. Routine dispensed can be resumed anytime upon submission of the previous log sheets.

The population of reference for this report is all patients who received doses of IVIG and/or SCIG for any indication.

5.2 Data Quality

The NSPBCP strives to continuously improve the quality of data obtained for analysis. To this end, the program reviews all of the submitted data for inconsistencies and to identify any incomplete data entry fields. Most of these checks are now completed using automated integrity queries. Any inconsistencies discovered by the queries are investigated and resolved. All cases with indications marked as "insufficient" or as "other" are identified on a quarterly basis so that the correct information pertaining to the diagnosis may be sought. This is done to minimize ambiguity in the categorization of disease indications; the appropriateness of IVIG and SCIG use is based on this information. Clinical experts are consulted electronically to assign an appropriateness category (L, UL-I, UL-N) whenever IVIG is used for any new indication.

As previously mentioned, this report includes data received by the NSPBCP for the fiscal year 2014/15 as of May 8, 2015. The data is extracted from the database and that is the source used for generating the report. Data for fiscal year 2014/15 can continue to be entered into the database but it will not be part of the extract used for generating the report. However for previous fiscal years, an updated or live database is used for a true reflection of the revisions, corrections and submissions on data that were completed after the generation of previous annual reports. This may reflect as a variation in the indications, utilized IVIG grams and overall appropriateness of use of IVIG from what was presented in the previous annual reports.

Data submissions were reviewed for missing data on a quarterly period which contributed to quality improvement of the Atlantic IVIG/SCIG Utilization report and must be continued.
Percent capture of the distribution data for the Atlantic Provinces during the time period of this report was greater than 95%. This is based on the amount of IVIG or SCIG reported as *utilized (transfused + discarded)* divided by the total amount of IVIG or SCIG *distributed.*

Table 2: Percent Capture for IVIG

Province	Percent Capture 2012-2013	Percent Capture 2013-2014	Percent Capture 2014-2015
New Brunswick	95.7	96.5	99.1
Nova Scotia	97.4	99.6	100.6
Prince Edward Island	95.7	100.1	100.9
Newfoundland and Labrador	98.2	99.5	99.7

Percent capture of the IVIG distribution data for the Atlantic Provinces during the time period of this report improved from what it was in 2013/14. The high percent capture of IVIG supports the fact that the utilization data in this report is representative of the actual overall utilization and a result of a continuous evaluation, reminders, support and mutual effort between the NSPBCP and the data submitters throughout the Atlantic Provinces.

Table 3 shows an improved Percent capture of the SCIG distribution data for all the Atlantic Provinces except Prince Edward Island during the time period of this report from what it was in 2013/14.

Table 3: Percent Capture for SCIG

Province	Percent Capture 2012-2013	Percent Capture 2013-2014	Percent Capture 2014-2015
New Brunswick	79.6	73.7	81.5
Nova Scotia	69.6	37.7	92.5
Prince Edward Island	59.2	98.6	91.2
Newfoundland and Labrador	117.3	92.1	92.4

6 Prevalence and Incidence of the Use of IVIG and SCIG in the Atlantic Provinces

The study of prevalence and incidence of cases using IVIG and SCIG is used to understand the variation in the trends of IVIG and SCIG distribution over a period of time. Population data used to calculate prevalence and incidence was taken from the website of Statistics Canada.

6.1 Incidence

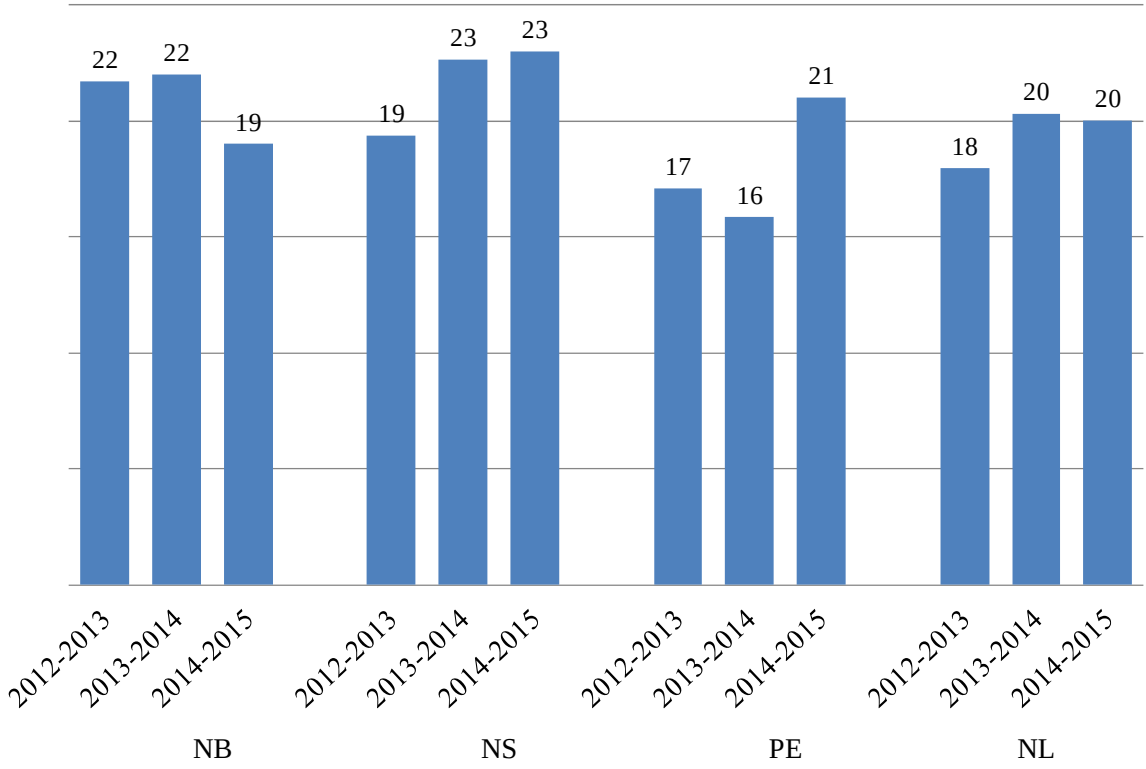
Incidence refers to the rate at which new cases of a disease occur in a population during a specified period. It is also calculated per 100,000 population to avoid display in decimals.

Figure 8 shows yearly provincial comparison of the incidence rates of patients requiring either IVIG or SCIG treatment in the Atlantic provinces over the last three fiscal years.
The incidence of cases requiring IVIG/SCIG decreased in New Brunswick from 22 new cases per 100,000 last year to 19 new cases this year. The incidence rate remained the same for Nova Scotia at 23/100,000 population and Newfoundland and Labrador at 20/100,000 in 2014/15 as it was in 2013/2014.

Prince Edward Island, exhibited a rise in the incidence from16/100,000 population in 2013/14 to 21/100,000 population in 2014/15.

Figure 8

Incidence of Cases on IVIG and SCIG
(per 100,000 pop)



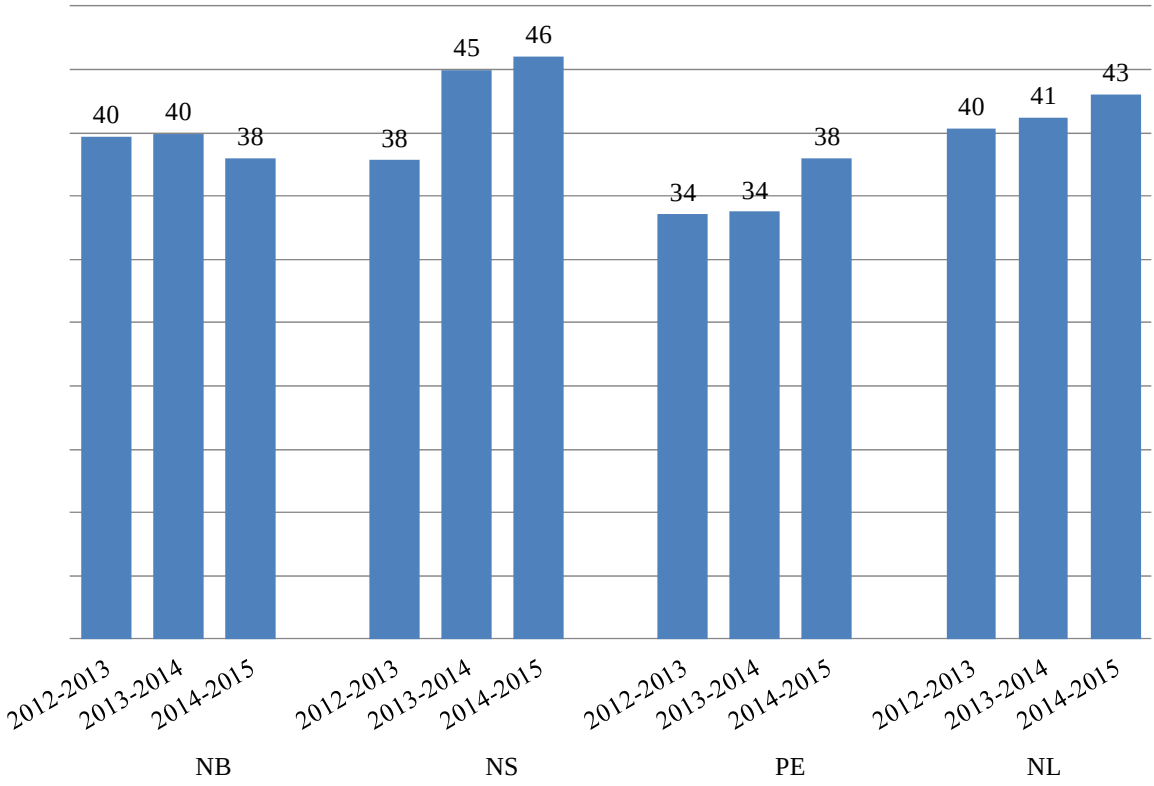
6.2 Prevalence

Prevalence is broadly defined as the proportion of individuals in a population having a disease. In this case, prevalence refers to the proportion of individuals (calculated per 100,000 population) that are receiving IVIG and/or SCIG.

Figure 9 shows that the prevalence rate for individuals requiring either IVIG or SCIG decreased for New Brunswick from 40 cases per 100,000 to 38 cases per 100,000 population. Prevalence rate increased the otherthree Atlantic provinces; for Prince Edward Island from 34 cases per 100,000 in 2013/14 to 38 cases per 100,000 in 2014/15; for Nova Scotia from45 to 46 cases per 100,000; and for Newfoundland and Labrador from 41 per 100,000 from 43 per 100,000 in 2014/15

Figure 9

Prevalence of Cases on IVIG and SCIG
(per 100,000 pop)



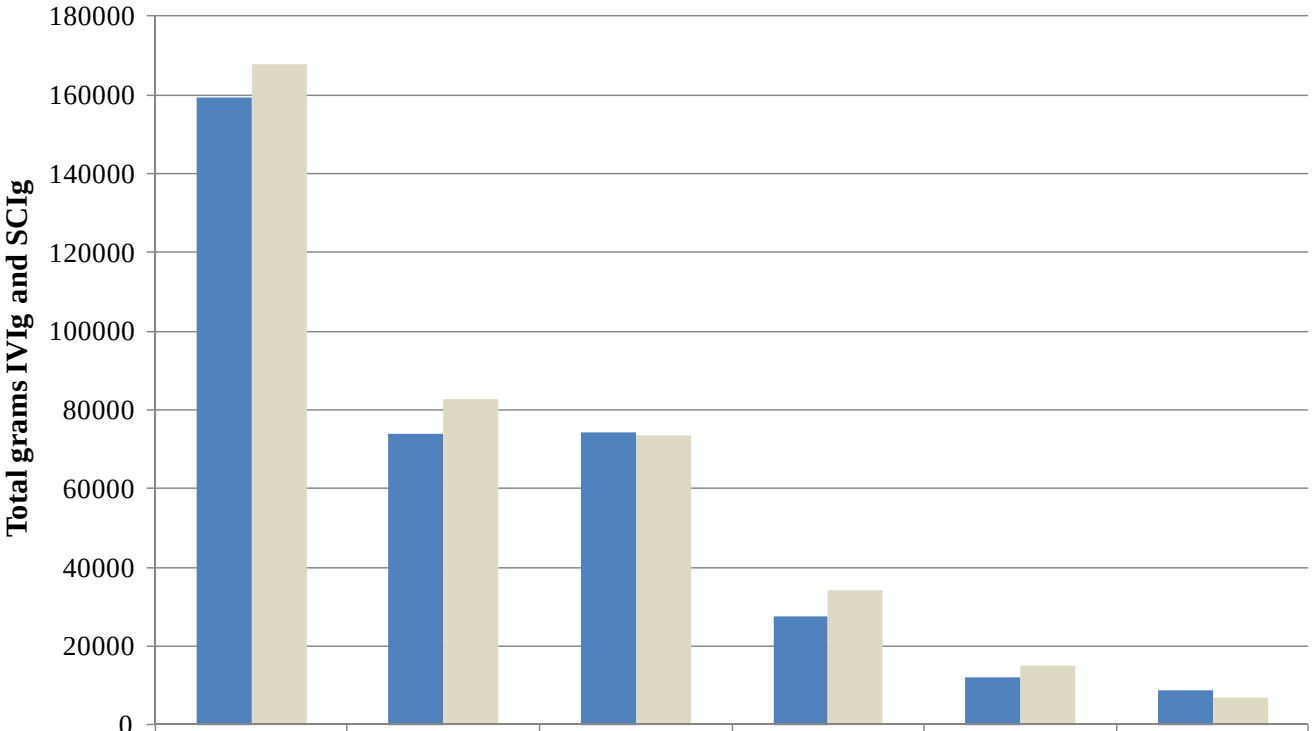
7 Disease Categories and Indications

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 10 shows the total grams of Atlantic IVIG and SCIG used by major disease categories in the last two fiscal years. It is important to consider that the disease category is based on the categorization of the indication for use and does not necessarily reflect the specialty of the ordering physician.

Figure 10

IVIG and SCIG (g) Use By Disease Category in the Atlantic Provinces



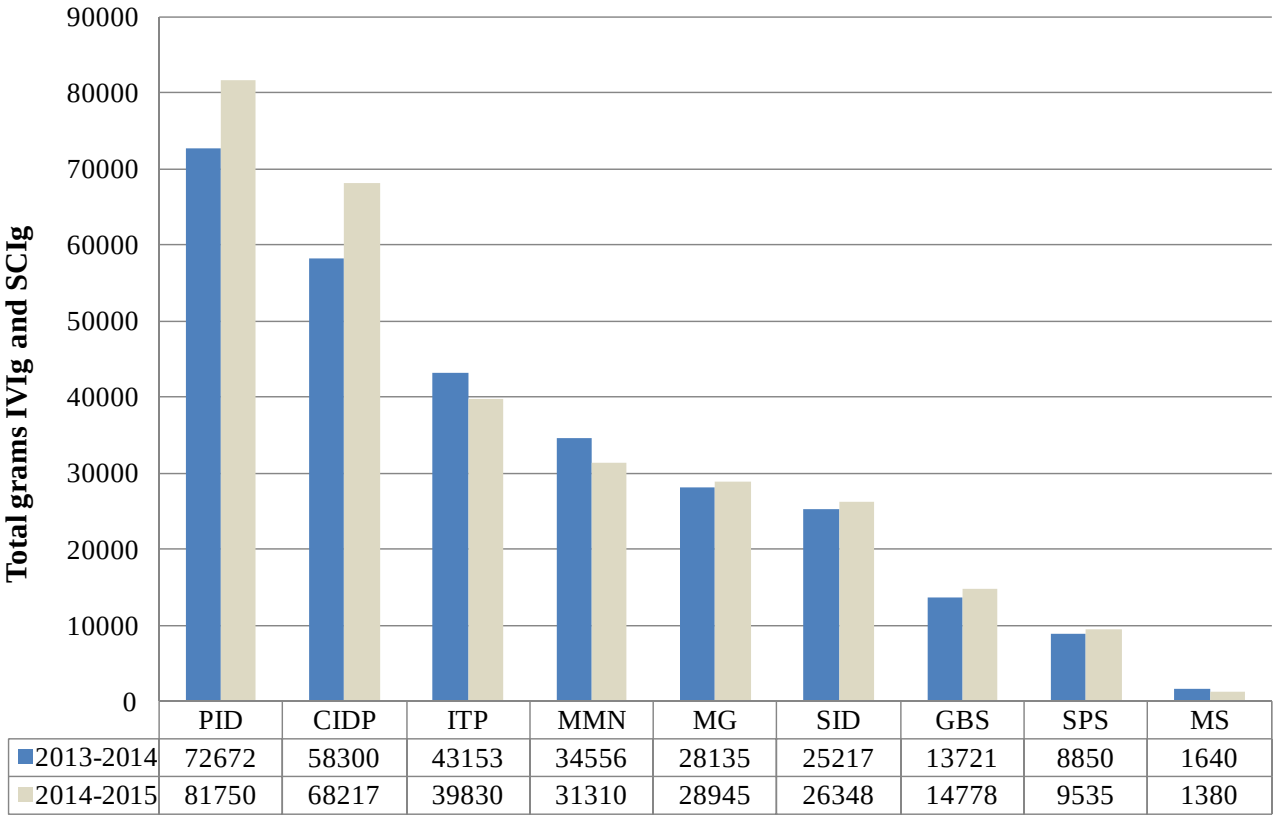
	Neurological	Immunological	Hematological	Rheumatological	Dermatological	Other
2013-2014	159415	74071	74187	27428	12258	8634
2014-2015	167702	82806	73532	34247	15117	7030

There was a rise in use of IVIG and SCIG for neurological conditions by 5%, immunological conditions by 12%, rheumatological conditions by 25%, and dermatological conditions by 23% in 2014/15 of what it was in 2013/14. Hematology conditions saw a *decrease* of 655 grams exhibiting a decline by 0.9% of what it was in the previousyear. All other disease categories are analyzed as a combined category named 'other', the use declined in this category by 18.6% in 2014/15 of what it was in 2013/14.

Figure 11 shows the total IVIG and SCIG used in each of the most common indications in the Atlantic Provinces in the last three fiscal years.

Figure 11

IVIG and SCIG Use by Indication in the Atlantic Provinces



	PID	CIDP	ITP	MMN	MG	SID	GBS	SPS	MS
2013-2014	72672	58300	43153	34556	28135	25217	13721	8850	1640
2014-2015	81750	68217	39830	31310	28945	26348	14778	9535	1380

The highest use was for Primary Immune Deficiency (PID) and Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP). In 2014/15 the use of IVIG/SCIG increased in Primary Immune Deficiency, Chronic Inflammatory Demyelinating Polyradiculoneuropathy, Myasthenia Gravis (MG), Guillain-Barre Syndrome (GBS) and stiff person syndrome . The use decreased for Immune Throbocytopenic Purpura (ITP), Multifocal Motor Neuropathy (MMN), and Myesthenia Gravis (MG) in 2014/15.

Graphs showing provincial utilization of IVIG and SCIG for all nine most common indications for IVIG/SCIG use can be found in Appendix A.

Table 4 shows the comparison of the top five indications by usage of IVIG and SCIG (g) in each Atlantic province during 2014/15. While not all provinces have the same top three indications for use, they do all share commonalities in their lists.

Table 4: Top Indications

NB		NS		PE		NL	
Indication	**g**	**Indication**	**g**	**Indication**	**g**	**Indication**	**g**
PID	18489	PID	47830	CIDP	8680	CIDP	17830
SID	14690	CIDP	27208	MMN	4310	PID	11740
CIDP	14499	ITP	15157	PID	3691	MG	11563
ITP	13918	MG	11645	SPS	2120	SLE	9959
MMN	6875	MMN	10980	PM	1680	ITP	9295

In 2014/15 the highest amount of IVIG/SCIG was used for Primary immune deficiency in Nova Scotia and New Brunswick. This was the second and third ranked indication by amount of IVIG/SCIG use in Newfoundland and Labrador and Prince Edward Island respectively. Use of IVIG for Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) was ranked highest in Newfoundland and Labrador and Prince Edward, second and third in Nova Scotia and New Brunswick respectively. High use of IVIG and SCIG for PID reinforces the importance of regularly monitoring IgG levels to ensure dosing is appropriate.

8 Request Approval Process

In an effort to optimize the appropriate use of IVIG, the Atlantic Blood Utilization Strategy (ABUS) Working Group developed an Atlantic-wide IVIG request approval system. Through this process, requests for IVIG are reviewed to determine if the indication, as well as the dosing, frequency and duration of treatment, meet the guidelines for its' use. In the event of a discrepancy, the ordering physician is contacted and discussion ensues regarding the variation. If the ordering physician continues to feel that a given case merits a change from the guidelines, he or she is asked to discuss the case with a consultant with the relevant clinical expertise. The pathway thus taken by the request is allocated a number representing the route it took for its approval. These pathway numbers are recorded and submitted for each and every new request of IVIG. A detailed guide of the request approval pathway numbers is attached as Appendix C at the end of the report.

The distribution of the Atlantic request approval pathways taken by new IVIG orders during 2014/15 is as follows: 1048 requests passed through the approval process. There were 979 (93%) requests that met the guidelines upon initial submission. Out of the remaining 69, 30 (43.5%) were for indications not listed in the guidelines (non neurology, non immunology and non hematology patients). Of the remaining, consultation occurred between Blood Transfusion Services staff and clinical expert in (36

out of 39=92% of the cases). Where consult happened, 15 (41.6%) were revised to meet the guideline after consultation with Blood Transfusion Services staff or clinical expert, 20 were dispensed as requested despite consultation with a clinical expert, 1 request was **withdrawn** after the ordering MD consulted with the clinical expert and 3 were dispensed as requested without a clinical expert consultation.

Generally speaking, the request approval process has improved compliance with the guidelines.

Pathway	Description	NB	NS	PEI	NL	Atlantic
1	Request was for an indication not listed in the guidelines	17	7	4	2	30
2	Request met the guidelines upon initial submission	233	424	45	277	979
3	Request was **revised** to meet the guidelines after discussion with BTS staff	1	7	4	1	13
4	Request was **withdrawn** after discussion with BTS staff	0	0	0	0	0
5	Request was **revised** to meet the guidelines after the ordering MD consulted with the clinical expert	0	1	1	0	2
6	Request was **withdrawn** after the ordering MD consulted with the clinical expert	0	0	0	1	1
7	The original request was granted even after the ordering MD consulted with the clinical expert	0	7	5	8	20
8	Consultation with the clinical expert was required but did not occur	1	2	0	0	3
Total		252	448	59	289	1048

9 Appropriateness of Use

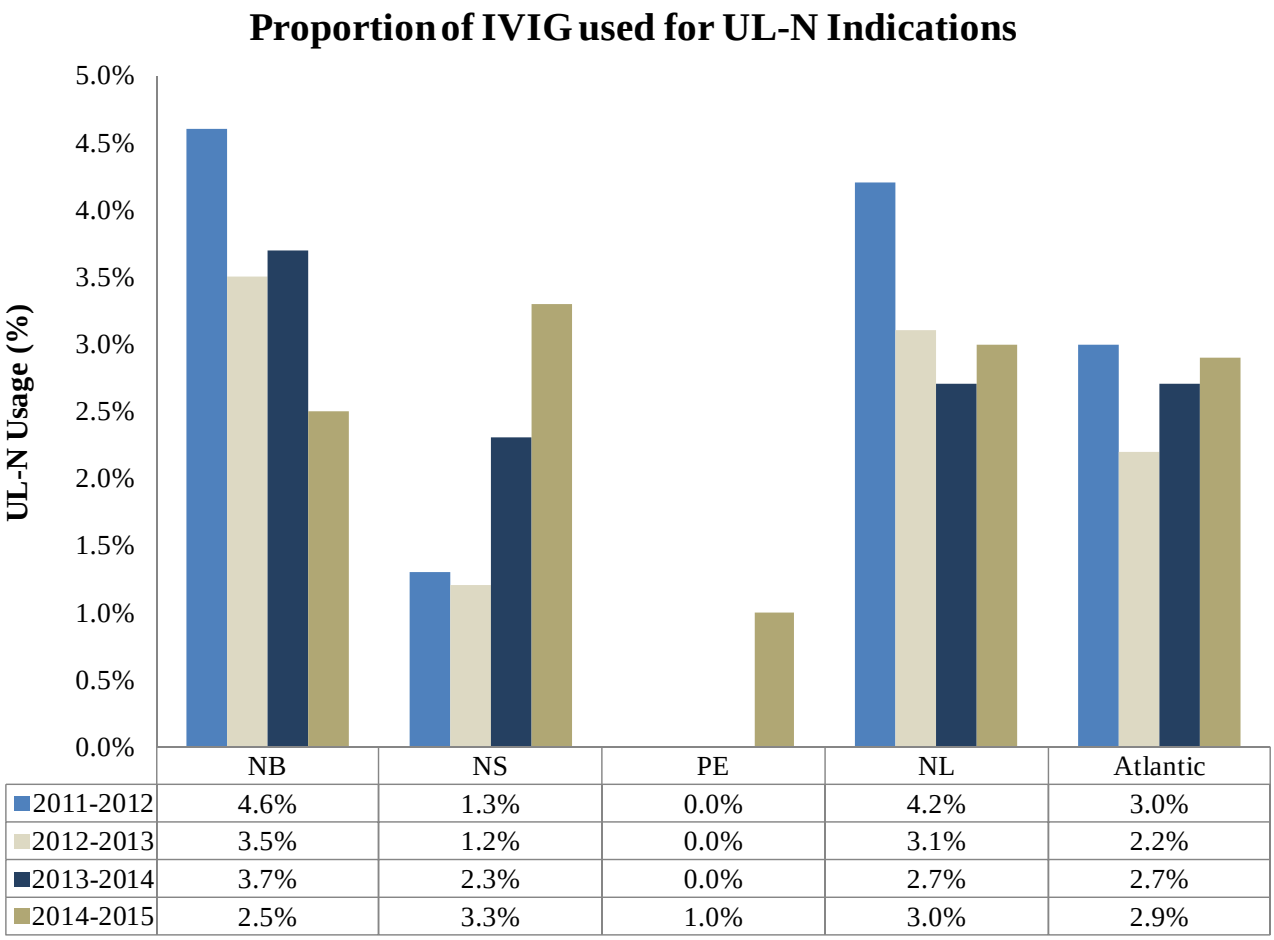
9.1 Appropriateness of Indications

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

Category	Explanation
L (labeled/licensed)	The manufacturer can advertise the use of IVIG for these conditions.
UL-I (unlabeled, indicated)	The manufacturer cannot advertise the use of IVIG for these conditions, but there is some evidence to support its use.
UL-N (unlabeled, not indicated)	There is no evidence to support the use of IVIG for these conditions.
II (insufficient information)	The NSPBCP was unable to obtain sufficient information. 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 12 shows the proportion of IVIG used for Unlabelled, not indicated (UL-N) conditions in the Atlantic Provinces.

Figure 12



	NB	NS	PE	NL	Atlantic
2011-2012	4.6%	1.3%	0.0%	4.2%	3.0%
2012-2013	3.5%	1.2%	0.0%	3.1%	2.2%
2013-2014	3.7%	2.3%	0.0%	2.7%	2.7%
2014-2015	2.5%	3.3%	1.0%	3.0%	2.9%

This year, Atlantic use of IVIG for UL-N indications was 2.9% of the total use. New Brunswick decreased the IVIG use for UL-N indications to 2.5% from 3.7% last year. Newfoundland and Labrador increased utilization of IVIG for UL-N indications to 3.0% from 2.7% last year; Prince Edward Island increased utilization of IVIG for UL-N indications to 1.0% from zero last year and Nova Scotia increased utilization of IVIG for UL-N indications to 3.3% from 2.3% last year

In 2014-15, SCIG was used for indications other than Primary immune deficiencies. 532 grams of SCIG was used for one patient with secondary immuned deficiency in Nova Scotia; and 362 grams of SCIG was used for one patient with Wegener's Granulomatosis in Newfoundland and Labrador. Prince Edward Island did not have any UL-N indications for IVIG in the previous three fiscal years.

Following are the Atlantic UL-N indications for IVIG during 2014/15 fiscal year by total grams utilized

Indication	IVIG(grams)
1. Chronic Urticaria	3,027.5
2. Rapid-Onset Obesity with Hypothalamic Dysfunction, Hypoventilation and Autonomic Dysregulation (ROHHAD)	1,350
3. Transverse Myelitis	1,045
4. Diabetic Neuropathy	845
5. Pure Red Cell Aplasia	570
6. Renal Failure	520
7. Crohn's Disease	502.5
8. Asthma	420
9. Bronchial infections	305
10. Polyarthritis/polychondritis/lytic bone lesions	275
11. Hematopoietic stem cell or bone marrow transplantation	270
12. Paraneoplastic Cerebellar Degeneration	237.5
13. Cellulitis	210
14. Thrombotic thrombocytopenic purpura	205
15. Acute Hemolytic Anemia	180
16. Anti-NMDA Receptor Encephalitis	125
17. Paraneoplastic Neuropathy	125
18. Leukemia	110
19. Acute Myeloid Leukemia	70
20. Mantle Cell Lymphoma	40
21. Viral Encephalitis	20
22. Pulmonary embolism	13.6
23. Rheumatoid Arthritis	10
Total	**10,476.1**

Because the price per gram varies depending on both availability and U.S. dollar exchange rates, it is imperative that IVIG be utilized appropriately with the goal being to reduce the amount used for conditions where it is not likely to be of clinical benefit (UL-N indications) to

as close to zero grams as possible. Approximately $501,281 was spent for UL-N indications in Atlantic Canada this year.

Using the details provided in the province specific reports, NSPBCP recommends that the Medical Directors of the respective Blood Transfusion Laboratories initiate a dialogue with the prescribing physicians to reconsider the use of IVIG in these UL-N inidications.

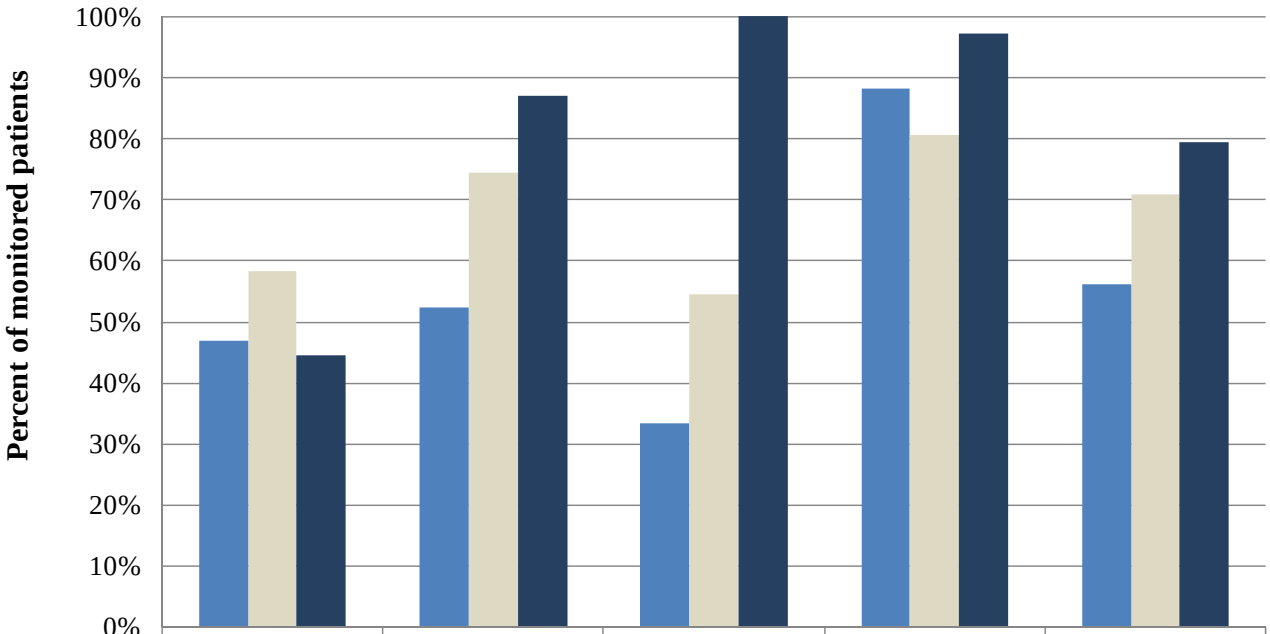
9.2 IgG Levels for Immune Deficiencies

When patients are receiving IVIG or SCIG for the treatment of immune deficiencies, it is recommended that serum IgG levels be measured on a regular basis and the dose of IVIG and SCIG be adjusted to keep the IgG level between the target range of 7 and 10g/L.

Figure 13 shows the proportion of patients with PID who had their IgG levels monitored. The frequency of monitoring cannot be inferred from this graph.

Figure 13

Proportion of Primary Immunodeficiency cases with monitored serum IgG levels



	NB	NS	PE	NL	Atlantic
2012-2013	47%	52%	33%	88%	56%
2013-2014	58%	74%	55%	81%	71%
2014-2015	44%	87%	100%	97%	79%

In 2014/15, 79% of Atlantic patients with primary immune deficiencies had their serum IgG levels monitored and reported. Improvement in monitoring and reporting of serum IgG levels was observed in Nova Scotia with a 13% increase, to 87% of cases this year; and in Newfoundland and Labrador with a 16% increase, to 97% of cases this year. In Prince Edward Island, 100% of their Primary immune deficiency patients had their serum IgG levels monitored. New Brunswick exhibited a decline in the monitoring and reporting of serum IgG levels from 58% in 2013/14 to 44% in 2014/15.

Figure 14

Proportion of serum IgG by the target levels

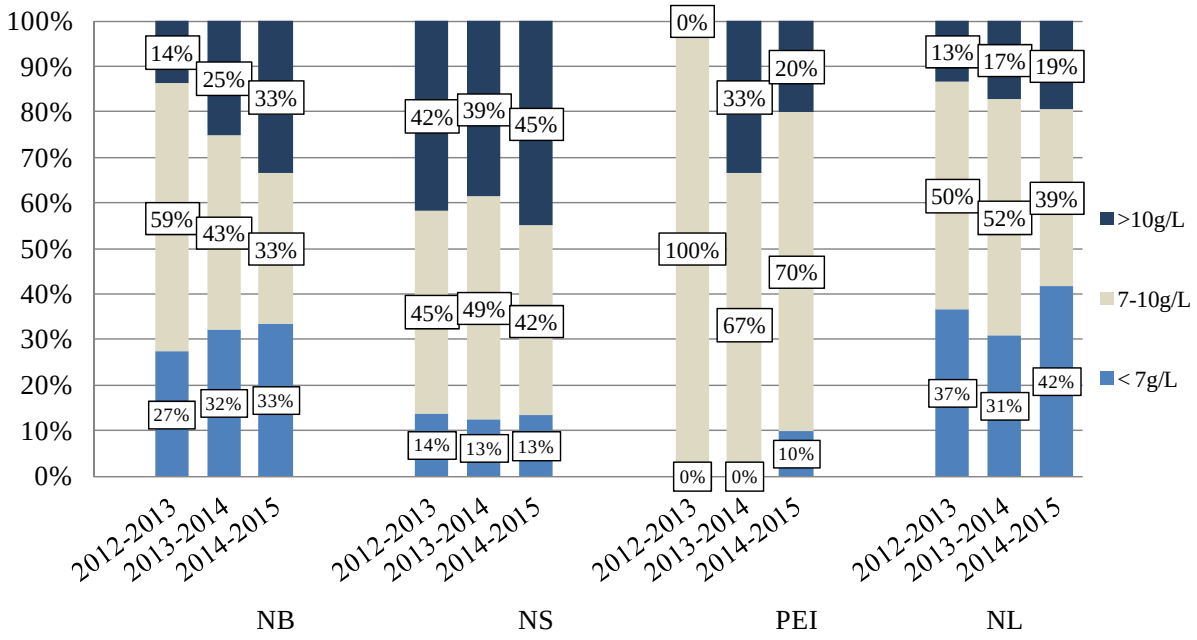


Figure 14 shows the total number of individuals (both pediatric and adult) with Primary Immune Deficiency, in each of the 4 provinces, who had their serum IgG levels monitored.

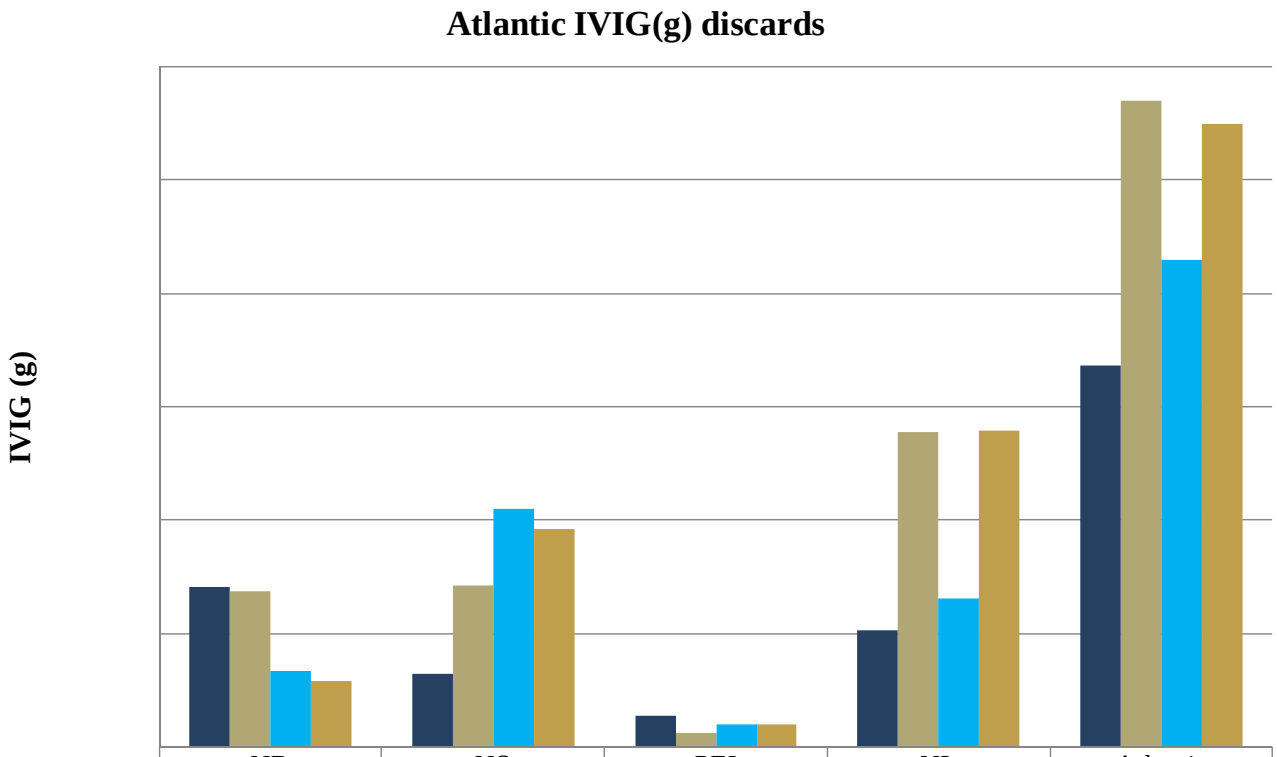
This monitoring helps identify those patients whose serum levels are above the target range of 7 to 10g/L and who *may* achieve the same clinical benefit with decreased dosing. In Nova Scotia, 45% of those monitored had their serum IgG level above 10g/L; likewise 33% in New Brunswick; 20% in Prince Edward Island and 19% in Newfoundland and Labrador had higher than target serum IgG levels.

For the first time this year, NSPBCP has included the details of the all the patients with serum IgG levels above the target range in the province specific reports NSPBCP recommends that the staff of the respective Blood Transfusion Laboratories share this information with the prescribing physicians and facilitate the follow up of these patients for dose adjustment.

10 Discards

The goal of the utilization management of the NSPBCP is to optimize appropriate use as well as to minimize wastage. Figure 15 shows a summary of the discarded IVIG during this past fiscal year in the Atlantic Provinces.

Figure 15



	NB	NS	PEI	NL	Atlantic
2011-2012	283	129	56	205	673
2012-2013	275	285	25	555	1140
2013-2014	135	420	40	263	858
2014-2015	115	385	40	558	1098

The total discards increased from 858 g in 2013/14 to 1,098 g in 2014/15.

Decreases in the discards were seen in New Brunswick and Nova Scotia from 135 grams and 420 grams in 2013/14 to 115 and 385 in 2014/15 respectively. Newfoundland and Labrador experienced a

rise in the discard from 263 grams to 558 grams. Prince Edward Island had 40 grams of discard, same as the discards for 2013/14.

The cause of the majority of wastage of IVIG in this fiscal year was breakage and in lab temperature/visually unacceptable.

Table 9 summarizes the reasons given for the amount (g) of discarded product discussed above.

Table 5: Reasons for IVIG discards

Reasons	NB	NS	PEI	NL	Atlantic
Broken	70	80	0	190	340
Expired	5	0	0	0	5
In lab temperature/visually unacceptable	0	0	0	340	340
Returned to lab temperature/visually unacceptable	40	85		15	140
Spiked not transfused/sterility/integrity of product compromised	0	220	40	13	273
Total	**115**	**385**	**40**	**558**	**1098**

The top most reason of discard in New Brunswick was “broken”; in Newfoundland and Labrador ‘in laboratory temperature/visually unacceptable’ and”, while “spiked, not transfused/sterility/integrity of product compromised” were cited as the top reason in Nova Scotia and Prince Edward Island. It is recommended that the data on discards continue to be collected and monitored. In order to minimize the discards, continuous education regarding the care for and the use of IVIG and early return of the unused products to the laboratory if not transfused should be emphasized.

As IVIG is safely stored at room temperature (between 2˚C-25˚C) according to the manufacturers’ inserts, it is recommended that product be stored at room temperature when possible to reduce wastage of product that has been returned to the lab more than 30 minutes after it was dispensed, and to reduce slippery condensation build up which has been anecdotally identified as a reason for breakage.

11 Dosing Intravenous Immune Globulin (IVIG) Based on Dosing Body Weight (DBW)

Adverse reactions like hemolysis are substantially more likely to happen when a high dose of IVIG is infused. Some Canadian jurisdictions have made recommendations to use adjusted weight based dosing instead of actual patient weight. Dosing weight, an intermediate between ideal body weight and actual body weight, was developed to more accurately dose IVIG. With most of the IVIG being used for appropriate indications and dosing, dosing IVIG based on an adjusted body weight rather than on actual weight may add to safety from hemolysis and may decrease the use of IVIG in patients with a high deviation from ideal body weight.

Actual body weight (which includes the weight of adipose tissue of the patient) is used for calculating the dose of fat soluble drugs. As intravenous immunoglobulin is not lipid soluble, an adjusted body weight is appropriate to use for dosing.

ABUS recommended the implementation of dosing of IVIG based on adjusted body weight in 2011/12 and a pilot implementation involving 131 patients was done. The following year, 2012/13, dosing body weight, or DBW, was implemented more widely across the Maritimes.

In order to calculate DBW implementation and savings, it was vital that all relevant data including pre-printed orders, patient demographics (including weight and height), and actual doses given, were all entered into the IVIN database. This was done either directly by the provinces (NS, NB, PEI) or via spreadsheet and uploaded by the NSPBCP (NL). In 2013/14, all patients receiving IVIG were included in the analysis of dosing body weight. In 2014/15 the order forms for patients with heights less than 5 feet are excluded. Since the patients with solid organ transplant and Gullian Barre syndrome are not dosed by dosing body weight they are also excluded from the analysis. If the order of IVIG is revised due to lack of clinical response then these are alse excluded from the analysis.
In 2013/14, the odd doses were not included in the analysis. In 2014/15 the corrections for the “odd doses” are made to the dosing body weight calculations.

Odd dose is a dose reported in IVIN that is different than actual ordered in the PPO. These doses are compared. Numbers are both rounded and truncated before comparison. For instance, if PPO dose is 20 and IVIN dose is 20.9 or 20.1 it will not fall into odd doses. If odd doses from IVIN can be converted into ordered dose then they are added to above calculations. For example if ordered dose is 50, but there are 2 doses of 25 in IVIN, it is considered as one dose of 50 for DBW savings analysis in the summary. Likewise, if AD = 50, but there is one dose of 100 in IVIN, 2 doses of 50 are included into the summary. Every time doses are added to the summary, corresponding Real Weight Dose (RWD) are also added.

The process for analysis of DBW data is as follows:

1. Get all PPOs up to the end of reporting period.

2. Exclude incomplete or invalid PPOs

3. Exclude PPOs with the following DBW reasons:

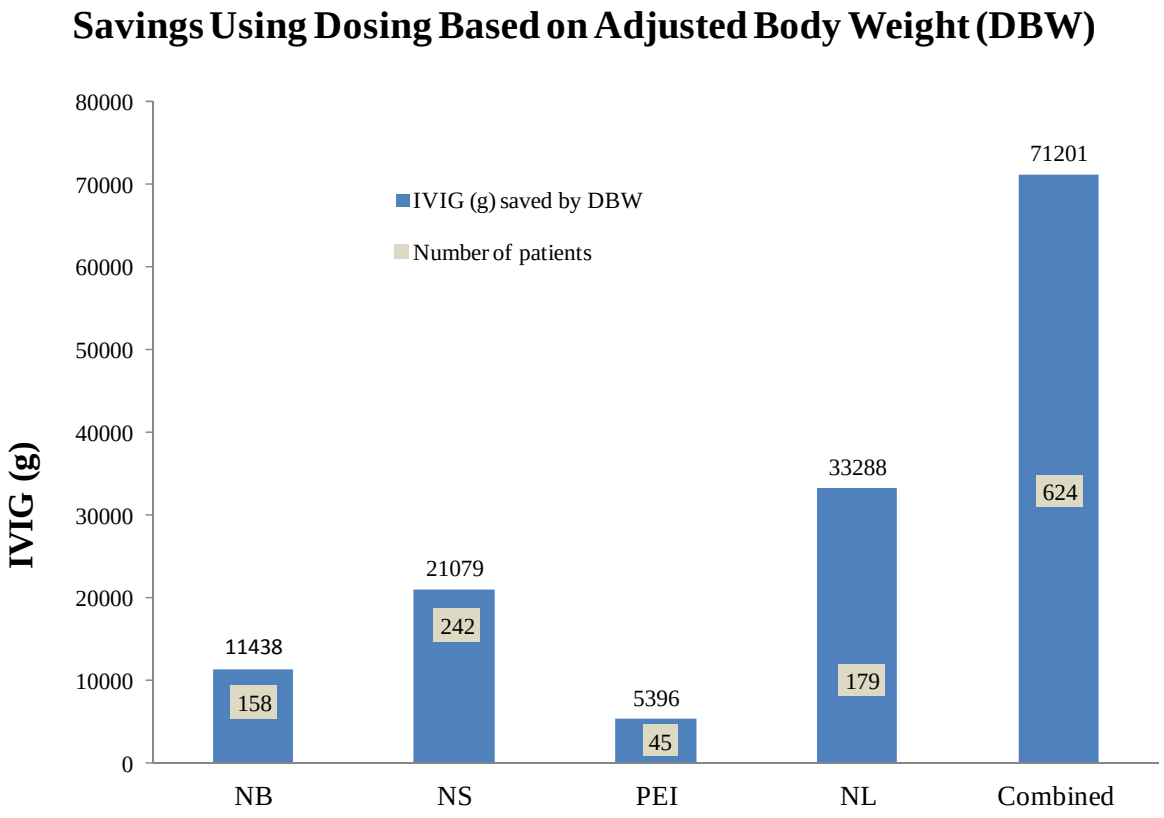
- GBS
- Lack of Expected clinical response
- height<152.3
- Solid Organ Transplant

4. Calculations are performed one patient at a time.
5. Calculate totals for each patient:
    - Number of doses is retrieved from IVIN = # IVIN doses
    - Real weight dose (RWD) = patient's weight times the dose in grams per kilogram from PPO
    - Total g by RWD = RWD multiplied # IVIN doses
    - Total g by AD = AD multiplied # IVIN doses
    - Ig (grams) avoided = Total g by RW – Total g by AD
    - Corrections for ODD doses is made

Challenges to analyzing this data experienced by all provinces included missing PPOs, missing heights, and odd doses (doses that did not match the order). It is because of one or more of these challenges that some doses or patients were not able to be included in the DBW analysis. The result of this is that the savings and number of patients affected as reported here may not represent the true value.

Figure 16 reveals the total grams saved of IVIG for this fiscal year and the number of patients dosed according to DBW.

Figure 16



In 2014/2015, 1008 Atlantic patients received immunoglobulin. Out of them 624 (62%) were dosed based on adjusted body weights resulting in an avoidance of 71, 201 grams worth $3,406,967

12 Subcutaneous Immunoglobulin

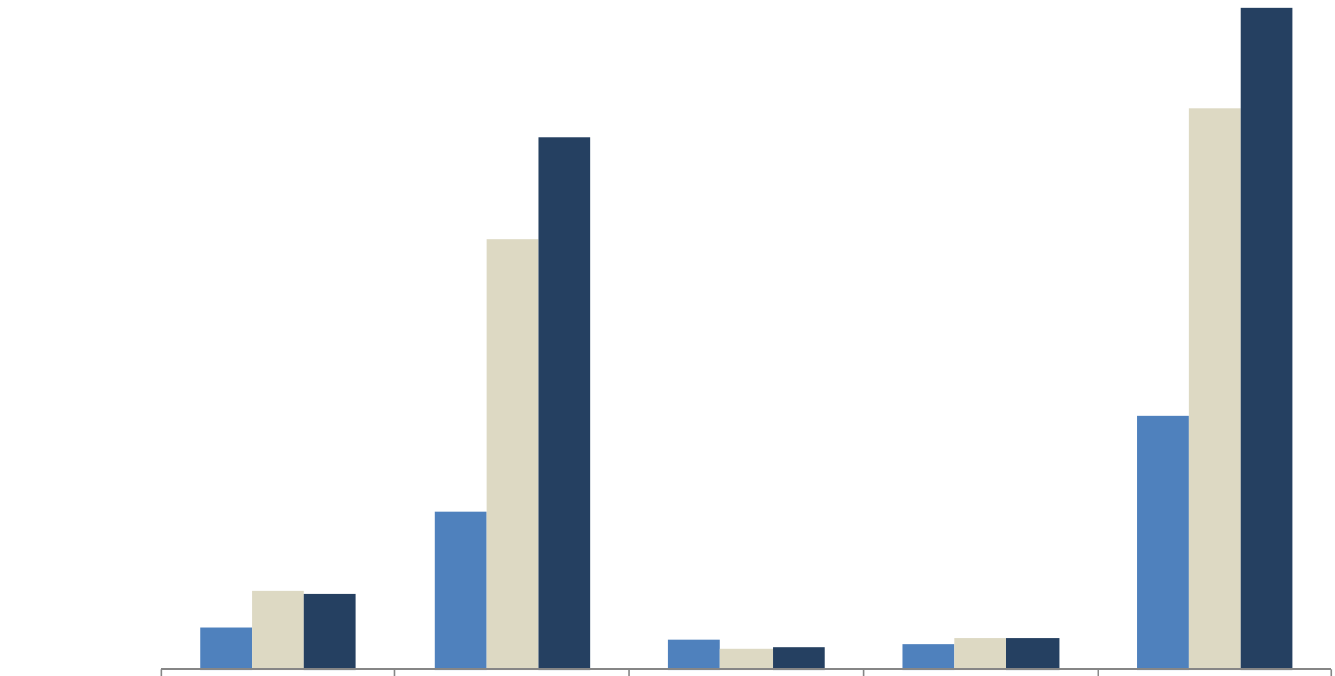
12.1 Atlantic Guidelines

In 2012, Atlantic guidelines for subcutaneous immunoglobulin Home Administration programs were approved and disseminated after stakeholder feedback and a pilot implementation. The guidelines included appropriate indications, dosing, and the patient education material for push and pump methods of self administration. At this time the only labeled use of SCIG is for PID. In Atlantic Canada, all but two patients are currently using it for treatment of PID. One patient in Nova Scotia is currently using it for Secondary immune deficiency and one patient in New found land and Labrador is using it for Wegener's Granulomatosis. To date there are no major issues reported with SCIG.

Figure 17 shows that there were 17518 grams of SCIG distributed in 2014/15, an increase from 14853g of SCIG distributed in the Atlantic Provinces in 2013/14. This is a marked increase by 18% from the previous year's distributed.

Figure 17

Distribution of SCIG (g) in the Atlantic Provinces



	NB	NS	PEI	NL	Atlantic
2012-2013	1120	4169	770	656	6715
2013-2014	2065	11393	558	837	14853
2014-2015	2010	14102	566	840	17518

In total there were 59 patients on SCIG in the Atlantic Provinces this year, up from 34 in 2013/14. There were 19 new patients on SCIG in Nova Scotia bringing a total to 45 cases in Nova Scotia. New Brunswick had 9 patients, Newfoundland and Labrador had 3, and Prince Edward Island had 2.

Home administration of SCIG has successfully helped transition patients from depending on hospital administration of this product to doing in the comfort of their own home.

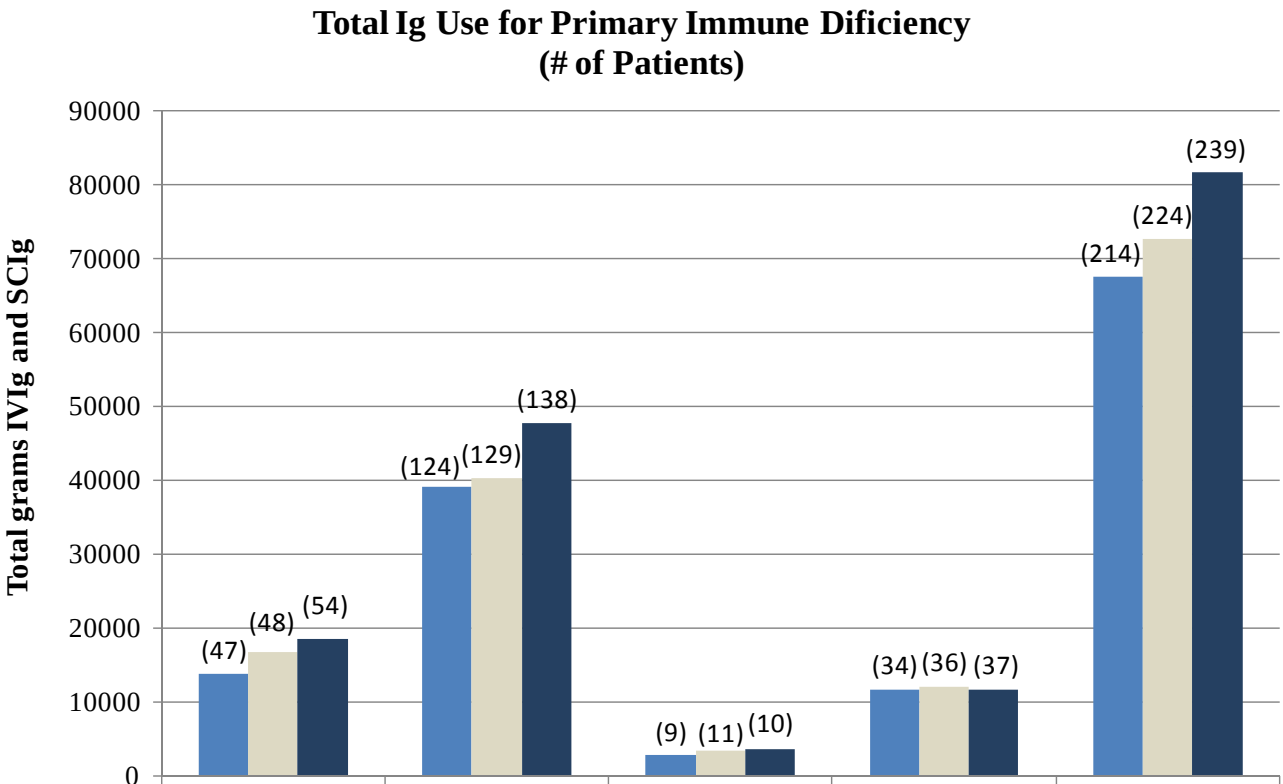
We expect this program to continue to grow in Atlantic Canada as patients and practitioners are becoming more aware of the health benefits and cost savings associated with home administration.

Table 6: Number of SCIG Patients

Fiscal Year	Province	# Patients Receiving SCIG	Number of New SCIG Patients	Failed SCIG
2013-2014	NB	6	2	0
	NS	27	6	2
	PE	2	0	0
	NL	3	1	0
	Atlantic	38	9	2
2014-2015	NB	9	2	0
	NS	45	19	0
	PE	2	0	0
	NL	3	0	0
	Atlantic	59	21	0

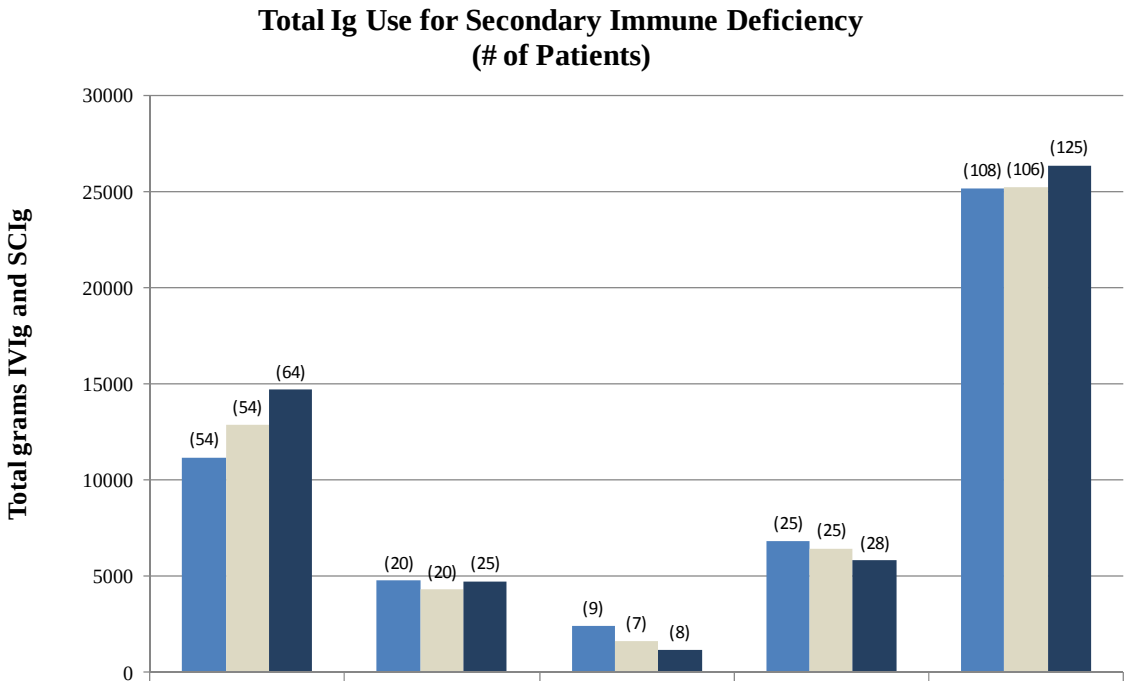
Appendix A per Capita Utilization of IVIG for Most Common Indications

Figure A1



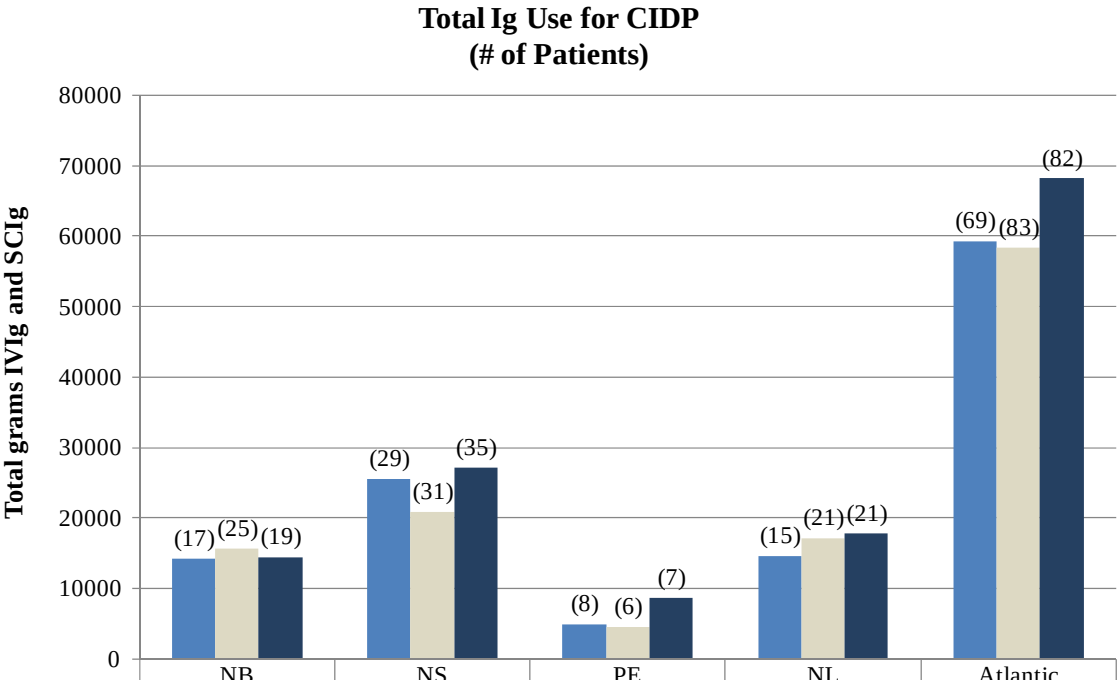
	NB	NS	PE	NL	Atlantic
2012-2013	13761	39165	2781	11752	67459
2013-2014	16884	40258	3460	12070	72672
2014-2015	18489	47830	3691	11740	81750

Figure A2



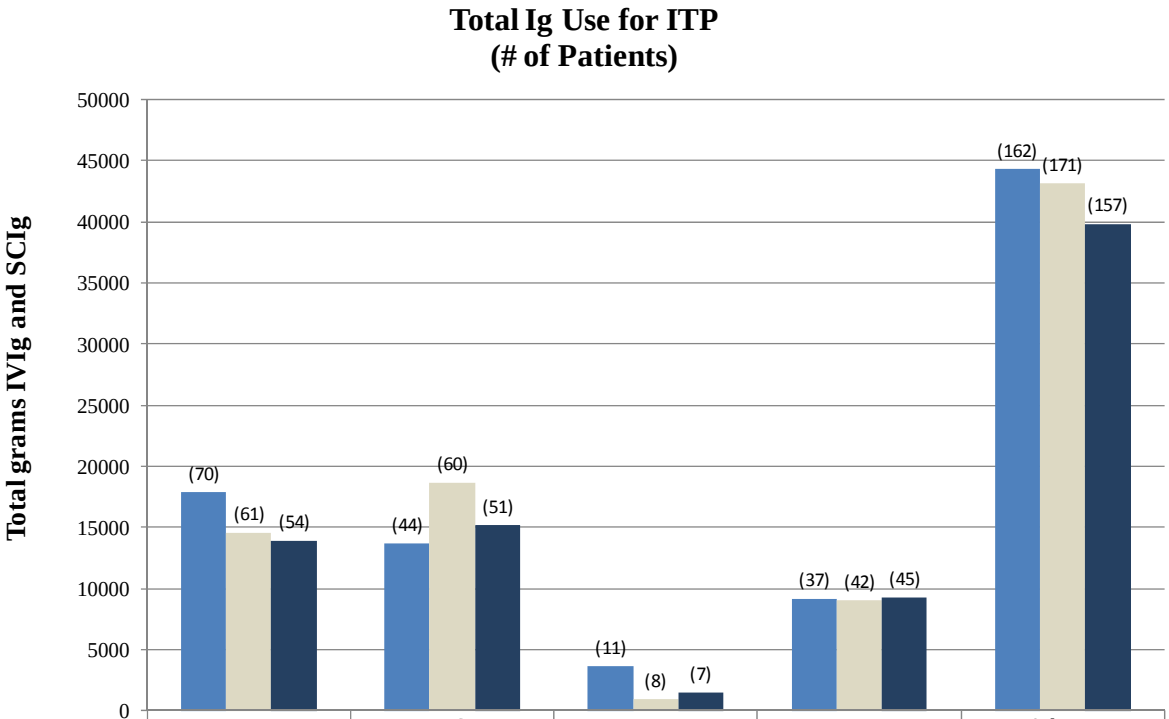
	NB	NS	PE	NL	Atlantic
2012-2013	11163	4753	2425	6833	25174
2013-2014	12855	4285	1640	6437	25217
2014-2015	14690	4722	1140	5796	26348

Figure A3



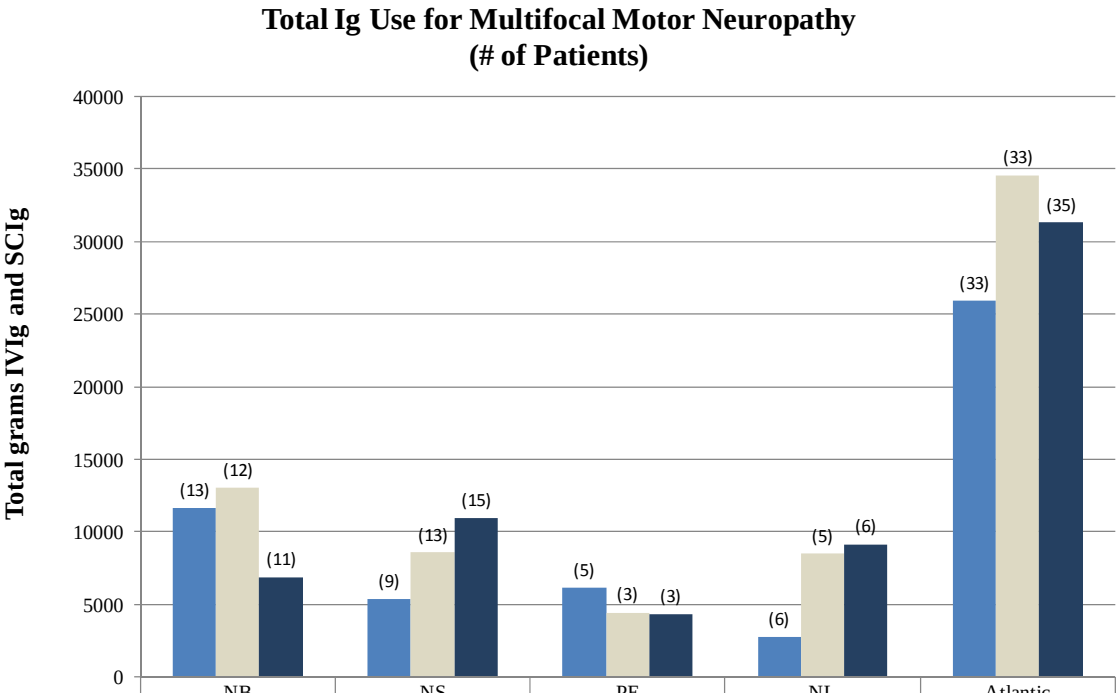
	NB	NS	PE	NL	Atlantic
2012-2013	14183	25547	4955	14635	59320
2013-2014	15585	20960	4590	17165	58300
2014-2015	14499	27208	8680	17830	68217

Figure A4



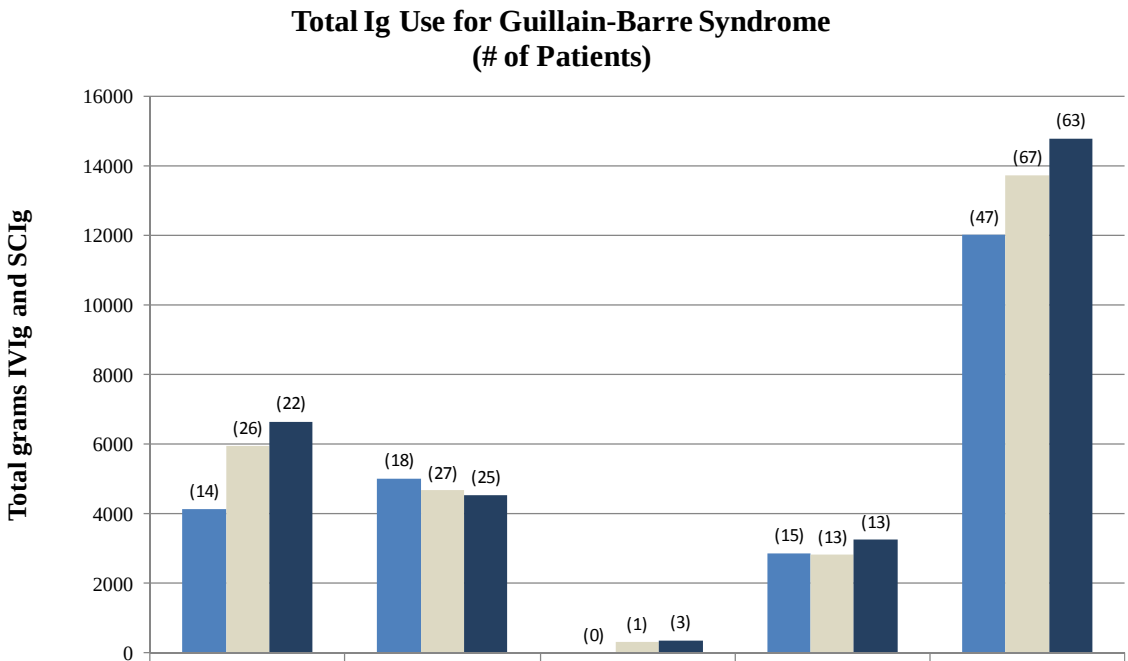
	NB	NS	PE	NL	Atlantic
2012-2013	17839	13670	3599	9193	44300
2013-2014	14547	18641	935	9030	43153
2014-2015	13918	15157	1460	9295	39830

Figure A5



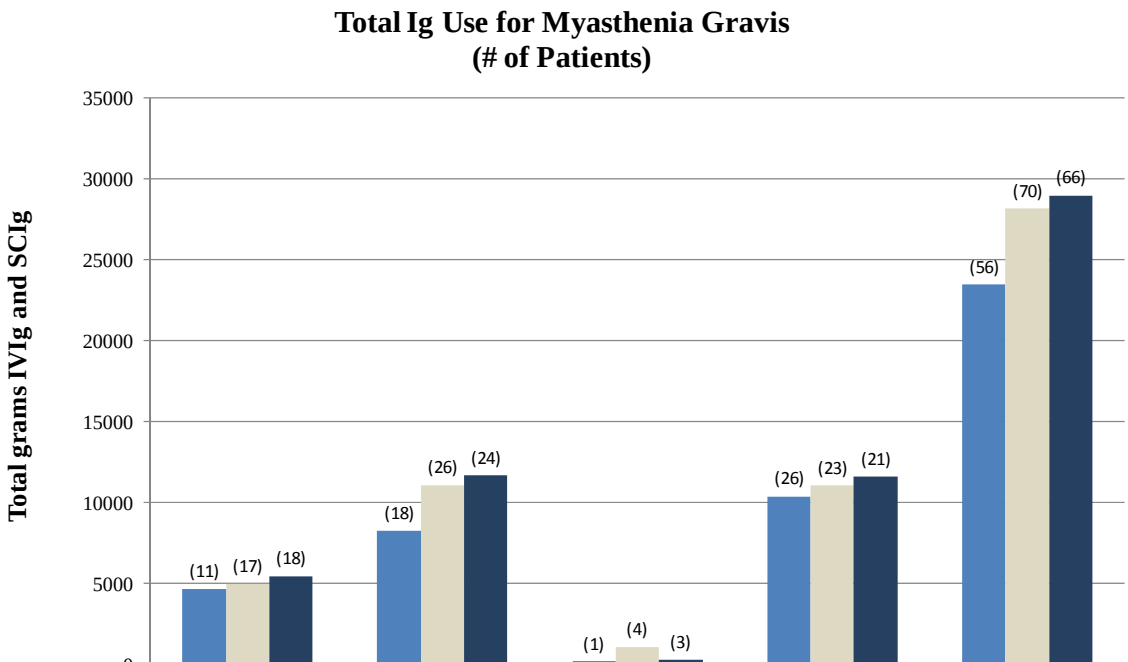
	NB	NS	PE	NL	Atlantic
2012-2013	11638	5395	6135	2725	25893
2013-2014	13061	8575	4450	8470	34556
2014-2015	6875	10980	4310	9145	31310

Figure A6



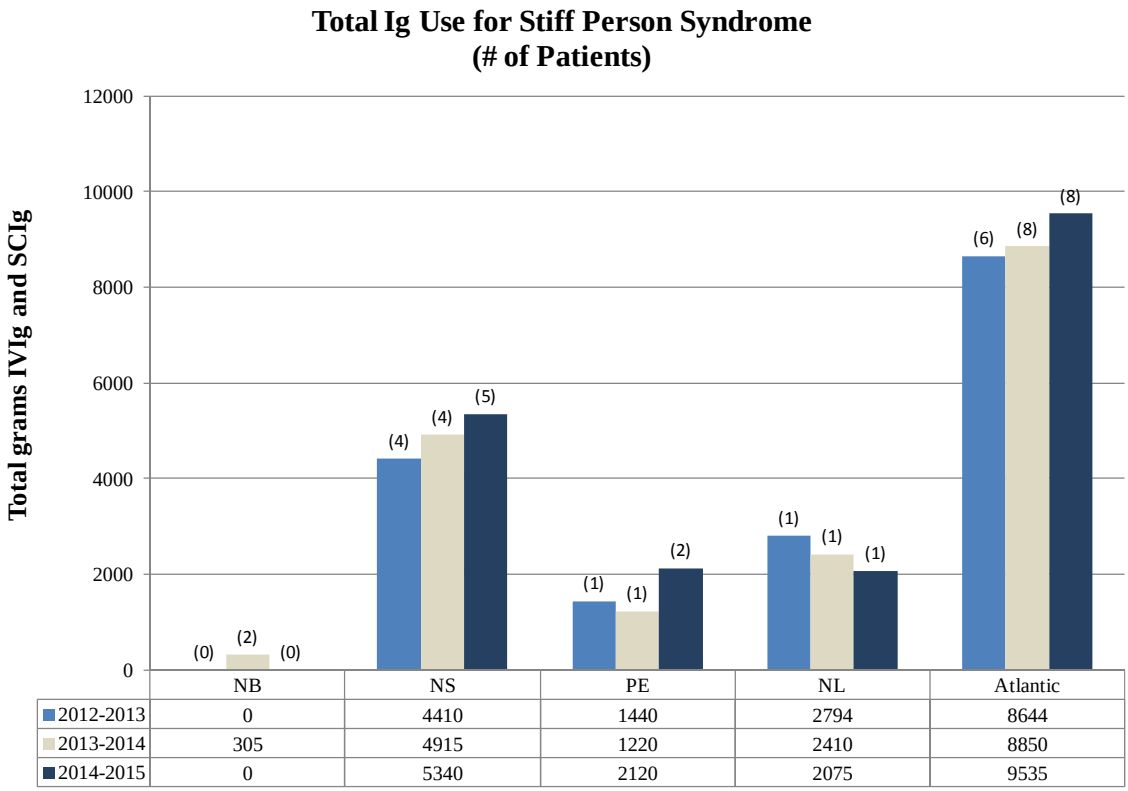
	NB	NS	PE	NL	Atlantic
2012-2013	4125	5011	0	2873	12008
2013-2014	5942	4655	300	2825	13721
2014-2015	6646	4523	355	3255	14778

Figure A7



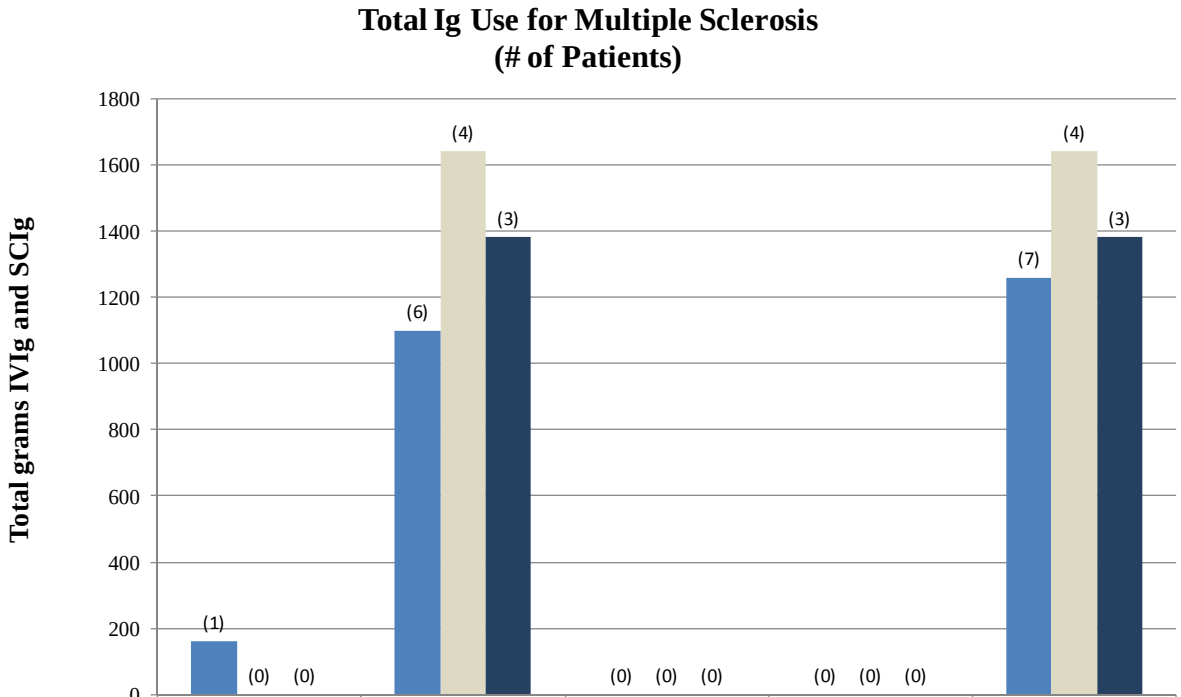
	NB	NS	PE	NL	Atlantic
2012-2013	4644	8218	175	10389	23426
2013-2014	4988	11065	1060	11022	28135
2014-2015	5438	11645	300	11563	28945

Figure A8



	NB	NS	PE	NL	Atlantic
2012-2013	0	4410	1440	2794	8644
2013-2014	305	4915	1220	2410	8850
2014-2015	0	5340	2120	2075	9535

Figure A9

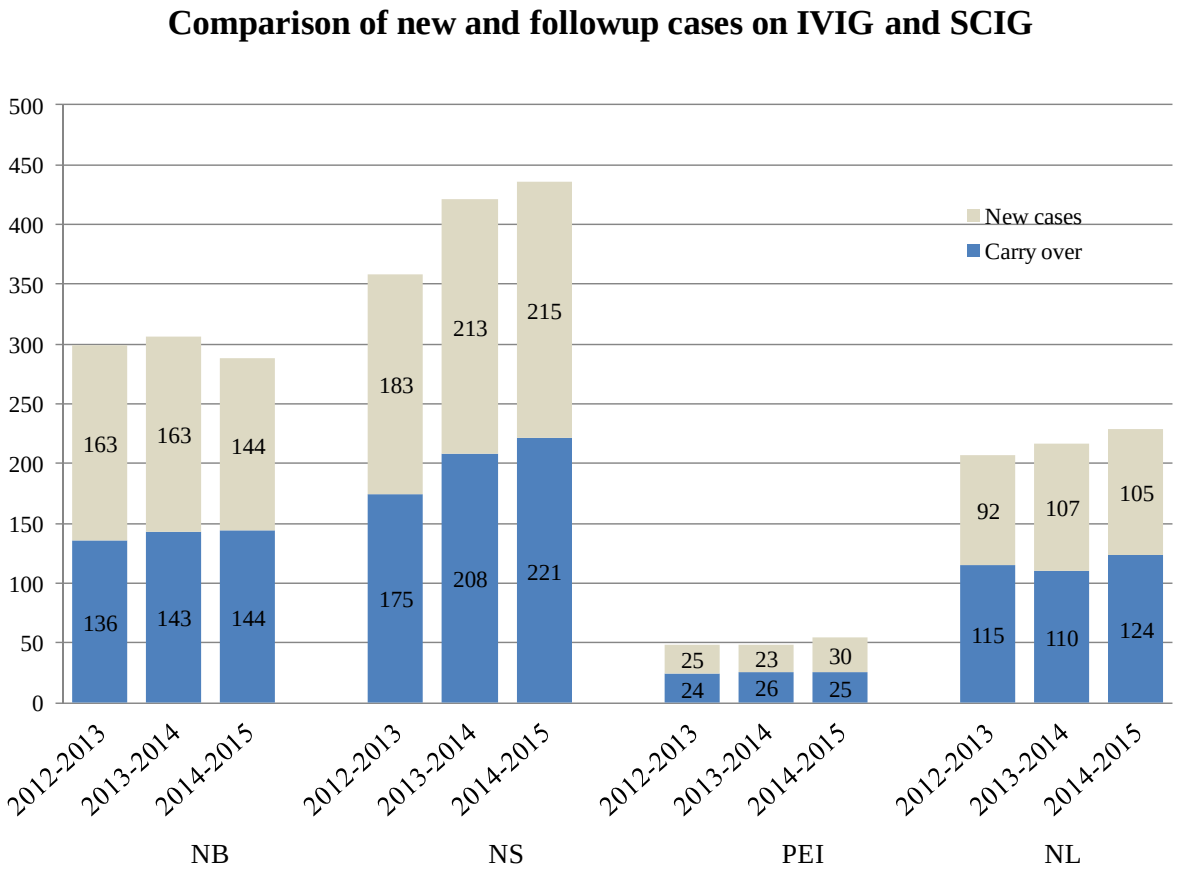


	NB	NS	PE	NL	Atlantic
2012-2013	160	1099	0	0	1259
2013-2014	0	1640	0	0	1640
2014-2015	0	1380	0	0	1380

Appendix B Year to Year New and Carry Over Patients on IVIG and SCIG

Figure B1 below shows the distribution of new and carry over patients (both Adult and Pediatric) in each Atlantic province from 2010/11 to 2013/14.

Figure B1



Appendix C Request Path Numerical Code Guide

1 Request was for an indication not listed in the guidelines

2 Request met the guidelines upon initial submission

3 Request was revised to meet the guidelines after discussion with BTS staff

4 Request was withdrawn after discussion with BTS staff

5 Request was revised to meet the guidelines after ordering MD consulted with the Clinical expert

6 Request was withdrawn after the ordering MD consulted with the clinical expert

7 The original request was granted even after the ordering MD consulted with the Clinical expert

8 Consultation with the clinical expert was required but did not occur