National Immunoglobulin Governance Program Impact Evaluation

National Blood Authority

Final Report - May 2021

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Evaluation summary of the Ig Governance Program

Introduction and context

Immunoglobulin (Ig) is a critical therapy used to support patient immune response for a wide array of conditions. Since 2004, the National Blood Authority (NBA) has been responsible for the provision of Ig products in Australia.

In 2014, NBA introduced the National Ig Governance Program (the Program) which aimed to ensure that the clinical needs of patients who need Ig can be met sustainably into the future. The Program comprises five elements: The National Policy (the Policy), The Criteria for the Clinical Use of Ig in Australia (the Criteria), The Blood System for Tracking Authorisations and Reviews (BloodSTAR), committees and interest groups; and the National Ig Governance Program Performance Improvement Strategy.

This evaluation and our approach

This evaluation has sought to assess the impact of the Program and three of its components (the Policy, the Criteria and BloodSTAR) on Ig usage in Australia, with a focus on: (1) how Ig use has changed since the introduction of the Program, (2) the drivers for the change, and (3) the impact of the Program components individually and collectively on Ig demand and costs. The period assessed includes data from Jul-2009 to Dec-2020 from STARS (owned by Australian Red Cross Lifeblood) and BloodSTAR.

Key findings

Prior to the introduction of the Program, Ig usage per 1,000 population grew at 8.0% pa on average from 2009 until 2013. While continuing to grow, the analysis identifies that the Ig growth rate per 1,000 dropped 9%, to a growth rate of 7.3% during the implementation of the Program (2014-2019). From 2019 onwards (the post implementation period), the growth rate per 1,000 dropped even further (31%) to an average of 5.1%. We note the shorter time period of the post implementation period. The total Ig usage growth rate pre-, during and post-implementation of the Ig Program is 10.4%, 9.6% and 7.3% pa, respectively. It dropped 7% during the implementation and then dropped further 24% after the implementation of the Program.

The reduction in Ig growth rate is primarily driven by a reduction in the growth rate of Ig patients of 66% from the implementation to post-implementation period of the Program. All other factors assessed related to Ig use such as Ig dosage, age and weight which have slightly increased during and post-implementation of the Ig Program. No major changes are observed in the top 10 medical conditions during the period analysed. Further, there is a correlation between the Program key components and decreasing use of Ig, most notably following the introduction of Version 3 of the Criteria and BloodSTAR.

Stakeholders to this evaluation observed that clinical awareness of the Program and its applicability has grown. BloodSTAR's inbuilt guidance has driven standardisation and the automation of components of the approval process appear to have delivered efficiency gains. Additionally, clinicians report to have greater opportunity to input to the Ig Governance framework.

Impact on Ig cost

The reduction of Ig growth, driven by the implementation of the Program, as well as other factors, is estimated to have delivered a cost saving of $71 million between July 2019 and December 2020. Year on year savings ranging from approximately $17 million in 2020-21 to $479 million in 2030-31 can be anticipated, representing a total of $2.2 billion of savings over the next eleven years.

Recommendations

The recommendations from this review are to:

- improve the use of data to further understand the drivers of Ig use, including patient numbers, dosage rates and use across specialties. Opportunities also exist to use data to drive standardisation across jurisdictions and define areas of research that could enhance the Ig evidence base
- consider opportunities to streamline BloodSTAR to enhance user experience, such as pre-population of patient data (from medical records) and supporting specific customisation
- improving patient education and awareness of Ig, including the development of patient resources in plain English and patient forums to promote patient engagement.

1 Executive summary

Implementation of the Program and its components correlates with a lower Ig growth rate

The objective of this evaluation was to assess the impact of the Program on Ig usage in Australia (the Program), using two datasets (STARS[1] and BloodSTAR) and supplemented with consultations with key stakeholders familiar with the dispensing and prescribing of Ig in Australia.

Introduced in 2014 and fully implemented in 2018, the Program aims to ensure that the clinical needs of around 19,000 patients each year can be met sustainably into the future. The Program comprises five components in total and three of them are considered key components (see table on the right for the introduction date of each key component):

- National Policy on Access to Government-funded Ig in Australia
- Criteria for the Clinical Use of Immunoglobulin in Australia (versions 1, 2 and 3)
- the online immunoglobulin management system, BloodSTAR (Blood System for Tracking Authorisations and Reviews).

This analysis has identified that Ig growth rate has decreased during the implementation of the Program (9%) and had an even higher decrease after its implementation (31%). However, the decrease in the observed Ig growth rate after the implementation should be considered together with an understanding of the short period available for the analysis.

Quarter by quarter data indicates that the Ig growth rate dropped between July 2017 to July 2019 aligning to the end of implementation of the Program. In the last four quarters (January to December 2020), the Ig growth rate has slightly increased; however, the growth rate remains lower than that observed in the pre- and implementation period of the Program (see page 20).

The data analysis of the growth rate along the timeline of implementing the key components of the Program show that version 2 of the Criteria and post-release of the National Policy had a moderate impact on Ig growth rate. Version 3 of the Criteria and implementation of BloodSTAR had a strong impact and was correlated to a strong decrease in Ig growth rate.

Consulted stakeholders noted that the Program has been a strong driver in the reduction in growth rates of Ig, but that other drivers (such as new treatments) may have also contributed to the impact on Ig demand.

The impact of the Program on Ig growth rates compared to previous period (not cumulative):

	Pre-implementation of the Program	Implementation of the Program	Post-implementation of the Program
Period	Jul-2009 to Dec-2013	Jan-2014 to Oct-2019	Nov-2019 to Dec-2020
Ig growth rate compared to previous phase	-	↓9%	↓31%

The impact of key components of the Program on Ig growth rates compared to previous period (not cumulative):

	Criteria (v.1)	Criteria (v.2)	Criteria (v.3)
Period	Jul-09 to Jun-12	Jul-12 to Sept-18	Oct-18 to Dec-20
Ig growth rate compared to previous phase	-	↓9%	↓50%

	Pre-BloodSTAR	Post-BloodSTAR[2]
Period	Jul-2009 to Jun-2016	Jan-2017 to Dec-2020
Ig growth rate compared to previous phase	-	↓46%

	Pre-policy	Policy (v.1)	Policy (v.2)	Policy (v.3)
Period*	Jul-2009 to Oct-2014	Nov-2014 to Jul-2016	Aug-2016 to Jun-2019	Jul-2019 to Dec-2020
Ig growth rate compared to previous phase	-	-	↓21%	↓35%

1. Supply Tracking and Reporting System (STARS): the national intranet web-based database on the use of immunoglobulin, used by Australia Red Cross Lifeblood before the implementation of BloodSTAR.
2. For NSW, implementation of BloodSTAR took place in 2018 and the period assessed was: from Jul-2009 to Sep-2018 (pre-BloodSTAR) and from Oct-2018 to Dec-2020 (post-BloodSTAR)

A decrease in the growth rate of total Ig patients has been the main driver of a lower Ig growth rate

All the factors below (growth rate of patients, Ig dosage, age, weight and medical conditions) are related to increase or decrease in use of Ig. During the implementation of the Program, there was a small increase in almost all factors. No major changes were observed in the top 10 medical conditions.

After the implementation of the Program, trends in almost all factors were the same as the previous period. However, growth rate of total number of Ig patients showed a considerable decrease, which is the main driver of the decrease of Ig growth rate seen during post-implementation of the Program (see page 4).

Summary of changes in different factors related to Ig demand: *number of arrows represent changes from previous period and width of column represents duration of the period*

2009-10 2010-11 2011-12 2012-13 2013-14 2014-15 2015-16 2016-17 2017-18 2018-19 2019-20 2020-21

	Pre-implementation of the Program (Jul-2009 to Dec-2013)	**Implementation of the Program** (Jan-2014 to Oct-2019)	**Post-implementation of the Program** (Nov-2019 to Dec-2020)
Growth rate of total number of Ig patients	-	↑	↓↓↓
Average Ig dispensed per Kg	-	↑	↑
Average age	-	↑	↑
Average weight	-	↑	↑

Legend: ↑ or ↓: Increase or decrease between 1% and 25%, ↑↑ or ↓↓: Increase or decrease between 26% to 50%, ↑↑↑ or ↓↓↓: Increase or decrease between 51% to 75%, ↑↑↑↑ or ↓↓↓↓: Increase or decrease from 76% to 100%

The reduced growth rate of Ig equates to an estimated cost saving of $71m between July 2019 and December 2020, and potential saving of up to $2.2b over the next 11 yrs

Ig costs from 2020-21 to 2030-31 have been projected assuming an annual growth rate of 8.4% as the base-case, which is the estimated annual growth rate from the last three quarters of data (Q4 2019-20 and Q1-2 2020-21 - see appendix B). The base-case scenario was compared to a scenario without the Program, with an annual Ig growth rate of 11%.

Forecasted savings are based on a national weighted average price for the cost per gram of Ig (adopted in a recent HTA Review, $94/gram).[1] Sensitivity analysis has also been applied to the Ig price per gram, considering a variation of plus and minus 20%.

Ig cost depends on the distribution of intravenous and subcutaneous Ig, distribution of different Ig products and ration between domestic and imported Ig. For this evaluation, it was assumed that all variables associated with the Ig cost per gram would be constant and the only difference being the total Ig dispensed per year.

The reduction of Ig growth, driven by the implementation of the Program, as well as other factors, is estimated to have delivered a cost saving of $71 million between 2018-19 and 2019-20 (which covers part of the implementation and the post-implementation period of the Program). The Ig growth rate was similar during the pre- and most of the implementation period of the Program and savings were not estimated for the period January-2014 to June-2017.

Comparing the total cost of the base-case scenario against the scenario without the Program, forecasts savings to ~$17 million in 2020-21 and ~$479 million in 2030-31, which represents a total of $2.2 billion across the forecast eleven years.

It is worth noting that the analysis here considers historical data and the estimated Ig growth rate in the future. The future savings predicted below relies on the assumption of future Ig growth rate of 8.4% per annum.

There are many factors that could drive changes in Ig growth rate in the future which can not be easily predicted. For instance, new treatments which could replace Ig and reduce its use, can have a significant impact on the estimated cost saving.

The analysis presented here focuses on what the future cost savings could be based on a fixed annual growth rate, considering all other factors equally. The potential savings should be considered together with an understanding of these assumptions. Figures should be interpreted with full understanding/acknowledgement of the assumptions or limitations.

Cost savings observed and predicted (in $ million):

2014-15	2015-16	2016-17	2017-18	2018-19	2019-20	2020-21	2021-22	2022-23	2023-24	2024-25	2025-26	2026-27	2027-28	2028-29	2029-30	2030-31
-				**$22**	**$49**	$17	$38	$62	$91	$125	$164	$210	$264	$326	$397	$479

Observed cost savings during implementation of the Program

Observed cost savings during post-implementation of the Program

Predicted cost savings

1. Australian Government. Medical Service Advisory Committee. Review of immunoglobulin use for Acquired Hypogammaglobulinaemia Secondary to Haematological Malignancies and haemopoietic stem cell transplantation. November 2019. Available from: <http://www.msac.gov.au/internet/msac/publishing.nsf/Content/1565-public>.

The Program's implementation has driven standardisation, but enhancement opportunities exist

Implementation of the Program

Stakeholders to this evaluation observed that:

Clinical awareness of the Program and its applicability has grown
The specific resources and the Criteria embedded through BloodSTAR has guided clinical teams to better monitor patients, improved access and anecdotally, increased equity in Ig use among patients.

BloodSTAR's inbuilt guidance has driven standardisation
BloodSTAR, in combination with the Criteria, has improved the use of Ig. The inbuilt guidance has driven improvements in prescription practices, including to 'force' clinicians to consider the evidence for prescriptions and dosage rates, as well as prompting review of patients with ongoing treatment.

Clinicians have greater opportunity to input to the Ig Governance framework
The Specialist Working Groups have increased the roles of clinicians in inputting into the Ig governance framework.

Gain in efficiency with BloodSTAR, as it automates components of the approval process
The BloodSTAR system partly automates the approval process for patients in that it provides clear indications to clinicians without the need to rely on phone support (although this is available if needed).

Recommendations

1. Improving use of data	This review has identified that the reduced growth rate in the total number of Ig patients and slight increase in Ig dispensed per kilogram has driven some of the observed changes in Ig demand. Further analysis should be undertaken into the drivers for: • the reduced growth in patient numbers, accounting for both new and continuing patients, and analysing patient numbers by medical speciality • the slight increase in Ig dispensed per kilogram during and in post-implementation of the Program. Further opportunities exist, more generally, to improve the use of data collected through BloodSTAR to continuously improve and tailor the Program, and drive standardisation across jurisdictions. Examples include: • using data to regularly review the Ig use by speciality to understand how effectively the Criteria are being applied and any differences that exist, including changes in treatment duration for the top ten medical conditions • analysing the changes and associated drivers in Ig use by condition to anticipate changing clinical practice • ongoing monitoring and potentially, auditing, of patient reviews • using data to inform research into the evidence base for the use of ideal body weight for dosage and patient outcomes for 'trial offs' for particular indications. Areas of research could be defined by NBA's Specialist Working Groups to identify opportunities for enhancing the Ig evidence base.
2. Consider opportunities to streamline BloodSTAR	There may be opportunity to continue to enhance the user experience of BloodSTAR, such as pre-population of patient data (from medical records) and supporting specific customisation. Enhancements could continue to be informed by NBA's user groups as a way to improve data quality and reduce barriers to its effective use.
3. Enhance patient education	Improve patient education and awareness of Ig, including the development of patient resources in plain English and patient forums to promote patient engagement. Patients are largely reliant on their clinical team for information and limited understanding of alternatives, the value of 'trial offs' (for fear of placebo effect), and limited incorporation of clinical and patient user needs in the Program may constrain future efficiencies.

2 Introduction

Supply of Ig in Australia

Immunoglobulin (Ig) is an antibody protein used by the immune system to identify and neutralise bacteria and viruses. Ig therapy is used to induce, enhance or suppress an immune response (modulation therapy) and is often used for patients with immune deficiency (replacement therapy) and can be administered intravenously (IVIg) or by injection into the layer of the skin directly below the dermis and epidermis: Subcutaneous Immunoglobulin (SCIg).[1]

Normal human immunoglobulin (NHIg)[2] is administered by intramuscular injection and is generally reserved for public health disease response activities and for use in defined circumstances where IVIg and SCIg are contraindicated.

In Australia, eligibility to access Ig products funded under the national blood agreement is strictly defined under rules (known as the Criteria) agreed by health experts from across Australia. The National Policy, the Criteria and processes to access Ig are managed nationally by the National Blood Authority (NBA) under its Immunoglobulin Governance Program.

Since 2004, the NBA has ensured uninterrupted supply of Ig products in Australia. In 2007, NBA released the first version of the evidence-based Ig criteria (the Criteria) that governs access, in order to provide clinically-appropriate access to government funded Ig products in Australia.

In 2012, NBA commissioned a review of the adequacy of the existing intravenous immunoglobulin (IVIg) authorisation and clinical governance arrangements. The review provided a series of recommendations to improve delivery against the government's objectives for the management of intravenous immunoglobulin (IVIg).

The review found, among other things:

- variation in IVIg management processes nationally
- limited evidence of alternative therapies being considered before prescription of Ig
- variation in diagnosis (high prescription rates in some conditions compared to international rates of use)
- limited transparency of cost implications and no accountability for cost with the prescriber.

In order to address the findings and recommendations of the 2012 review of IVIg authorisation and clinical governance arrangements, the NBA introduced in 2014 the National Ig Governance Program (the Program).

The Program's aim was to ensure that the clinical needs of around 19,000 patients yearly can be met sustainably into the future. More specifically, the Program aimed that access to Ig products would:[3]

- deliver optimal benefit to patients with various chronic and acute medical conditions
- reflect appropriate clinical practice
- represent efficient, effective and ethical expenditure of government funds and
- be in accordance with relevant national safety and quality standards for health care

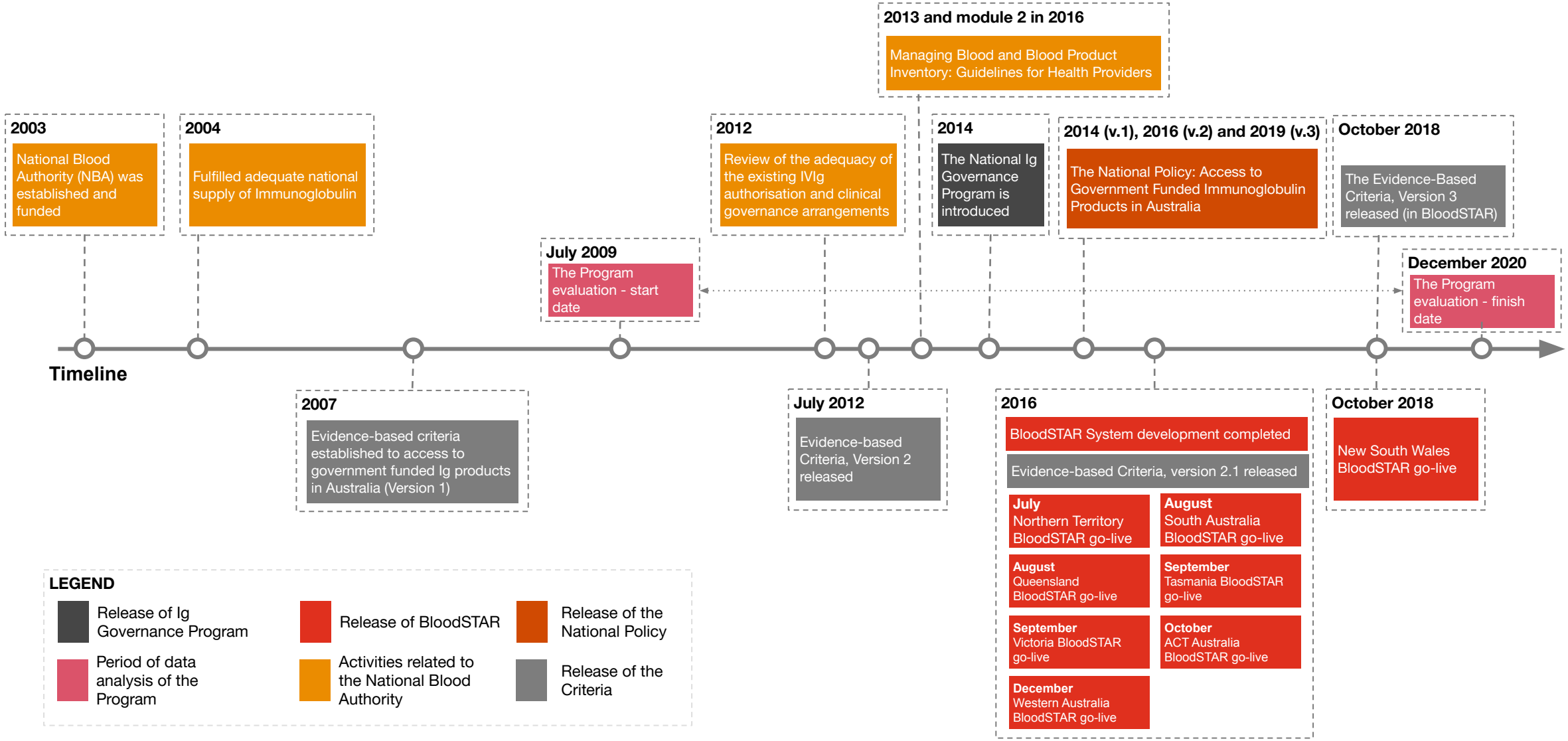
The Program comprises five main elements (the first three - key components, are being considered for this review):

1. **National Policy** on access to government-funded Ig in Australia, which describes the roles and responsibilities of key participants in the governance and management framework for Ig products.
2. **Criteria for the Clinical Use of Immunoglobulin in Australia (the Criteria),** which identifies the conditions and circumstances for which the use of Ig is considered to be clinically appropriate and for which Ig products are able to be accessed under the National Policy.
3. **BloodSTAR** (Blood System for Tracking Authorisations and Reviews), which is an online immunoglobulin management system. Through BloodSTAR, Ig prescribers are able to determine whether patients are eligible to receive government-funded product and seek authorisation for access, and dispensers use it and associated systems to manage infusions and dispensing practices to approved patients.
4. **Committees and interest groups,** a network of committees and interest groups which provide formal and informal forums for informing the work of the national immunoglobulin (Ig) governance program. These committees interact with national health policy committees and forums, as appropriate.
5. **Performance Improvement Strategy,** which promotes a nationally consistent approach to monitoring performance and identifying obstacles and challenges to performance. As part of the Strategy, the NBA will develop tools and mechanisms to promote continuous improvement amongst all those involved in the prescription, management and use of government-funded Ig products. Where issues are identified, the NBA will develop and implement solutions.

On the next page there is a timeline with the implementation date of each component of the Program and other key milestones in the supply of Ig in Australia.

1. Currently approved for a limited range of conditions through specific hospital-based programs that may support home therapy being administered by patients or carers.
2. The product is approved in Australia for use in the management of hypogammaglobulinaemia and for the public health purposes to treat susceptible contacts of hepatitis A, measles, poliomyelitis and rubella.
3. The National Blood Authority. National Immunoglobulin Governance Program. Available from: <https://www.blood.gov.au/Ig-program>.

National Blood Authority and the Program timeline



Project objectives and approach

This evaluation

The objective of this evaluation was to assess the impact of the Program on Ig usage in Australia. This evaluation seeks to:

- confirm the effect observed to identify how Ig use has changed since the introduction of the Program
- understand the drivers for the change and quantify them
- analyse the impact of the Program components individually and collectively on Ig demand and costs

More specifically, this evaluation aims to answer seven evaluation questions listed on the next page.

Our approach

The evaluation has been undertaken over an eight-week period, using datasets sourced from NBA from STARS and BloodSTAR systems. It has been supplemented with consultations with the NBA, jurisdictional representatives, Lifeblood and medical specialists. Consultations were undertaken as a blend of one-on-one meetings, workshops and an online questionnaire (further information can be found at Appendix A).

Information presented in this evaluation provides a synthesis of this data and consultation insights. This report should be read noting the following treatments applied to the data:

Data periods: Ig demand changes have been assessed using data from between July-2009 to December-2020.

Quarter by quarter growth: in order to assess changes in Ig demand in periods which end/start at different parts of the year, a quarterly growth rate has been used. These rates have been multiplied by 4 to estimate an effective annual growth rate. Additionally, as there is seasonality in the use of Ig, 12-month growth rate by quarter has been used (see page 20 for more information on this calculation and approach).

Aging population adjustments: in order to isolate Ig growth rate from population growth and aging population, Ig growth rates of total Ig in grams per 1,000 population has been used and adjusted for aging to the Australian population age profile in June 2010.

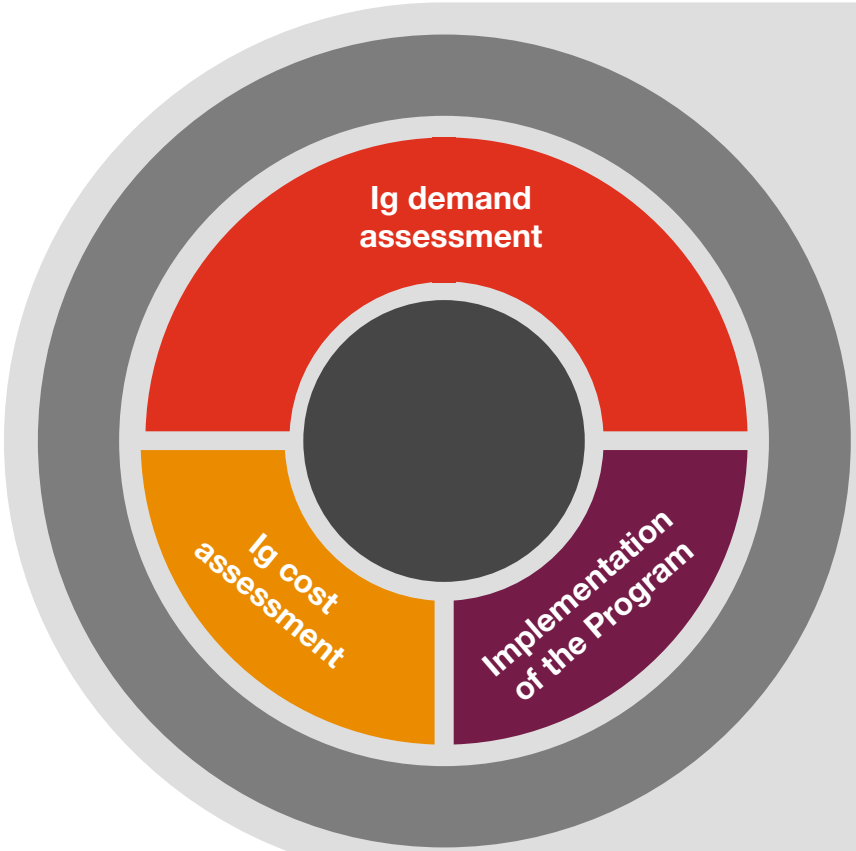
Removal of blanks/strange data: blank records, negative age and above 100 years old, negative weight and records with zero or above 110 Kgs values have been removed from the analysis because there is a risk of them being a data error entry. Ig grams dispensed per kilogram has also been limited to 5. Any value above this value was considered invalid.

Estimating future Ig demand: past trends have been used to estimate future Ig demand and costs. However, there are many unpredictable factors that could influence future trends; estimations presented in this report can not be interpreted as a prediction of what will happen in the future.

Key evaluation questions

Seven evaluation questions, covering Ig demand and costs, and the implementation of the Program, are explored in this evaluation. The evaluation framework to address each evaluation question is detailed in section 3 of this report.

For each of the cost and demand evaluation questions, there are specific lines of enquiry which have been used to answer the question. For the question around the implementation of the Program, consultation with key stakeholders has been used to understand the impact of implementation.



Ig demand assessment

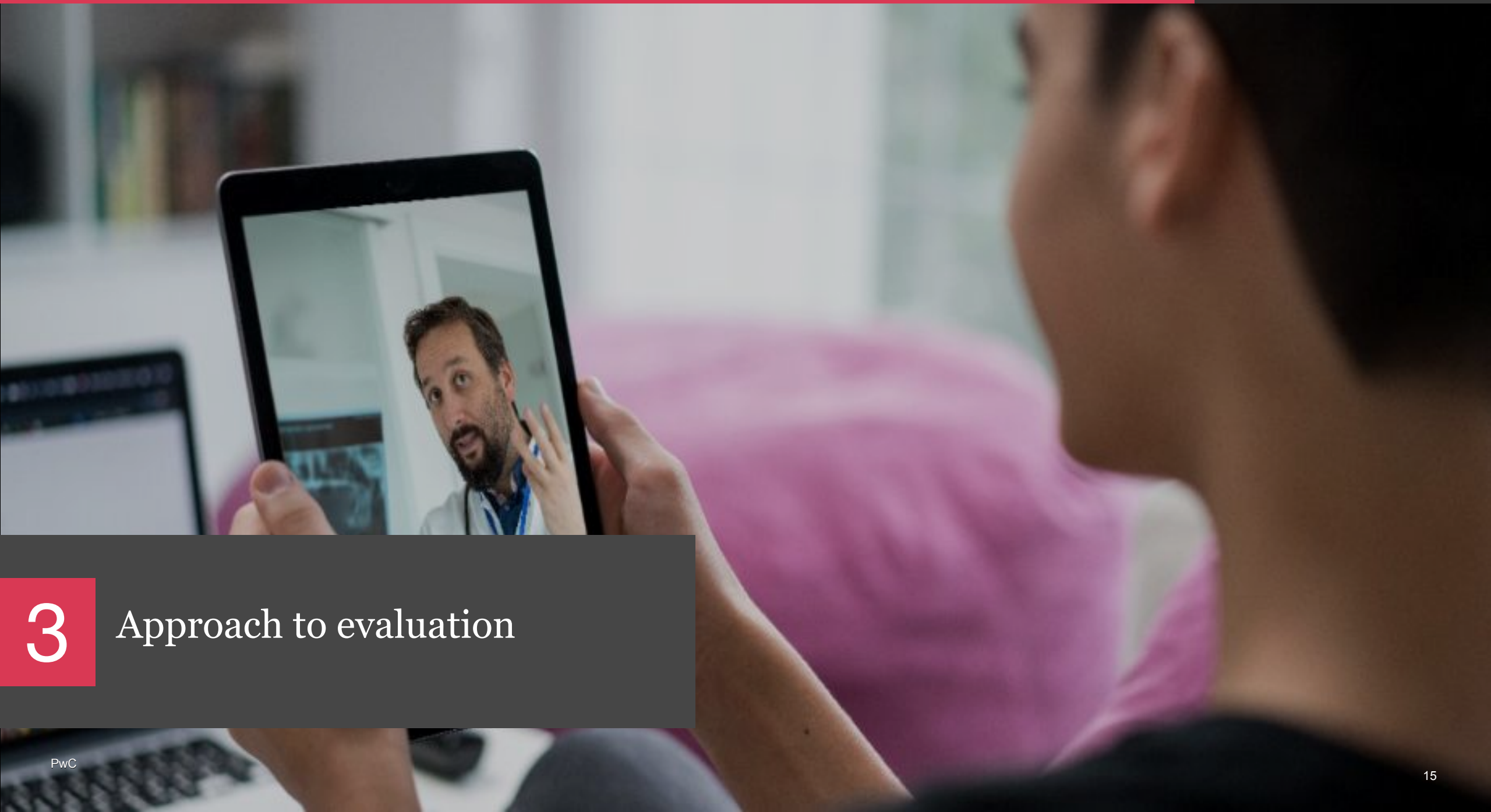
1. What effect has the Program had on the **demand for use of Ig products** in Australia **since it was introduced in 2014**?
2. What are the **factors that contributed to the observed change in demand** (changes in patient numbers, changes in dose prescribing practices or other factors)? Quantify the contribution of these factors.
3. What **contribution has each of the Program components** (the National Policy, the Criteria and BloodSTAR) had on the change in demand, where possible?
4. Is the **change in demand** consistent **across the top 10 medical conditions**, or is there variation of interest?

Ig cost assessment

5. What is the **cost saving of the effects observed?**
6. What is the **estimated cost saving** if the demand trend were to continue?

Implementation of the Program

7. Has the Program implemented/achieved what the 2012 Review of the Authorisation and Clinical Governance Framework recommended?



3 Approach to evaluation

Ig demand assessment

	Evaluation questions	Lines of enquiry	Proof point
1	**What effect has the Program had on the demand for use of Ig products in Australia since it was introduced in 2014?**	Has the growth of Ig demand decreased since 2014 after the introduction of the Program?	Compare growth of Ig demand pre-, during and post-implementation of the Program.
		Has any of the Ig use shifted to Jurisdictional Direct Order (JDO), which is provided by states and territories and outside of the Criteria?	Assess Ig demand accessed through JDOs.
2	**What are the factors that contributed to the observed change in demand (changes in patient numbers, changes in dose prescribing practices or other factors)? Quantify the contribution of these factors**	Is there any change in terms of number of patients using Ig before and after the Program?	Compare the number of patients per year and patient annual growth pre-, during and post-implementation of the Program.
		Is there any change in terms of dispensed Ig per kg before and after the Program?	Compare the average, minimum and maximum grams per Kg dispensed pre-, during and post-implementation of the Program.
		Is there any change in terms of patient characteristics (age and weight) before and after the Program?	Compare the average, minimum and maximum age and weight pre-, during and post-implementation of the Program.
		Is there any change in terms of number of registered Ig prescribers before and after the Program?	Compare the number of prescribers per year.
3	**What contribution has each of the Program components (the National Policy, the Criteria and BloodSTAR) had on the change in demand, where possible?**	Is there any change in Ig demand growth before and after the release of each version of the Criteria (versions 1, 2 and 3)?	Compared growth of Ig use, growth of number of patients, average Ig grams per Kg during the period of each version of the Criteria.
		Is there any change in Ig demand growth before and after the introduction of Ig National Policy?	Compare growth of Ig use, growth of number of patients, average Ig per Kg pre- and post-Policy.
		Is there any change in Ig demand growth before and after the introduction of BloodSTAR?	Compare growth of Ig use, growth of number of patients, average Ig per Kg pre- and post-BloodSTAR.
4	**Is the change in demand consistent across the top 10 medical conditions, or is there variation of interest?**	Is there any change in the top 10 conditions before and after the Program?	Compare the top 10 medical conditions from pre- and post-implementation of the Program.
		For the top 10 medical conditions, is there any change in Ig prescribed per Kg?	Compare average Ig gram/Kg per each top 10 medical conditions pre-, during and post-implementation of the Program.
		For the top 10 medical conditions, Is there any change in terms of treatment duration?	Due to data limitations, it was not possible to assess the treatment duration during the different periods of implementation of the Program.

Ig cost assessment

	Evaluation questions	Lines of enquiry	Proof point
5	**What is the cost saving of the effects observed?**	What has been the cost saving since the introduction of the Program in 2014?	Ig annual growth rate has not changed significantly from 2009-10 to 2017-18 (around 11%): • Projected costs in the last two financial years (2018-19 and 2019-20) with an annual Ig growth of 11% (pre-implementation of the Program) minus current Ig costs (Ig annual growth of around 7%)
		Has the potential savings estimated by the 2012 Review of the Authorisation and Clinical Governance Framework been achieved?	Compare grams of Ig per 1,000 population associated with six different medical conditions with those modelled by the 2012 Review.
6	**What is the predicted cost saving if the demand trend were to continue?**	What is the estimated future cost saving of the Program?	• **Scenario 1**: Ig annual growth rate of 6.7%, which is the annual growth rate of 2019-20 and reflects the best-case scenario • **Scenario 2:** Ig annual growth rate of 8.4%, which is the estimated annual growth rate from the three last quarters of data (Q4 2019-20 and Q1-2 2020-21 - see appendix B) and represents the base-case • **Scenario 3**: Ig annual growth rate increasing from 8.4% to a maximum of 11%, following the trajectory of the last three quarters of data three quarters of data (Q4 2019-20 and Q1-2 2020-21 - see appendix B). This is the worst-case scenario • **No Program scenario:** Ig annual growth rate increasing of 11%. **Cost saving calculation:** no Program minus Program scenarios.

Implementation of the Program

	Evaluation questions	Consultation topics
7	**Has the Program implemented/achieved what the 2012 Review of the Authorisation and Clinical Governance Framework recommended?**	Are patients more informed about their IVIg treatment (requirements for IVIg treatment, risks and costs)?
		After the implementation of the Program, were there any patients that are ineligible to access Ig through the Program?
		Has the Program provided more efficient approval process, deeper clinical knowledge base, and more informed support staff and patients?
		Have clinicians been given greater opportunity to input into the Ig Governance framework through participation in the Specialist Working Groups, local Ig Advisory Groups or, in particular, by contributing to updating the Criteria as part of the clinical expert networks? And opportunities to undertake research and trials?
		Has BloodSTAR improved the evidence base upon which treatment decisions are based or lead to improve treatment for patients? Is it helpful to guide clinicians through the life cycle of IVIg treatment?
		Does the Criteria ensure that IVIg is being used only where it is demonstrated to be providing clinical benefit?
		Was BloodSTAR able to efficiently automate approvals and promote national prescribing consistency and centralising knowledge?
		Has centralising the ordering of IVIg for on-going patients to AHPs' blood banks and pharmacies reduced inappropriate movement, storage and holding of product?
		Does BloodSTAR, in connection with BloodNet, provide greater clarity over the product life cycle, from ordering to infusion?

4 Findings

4.1 Immunoglobulin demand assessment

Trends in Ig dispensed in Australia

Overall trends

Total Ig dispensed in Australia has grown over time, from 2.7 tonnes in 2009-10 to 7.0 tonnes in 2019-20. While the annual growth of total Ig dispensed per financial year has not changed considerably between 2009-10 to 2017-18 (fluctuated around 11%), in the last two financial years (from 2018-20), annual growth has reduced to around 7% each year (Figure 1).

Total Ig dispensed per 1,000 population has also grown over time; from 121 to 274 grams between 2009-10 to 2019-20. When assessing growth using the total Ig grams per 1,000 population (compared to the annual growth of total Ig dispensed) it reduces to around 9% between 2009-10 to 2017-18 and to around 5% in the last two financial years reported (Figure 2). Population data were sourced from Australian Bureau of Statistics.[1]

Note that Figures 1 and 2 do not include 2020-21 data as there are only 6 months of data available at the time of this review (July to December).

Adjusting for age distribution of patients

This reduction in the annual Ig growth rate by half between 2009-18 and 2018-20 is despite increases in population growth and an aging population. In order to isolate Ig growth rate, we have used Ig dispensed per 1,000 population and also adjusted it to account for the population aging. The Ig dispensed per 1,000 population has been calculated for each different age group and, to estimate the total Ig dispensed per population, we have weighted each age group with its distribution in the Australian population at June 2010 (standard population). This age-adjustment has been applied throughout this report.

Tables 1 and 2 show a hypothetical scenario of adjusting Ig per 1,000 population in 2019-20, using a standard population (as at June 2010) to demonstrate how the age-adjustment has been undertaken. In the analysis presented in this report, this approach has been applied, but has used twenty-one different age groups.

Figure 1: Total Ig dispensed and annual growth in Australia from 2009-10 to 2019-20

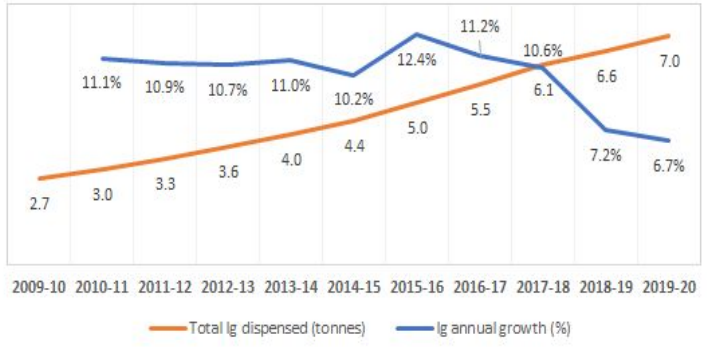


Figure 2: Total Ig dispensed per 1,000 population and annual growth in Australia from 2009-10 to 2019-20

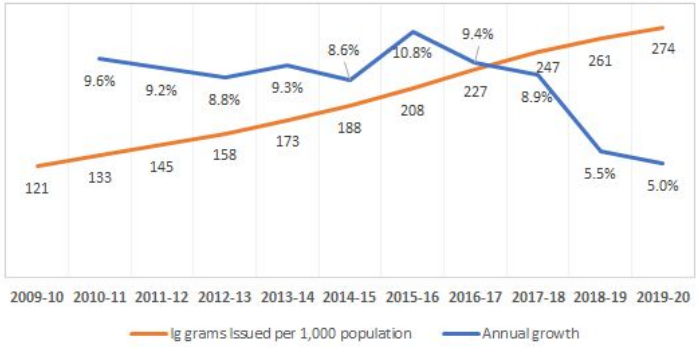


Table 1: Hypothetical calculation of total Ig dispensed without adjusting age distribution

	Age distribution (2019-20)	Ig grams per 1,000 population (2019-20)	Ig per 1,000 population in 2019-20
0-34	46%	150	70.5
35-69	45%	170	73.1
70 and over	9%	200	20.0
Total Ig per 1,000 in 2019-20			163.6

Table 2: Hypothetical calculation of total Ig dispensed with adjusting age distribution

	Age distribution in a standard population	Ig grams per 1,000 population (2019-20)	Ig per 1,000 population in 2019-20 adjusted
0-34	47%	150	69.0
35-69	43%	170	76.5
70 and over	10%	200	18.0
Total Ig per 1,000 in 2019-20 adjusted to standard population (aging)			163.5

1. ABS. Australian Bureau of Statistics. Population Projections, Australia. Available from: <https://www.abs.gov.au/statistics/people/population/population-projections-australia/latest-release#data-download>.

Ig trends in this report have been analysed by quarter and adjusted by age (presented as annual changes)

Data in this report should be read understanding that growth is based on quarterly analysis throughout

It is challenging to determine the impact of the Program and its components on Ig demand assessing the yearly Ig growth rate given the Program's components were introduced at different time increments that do not align perfectly with the advent of financial years.

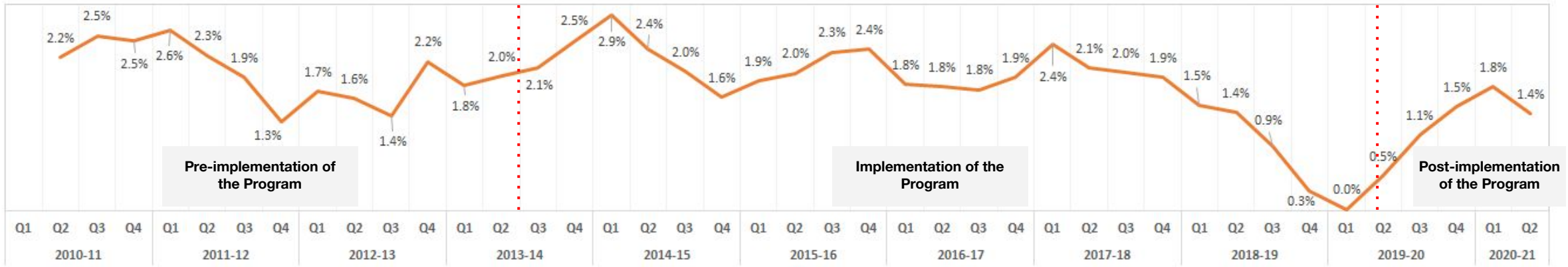
To analyse the effects throughout this report, we have assessed the 12-month growth rate, quarter by quarter. For instance, the 2.2% Ig growth from Q1 to Q2 of 2010-11 is shown in table 3. This approach has been adopted throughout this report.

The quarter growth shows the same trends as the yearly growth rate, with a decrease in growth rate from 2017-18. However, from the first quarter of 2019-20, the Ig growth rate increases, reaching 1.8% growth in the first quarter of 2020-21.

Table 3: Calculation of the 12-month Ig growth of Ig dispensed by 1,000 population and adjusted by age group, quarter by quarter

12-month period	Month	Ig per 1,000 population (grams)*	Quarter	Average per quarter (grams)	Growth Q1 to Q2
June-09 to Jul-10	July-10	120.8			
July-09 to Aug-10	Aug-10	122.1	Q1 2011	121.8	
Aug-09 to Sept-10	Sept-10	122.6			2.2%
Sept-09 to Oct-10	Oct-10	123.2			
Oct-09 to Nov-10	Nov-10	124.7	Q2 2011	124.5	
Nov-09 to Dec-10	Dec-10	125.7			

Figure 3: Twelve-month Ig growth by quarter of Ig per 1,000 population, adjusted by aging



The Ig growth rate has decreased since the introduction of the Program

We have compared Ig growth rate in three different periods:

- Pre-implementation of the Program: from Jul-2009 to Dec-2013
- Implementation of the Program: from Jan-2014 to Oct-2019
- Post-implementation of the Program: from Nov-2019 to Dec-2020

The Program was introduced in 2014 after a review of the adequacy of the intravenous immunoglobulin (IVIg) authorisation and clinical governance arrangements showed significant variation in IVIg use, management and processes nationally. Since the introduction of the Program, the growth of Ig, in both total annual terms and on a per capita basis demonstrate decreased growth. This effect is more substantive in the post-implementation period analysed in this evaluation.

Table 4: Summary of evaluation question 1: difference from previous period

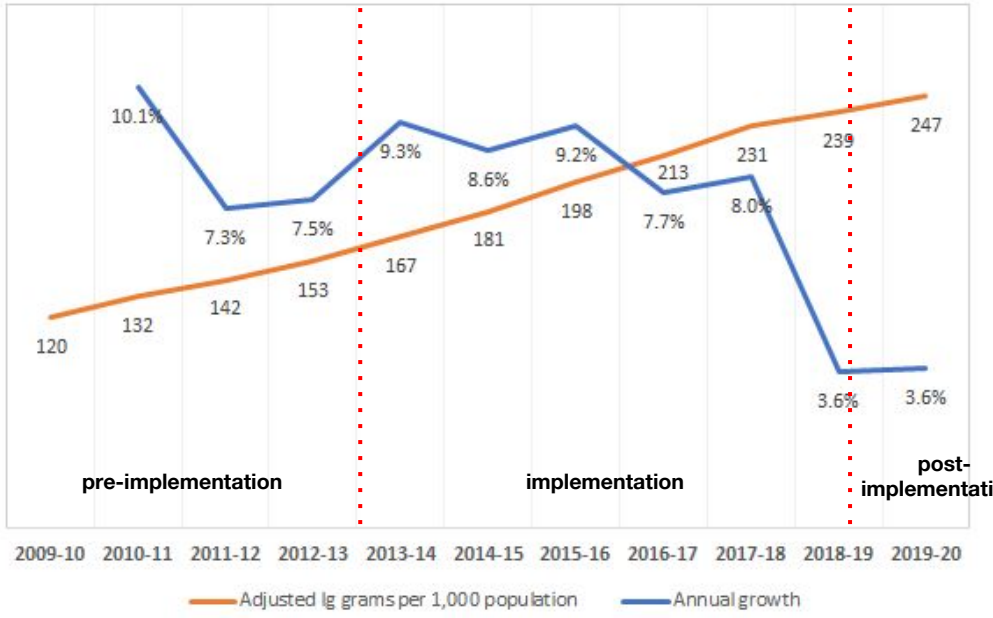
	Pre-implementation of the Program	Implementation of the Program	Post-implementation of the Program
Ig growth rate (total)	-	↓	↓
Ig growth rate (Ig per 1,000 population)*	-	↓	↓↓

Legend:

↑ or ↓: Increase or decrease between 1% and 25%
↑↑ or ↓↓: Increase or decrease between 26% to 50%
↑↑↑ or ↓↓↓: Increase or decrease between 51% to 75%
↑↑↑↑ or ↓↓↓↓: Increase or decrease from 76% to 100%

The Ig growth rate has decreased during implementation of the Program (2009-13) and has had an even greater decrease in the post implementation period (2019-20).

Figure 4: Total Ig dispensed per 1,000 population and adjusted for aging* and annual growth of Ig dispensed per 1,000 population in Australia from 2009-10 to 2019-20



* See page 19 for more information about adjusting Ig dispensed per 1,000 population by age group distribution. This figure does not include data from 2020-21 because there are only 6 months data available for this financial year (July to December)

Since the Program was implemented, the Ig growth rate has reduced by 31% compared to the implementation phase

Table 5: Ig quarter and estimated annual growth rates - total Ig dispensed

	Pre-implementation of the Program	Implementation of the Program	Post-implementation of the Program
Period assessed (quarters)	13	23	5
Average quarter Ig growth	2.6%	2.4%	1.6%
Estimated annual growth**	**10.4%**	**9.6%**	**6.3%**
Difference from previous period	**-**	**-7%**	**-24%**

** To assess the Ig growth rate, the 12-month growth rate (based on quarter by quarter growth) has been used (see page 20 for more information).

Table 6: Ig quarter and estimated annual growth - Ig dispensed per 1,000 population adjusted by aging*

	Pre-implementation of the Program	Implementation of the Program	Post-implementation of the Program
Number of quarters assessed	13	23	5
Average quarter Ig growth	2.0%	1.8%	1.3%
Estimated annual growth**	**8.0%**	**7.3%**	**5.1%**
Difference from previous period	**-**	**-9%**	**-31%**

* See page 19 for more information about adjusting Ig dispensed per 1,000 population by age group distribution.

We have compared the Ig growth rate pre-, during and post-implementation of the Program. In the analysis shown in tables 5 and 6, growth rates of total Ig dispensed and total Ig dispensed per 1,000 population adjusted by aging growth are presented for these three different periods. See page 19 for more information about adjusting by aging.

Considering the total Ig growth rate, the Program's implementation is correlated with a reduction in the estimated annual growth rate of 7%. A 24% reduction in the growth rate, compared to pre-implementation, is observed in the post-implementation period.

After adjusting the growth rate for population growth (grams per 1,000 population) and by aging (using age group distribution of Australia population in June 2010), implementation of the Program is associated with a 9% reduction in estimated annual growth rate and a 31% reduction in the post-implementation period.

Note that the reduction in estimated annual growth rate post-implementation should be considered together with the understanding of it relating to a shorter period assessed (five quarters only).

The continued growth of Ig demand is anticipated by stakeholders to this review. However, it is unclear to them at what level this growth will continue in the future. Among the perspectives noted in consultation were that the aging population, growing prevalence of neurological conditions and longer-term survivors of indications for Ig are likely to continue to drive the need for Ig over time. Further insights on future demand are provided on slide 46.

Total Ig dispensed via JDOs account for around 62 kilograms over the past two and a half years

Table 7: Total Ig dispensed through JDOs

Financial year	Ig dispensed (grams)
2018-19*	16,155
2019-20	28,050
2020-21 (Jul-Jan)	17,892
Total	62,096

* Data from Grifols from July to January was not available.

Clinicians who wish to prescribe Ig for medical conditions that are not funded under the Criteria can seek access for Ig through their local arrangements between hospitals and jurisdictions. This arrangement is called Jurisdictional Direct Orders (JDO). These costs are borne by jurisdictions.

We have used data from 2018-19 to 2020-21, covering Ig distributed under the JDOs from CSL Behring and Grifols, to understand demand over the past few years over which data is available. (We note that the data source is incomplete - data for 2018-19 does not include total Ig supplied by Grifols from July to January and for 2020-21 it includes only data from July to January). In all, a little over 62 kilograms of Ig has been dispensed through JDOs over the past two and a half years, which represents only a small fraction of total Ig dispensed in Australia over the same time period.

Stakeholders to this evaluation noted that the JDO process in each jurisdiction varies and is often decentralised to local health networks/hospitals. This means that the indications for use are not well documented and are driven largely by the private sector (primarily in haematological applications). However, in some jurisdictions, there is strict adherence to the clinical indications mentioned by the Criteria, while in others, Ig may be accessed for other indications (including haemolytic disease of the newborns and for use in fertility clinics).

Line of enquiry:
Has any of the Ig use shifted to Jurisdictional Direct Order (JDO), which is provided by states and territories and outside of the Criteria?

A reduction in the growth rate of Ig patients has contributed to decreases in Ig growth rates

Table 8: Summary of evaluation question 2: difference from previous period

	Pre-implementation of the Program	Implementation of the Program	Post-implementation of the Program
Growth rate of total number of Ig patients	-	↑	↓↓↓
Average Ig dispensed per Kg	-	↑	↑
Average age	-	↑	↑
Average weight	-	↑	↑

Legend:

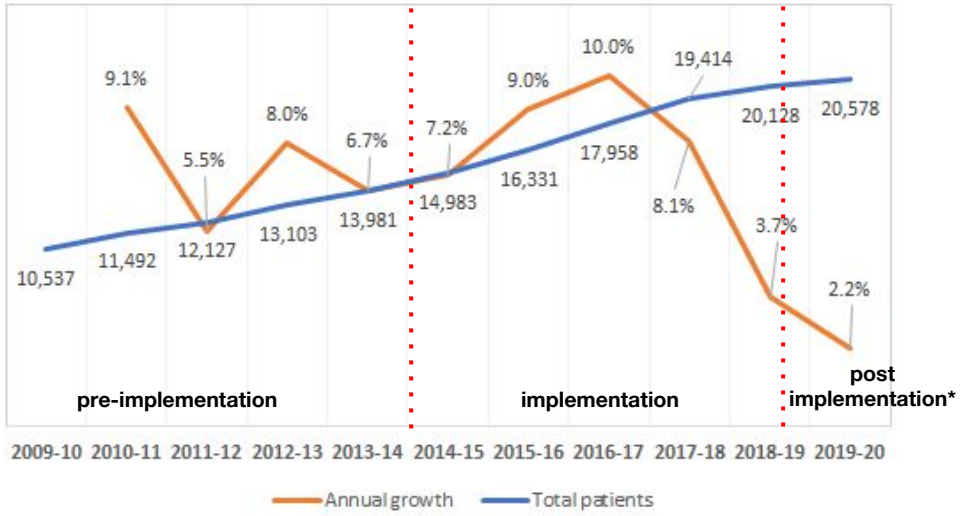
↑ or ↓: Increase or decrease between 1% and 25%
↑↑ or ↓↓: Increase or decrease between 26% to 50%
↑↑↑ or ↓↓↓: Increase or decrease between 51% to 75%
↑↑↑↑ or ↓↓↓↓: Increase or decrease from 76% to 100%

We have compared factors that contributed to changes in Ig demand in three different periods:

- Pre-implementation of the Program: from Jul-2009 to Dec-2013
- Implementation of the Program: from Jan-2014 to Oct-2019
- Post-implementation of Program: from Nov-2019 to Dec-2020

During the implementation of the Program, there has been a slight increase in the growth rate of the total Ig patients, average Ig grams per kilogram dispensed, average patient age and weight. However, there has been a significant decrease in the growth rate of the total number of patients in the post implementation period.

Figure 5: Total number of Ig patients and annual growth in Australia from 2009-10 to 2019-20



* This figure does not include data from 2020-21 because there are only 6 months data available for this financial year (July to December)

Between implementation and post-implementation phases, the Ig patient growth rate has reduced by 66%

Table 9: Total patients - average quarter growth and estimated annual growth rates

	Pre-implementation of the Program	Implementation of the Program	Post-implementation of the Program
Period assessed (quarters)	13	23	5
Average quarter growth	1.7%	1.8%	0.6%
Estimated annual growth	**6.6%**	**7.0%**	**2.4%**
Difference from previous period	**-**	**6%**	**-66%**

We have compared the growth rate of Ig patients in three different periods:

- Pre-implementation of the Program: from Jul-2009 to Dec-2013
- Implementation of the Program: from Jan-2014 to Oct-2019
- Post-implementation of Ig Governance Program: from Nov-2019 to Dec-2020

The growth rate of Ig patients grew by 6% between pre-implementation and implementation phases of the Program (annual growth rate). However, it dropped by 66% between the implementation and post-implementation periods.

Through consultations, some stakeholders suggested that this drop is associated with a stricter application of the Criteria, limiting the number of new patients enrolled, and patients continuing with Ig treatment. Data from this evaluation shows that version 3 of the Criteria reduced the growth rate of Ig patients by almost 90% (see page 31). Release of BloodSTAR was also associated with a reduction of growth rate of Ig patients of almost 60% (see page 33).

Consultations also suggested that due to new treatment options, some patients that would be candidates for Ig may access alternative treatments. Overall, this is contributing to a decline in annual growth rates in total patients.

Since the Program was implemented, average Ig dispensed per kg has increased by 12%

Table 10: Average, minimum, maximum and median Ig grams dispensed per kilogram*

	Pre-implementation of the Program	Implementation of the Program	Post-implementation of the Program
Dispensing activities	287,507	628,871	168,154
Average (Ig grams / Kg)	0.53	0.58	0.65
Difference from previous period	**-**	**9%**	**12%**
Maximum (Ig grams / Kg)*	4.92	4.98	4.97
Minimum (Ig grams / Kg)	0.02	0.01	0.02
Median (Ig grams / Kg)	0.40	0.41	0.42

Table 11: Average, minimum, maximum and median Ig grams dispensed per kilogram for the top 4 medical conditions* and the maintenance dose allowed under the version 3 of Criteria

	% of the total Ig dispensed	Maintenance Dose (IVIg) (Criteria v.3)	Pre-implementation of the Program		Implementation of the Program		Post-implementation of the Program	
			Median	Average	Median	Average	Median	Average
Acquired hypogammaglobulinemia haematological malignancy and/or post HSCT (Ig gram/Kg)	23%	0.4-0.6 g/kg	0.39	0.37	0.40	0.41	0.40	0.45
Chronic inflammatory demyelinating polyneuropathy (Ig gram/Kg)	22%	0.4-1.0 g/kg	0.41	0.58	0.42	0.65	0.63	0.81
Primary immunodeficiency diseases (Ig gram/Kg)	12%	0.4-0.6 g/kg	0.40	0.43	0.41	0.48	0.42	0.56
Myasthenia gravis (Ig gram/Kg)	8%	0.4-1.0 g/kg	0.41	0.58	0.42	0.63	0.53	0.71

We have compared the Ig grams dispensed by kilogram for each dispensing activity pre-, during and post-implementation of the Program.

The average Ig grams per kilogram per dispensing activity has increased 9% through implementation of the Program and by 12% after its implementation (2019-20). The median has slightly increased from 0.40 prior the implementation period to 0.41 during and 0.42 after the implementation of the Program.

When considering the top four medical conditions in terms of average Ig/kg dispensed per dispensing activity during the total period, the increase in Ig grams per kilogram is higher among Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) and Myasthenia Gravis (MG) patients. These two conditions represent almost one third of the total Ig dispensed from Jul-2009 to Dec-20. Averages and means of Ig/kg dispensed per dispensing activity are within the recommended maintenance dose under the Criteria (version 3).

Consultations suggest that the increase in grams of Ig dispensed per kilogram is driven by the historically low dosage rates among some clinical indications, which has since evolved to adopt higher dosage rates, particularly among neurologists.

Increase in Ig grams per kilogram post-implementation should be considered together with the understanding of it relating to a shorter period of assessment (fourteen months).

* Blank records and negative values were excluded from our analysis. We have set 5 grams per kilogram as a maximum, as there are a number of outliers with greater values and are treated as typos.

Average age and weight have increased by 1-5% since the Program was implemented

Table 12: Average, minimum, maximum and median weight for patients using Ig*

	Pre-implementation of the Program	Implementation of the Program	Post-implementation of the Program
Number of patients	26,935	38,638	7,608
Average (kg)	66.4	66.6	69.2
Difference from previous period	**-**	**<1%**	**4%**
Maximum (kg)	110	110	110
Minimum (kg)	<5	<5	<5
Median (kg)	70	70	72

Table 13: Average, minimum, maximum and median age for patients using Ig*

	Pre-implementation of the Program	Implementation of the Program	Post-implementation of the Program
Number of patients	29,700	40,498	8,052
Average (years)	50.5	51.3	53.9
Difference from previous period	**-**	**2%**	**5%**
Maximum (years)	100	100	100
Minimum (years)	0	0	0
Median (years)	57	59	61

* The increase in weight is only relevant in the cases where clinicians don't use the ideal body weight.
For this analysis, we have removed blanks records, negative age, weight above 110 kgs and age above 100 years.

We have compared patient age and weight pre-, during and post-implementation of the Program.

Aging of the Ig population is not likely to change Ig demand itself. However, it might indicate a new group of patients for which Ig therapy has been considered a treatment option for. Stakeholders have indicated that efficacy of Ig is not well established.

Incremental changes are observed in the patient characteristics of those accessing Ig. The average weight of patients using Ig has slightly increased (<1%) during the implementation of the Program and after its implementation (4%). The median had a slight increase from 70 kilograms prior and during the implementation period to 72 kilograms after the implementation of the Program.

For those treating clinicians using actual bodyweight, Ig patient's weight has the potential to increase the total Ig dispensed and therefore influence Ig demand. Due to data limitations, the percentage of patients using ideal *versus* actual bodyweight has not been considered in this analysis.

The average age of patients using Ig shows a similar trend, with a slight increase during the implementation of the Program (2%) and after its implementation (5%). The median also shifted slightly from 57 years of age prior to the implementation period to 59 and 61 years of age during and after the implementation of the Program, respectively.

Clinicians consulted as part of this evaluation noted that:

- Patients being treated, or who are suitable for treatment, are anecdotally getting older and slightly heavier
- The application of Ig is expanding across patients; for example, the use of haemopoietic stem cell transplants is now more commonly used in older patients, which in turn, generates new demand for Ig among patients not traditionally accessing Ig.

The number of Treating Medical Specialists has been stable in most jurisdictions over the past three years

Figure 6: Number of prescribers in Australia from 2016-17 to 2019-20

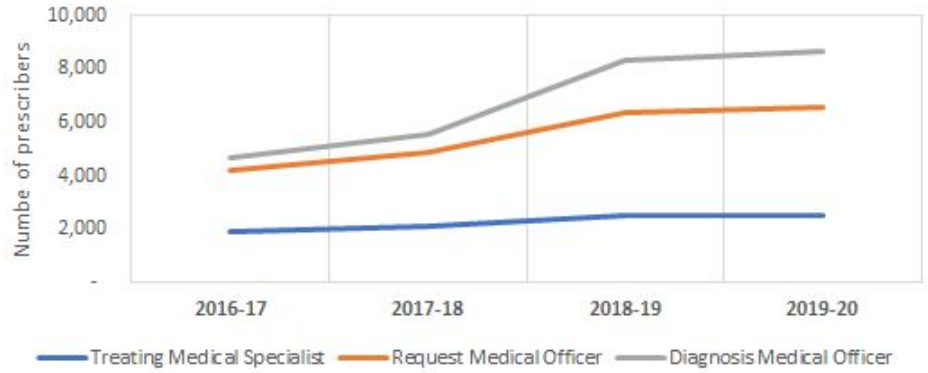
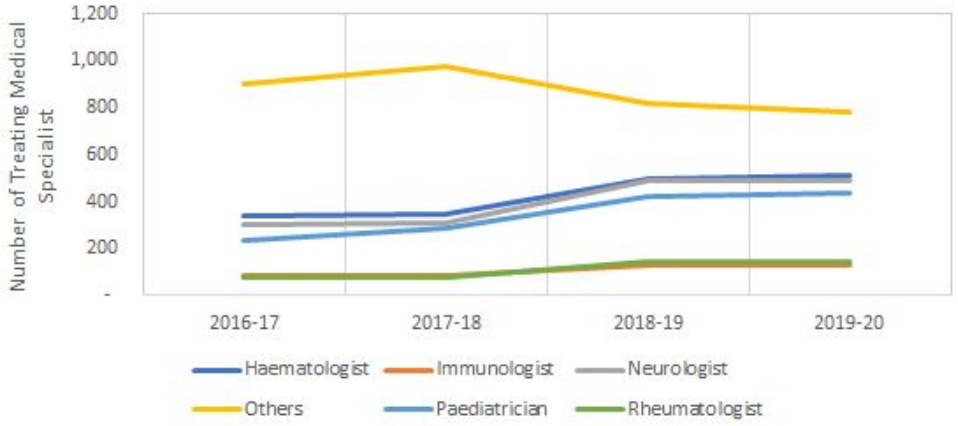


Figure 7: Number of Treating Medical Specialist per specialty in Australia from 2016-17 to 2019-20



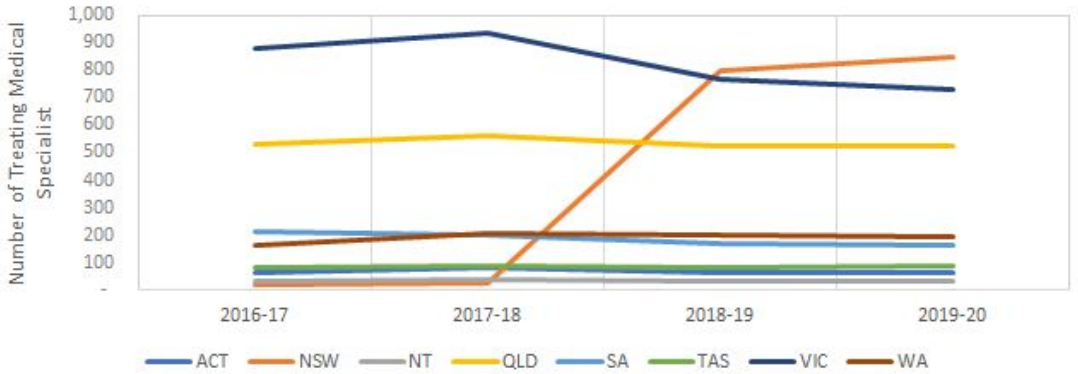
The term Prescriber collectively refers to all types of medical officers that have a role in the process of seeking patient-specific authorisation to access Ig products under the National Policy. This includes the BloodSTAR roles of Treating Medical Specialist (TMS), Diagnosing Medical Officer (DMO), Requesting Medical Officer (RMO) and Reviewing Medical Officer (RvMO).

We have assessed the number of Prescribers (except RvMO) with authorisation in BloodSTAR from 2016-17 to 2019-20. As there is no data available from STARS, it is not possible to test specific changes related to the Program.

The number of TMS has slightly grown during the period assessed, while the number of DMO and RMO has increased considerably between 2017-18 to 2018-19. However, these changes probably reflect the transition between STARS and BloodSTAR in NSW.

The number of TMS by speciality observes similar stable to slight growth trends; however, it is also probably linked with the transition from STARS to BloodSTAR. When assessed by jurisdiction, the number of TMS from 2016-17 to 2019-20 has been stable, with the exception of Victoria, which had a slight decrease from 2017-18 to 2018-19. Changes in NSW are due to its transition from STARS to BloodSTAR.

Figure 8: Number of Treating Medical Specialist per jurisdiction from 2016-17 to 2019-20



Version 3 of the Criteria and BloodSTAR appear to have had the biggest impact on the Ig growth rate

See periods of implementation of each component of the Program in the next slides.

The Program comprises three main components: the National Policy, the Criteria and BloodSTAR. We have assessed the impact of each component on the change of Ig demand by considering the timeline they were all implemented (refer following page for details).

Table 14: Summary of evaluation question 3: difference from previous period

	Version 1	Version 2	Version 3
Ig growth rate (Ig per 1,000 population)*	-	↓	↓↓
Growth rate of total number of Ig patients	-	↑↑↑	↓↓↓↓
Average dispensed Ig per Kg	-	↑	↑

	Pre-policy	Policy (v.1)	Policy (v.2)	Policy (v.3)
Ig growth rate (Ig per 1,000 population)*	-	-	↓	↓↓
Growth rate of total number of Ig patients	-	↓↓	↑↑	↓↓↓
Average dispensed Ig per Kg	-	-	↑	↑

All Program components appear to have impacted Ig growth rate. The greatest impact is observed by version 3 of the Criteria and BloodSTAR in reducing Ig growth rate comparative to earlier versions of the Criteria, and pre-implementation of BloodSTAR. This impact was echoed by stakeholders to this evaluation who considered that version 3 of the Criteria tightened requirements for Ig, while BloodSTAR has driven compliance, together contributing to a reduction in Ig growth rate.

Ig demand changes are driven by an overall decrease in the growth rate of Ig patients. While, the average dispensed Ig grams per kilogram slightly increased following implementation of each Program component, the number of patients drove greater effect.

	Pre-BloodSTAR	Post-BloodSTAR
Ig growth rate (Ig per 1,000 population)*	-	↓↓
Growth rate of total number of Ig patients	-	↓↓↓
Average dispensed Ig per Kg	-	↑

Note: BloodSTAR was implemented at different time periods across the jurisdictions. This analysis has been undertaken accounting for these differences to infer the impact of BloodSTAR. * Adjusted to age profile of Australian population in June 2010.

Legend:

↑ or ↓: Increase or decrease between 1% and 25%
↑↑ or ↓↓: Increase or decrease between 26% to 50%
↑↑↑ or ↓↓↓: Increase or decrease between 51% to 75%
↑↑↑↑ or ↓↓↓↓: Increase or decrease from 76% to 100%

The Version 3 Criteria has correlated with reduced Ig use and Ig patient growth rates

Table 15: Ig growth and number of patients during different versions of the Criteria*

		Version 1	Version 2	Version 3
Period assessed (quarters)		7	25	9
Ig growth rate	Average quarter Ig growth	2.2%	2.0%	1.0%
	Estimated annual growth	8.8%	8.0%	4.0%
	Difference from previous period		**-9%**	**-50%**
Growth rate of total number of Ig patients	Average quarter Ig growth	1.3%	2.1%	0.3%
	Estimated annual growth	5.1%	8.5%	1.1%
	Difference from previous period		**66%**	**-87%**

Table 16: Average, minimum, maximum and median Ig grams dispensed per kilogram during different versions of the Criteria*

	Version 1	Version 2	Version 3
Dispensing activities	177,742	609,208	297,582
Average (Ig grams / Kg)	0.53	0.55	0.64
Difference from previous period	**-**	**4%**	**16%**
Maximum (Ig grams / Kg)	4.92	4.98	4.98
Minimum (Ig grams / Kg)	0.02	0.01	0.01
Median (Ig grams / Kg)	0.40	0.40	0.41

The first version of the evidence-based Criteria to access government funded Ig products in Australia was published in 2007. In July 2012, the second version of the Criteria was released and, in October 2018, the third version was released (implemented via BloodSTAR).

The NBA dataset covers all three versions of the Criteria, from July 2009 to December 2020. With the second version having the longest period available. To review the impact of the Criteria, we have analysed the following periods:

- Criteria version 1: from Jul-09 to Jun-12
- Criteria version 2: Jul-12 to Sept-18
- Criteria version 3: from Oct-18 to Dec-20

The annual estimated growth rate was lower during versions 2 and 3, when compared with the previous version, (9% and 50%, respectively). In terms of number of patients using Ig, the growth rate increased for version 2 compared to version 1 (66%) and then decreased significantly with the introduction of version 3 of the Criteria (87%, compared to version 2).

We have also assessed the average, median, maximum and minimum grams of Ig per kilogram dispensed to patients during the three versions of the Criteria. During versions 2 and 3, there was a slight increase in the average grams of Ig per kilogram (4% and 16%, respectively).

Stakeholders to this evaluation noted that when the governing rules for Ig were introduced in 2014, Ig use increased, reflecting the 'normalisation' and greater awareness of Ig. The Criteria has driven appropriate dosage rates and, in some cases, reduced demand in certain indications. For example, version 3 of the Criteria was noted to have been tightened for autoimmune diseases with access to Ig permitted only after other treatments have been tried and failed, according to clinical evidence and best clinical practice.

* In order to assess the growth rates of Ig dispensed and number of Ig patients using Ig during the three different versions of the Criteria, the 12-month growth rate, quarter by quarter, was used (see page 20 for more information). The quarter growth rate was then multiplied by 4 to estimate the annual growth rate in each period.

In the NBA dataset, the period covering version 2 of the Criteria is almost three times longer than those covering versions 1 and 3. This difference also reflects the total number of dispensing activities during each version of the Criteria.

In the analysis of Ig grams per kilogram, blank records and negative values were excluded from our analysis. We have set 5 grams per kilogram as a maximum, as there were a few outliers with value above this which may be a typo.

Since the National Policy was implemented in 2014, growth rate in Ig use has decreased

Table 17: Ig growth and number of patients pre- and post-implementation of the National Policy*

		Pre-policy	Policy (v.1)	Policy (v.2)	Policy (v.3)
Period assessed (quarters)		16	7	12	6
Ig growth rate	Average quarter Ig growth	2.1%	2.1%	1.7%	1.1%
	Estimated annual growth	8.4%	8.4%	6.6%	4.2%
	Difference from previous period		**-**	**-21%**	**-36%**
Growth rate of total number of Ig patients	Average quarter Ig growth	1.9%	1.2%	1.8%	0.6%
	Estimated annual growth	7.6%	5.0%	7.3%	2.5%
	Difference from previous period		**-34%**	**47%**	**-65%**

Table 18: Average, minimum, maximum and median Ig grams dispensed per kilogram pre- and post-implementation of the National Policy**

	Pre-policy	Policy (v.1)	Policy (v.2)	Policy (v.3)
Dispensing activities	363,081	181,251	326,817	213,383
Average (Ig grams / Kg)	0.53	0.53	0.61	0.64
Difference from previous period	**-**	**0%**	**15%**	**7%**
Maximum (Ig grams / Kg)	4.98	4.93	4.97	4.98
Minimum (Ig grams / Kg)	0.02	0.01	0.01	0.02
Median (Ig grams / Kg)	0.40	0.40	0.41	0.42

The National Policy was first released in 2014 and revised for the BloodSTAR release in 2016. The latest edition of the National Policy replaces all previous editions effective from 15 July 2019.

We have analysed the Ig growth rate, growth of Ig patients and average Ig grams per kilogram in the following periods:

- Pre-policy: from Jul-2009 to Oct-2014
- Policy (version 1): from Nov-2014 to Jul-2016
- Policy (version 2): from Aug-2016 to Jun-2019
- Policy (version 3): from Jul-2019 to Dec-2020

The Ig growth rate has decreased during the versions 2 and 3 of the National Policy. A lower growth rate in the total number of Ig patients was also observed during the versions 1 and 3 of the National Policy.

We have also assessed the average, median, maximum and minimum grams of Ig per kilogram per dispensing activity to patients pre- and post-implementation (versions 1 to 3) of the National Policy. There was a slight increase in the average grams of Ig per kilogram after introduction of versions 2 and 3 of the National Policy.

* In order to assess the growth rates of Ig dispensed and number of Ig patients pre- and post-implementation of the National Policy, the 12-month growth rate, quarter by quarter, was used (see page 20 for more information). The quarter growth rate was then multiplied by 4 to estimate the annual growth rate in each period.
** In the analysis of Ig grams per kilogram, blank records, negative values and Ig grams per kgs above 5 were excluded from our analysis.

The Ig use growth rate and Ig patient growth rate have decreased since BloodSTAR was implemented

Table 19: Ig growth and number of patients

		Pre-BloodSTAR	Post-BloodSTAR
Period assessed (quarters) - NSW*		32	9
Period assessed (quarters) - all other jurisdictions*		23	16
Ig growth	Average quarter Ig growth	2.1%	1.1%
	Estimated annual growth	8.4%	4.6%
	Difference from previous period	**-**	**-46%**
Growth rate of total number of Ig patients	Average quarter Ig growth	1.8%	0.8%
	Estimated annual growth	7.3%	3.2%
	Difference from previous period	**-**	**-57%**

* BloodSTAR was introduced in 2018 in NSW and 2016 in all other jurisdictions.

In order to assess the growth rates of total Ig dispensed and number of Ig patients pre- and post-introduction of the BloodSTAR, the 12-month growth rate, quarter by quarter, was used (see page 20 for more information).

Table 20: Average, minimum, maximum and median Ig grams dispensed per kilogram *

	Pre-BloodSTAR	Post-BloodSTAR
Dispensing activities	642,080	442,452
Average (Ig grams / Kg)	0.53	0.64
Difference from previous period	**-**	**21%**
Maximum (Ig grams / Kg)	4.98	4.98
Minimum (Ig grams / Kg)	0.01	0.01
Median (Ig grams / Kg)	0.40	0.41

BloodSTAR was developed by the NBA to serve the needs of health providers and support users to meet their obligations under the National Policy. Through BloodSTAR, Ig prescribers are able to determine whether patients are eligible to receive government-funded Ig product and seek authorisation for access, and dispensers use it and other associated systems to manage infusions and dispensing to approved patients.

BloodSTAR was introduced from July to December 2016 in almost all jurisdictions, with the exception of NSW, which introduced it in October 2018. It replaced a previous system, called STARS.**

Annual growth rate in Ig usage was considerably lower after the introduction of BloodSTAR (reduction of 46%). The growth rate of total number of Ig patients was also lower during the period of BloodSTAR (reduction of 57%).

We have also assessed the average, median, maximum and minimum grams of Ig per kilogram dispensed to patients pre- and post-implementation of BloodSTAR. This shows that there was an increase in the average grams of Ig per kilogram post-implementation (21%).

Anecdotally, clinicians and jurisdictional representatives observed that BloodSTAR:

- has encouraged greater adoption and consistency of patient treatment in line with the Criteria
- assisted in the review of patients, and/or prompt of dosage and evidencing of treatment need

*In the analysis of Ig grams per kilogram, blank records and negative values have been excluded. We have set 5 grams per kilogram as a maximum, as more there few outliers with value above this value and it is probably typo.

** STARS is not an NBA system, but NBA have access to data from STARS.

Line of enquiry: Is there any change in Ig demand growth before and after the introduction of BloodSTAR?

The average Ig grams dispensed per kg has slightly increased over time

Table 21: Summary of evaluation question 4: difference from previous period

	Pre-implementation of the Program	Implementation of the Program	Post-implementation of the Program
Changes in the composition of top 10 medical conditions	-	**No major changes observed**	**No major changes observed**
Dispensed Ig per Kg for top 10 medical conditions	-	↑	↑

Legend:

↑ or ↓: Increase or decrease between 1% and 25%
↑↑ or ↓↓: Increase or decrease between 26% to 50%
↑↑↑ or ↓↓↓: Increase or decrease between 51% to 75%
↑↑↑↑ or ↓↓↓↓: Increase or decrease from 76% to 100%

There have been no major changes in the composition of the top 10 medical conditions in terms of total Ig use during or after the implementation of the Program.

There is a slight increase in the average Ig grams dispensed by kilogram during and after the implementation of the Program.

Stakeholders to this evaluation noted the following observations regarding clinical practice over the period analysed:

- Primary Immunodeficiency disorders (PID) definitions and criteria changed, resulting in tightening of eligibility. Additionally, many more PID patients are undergoing haemopoietic stem cell transplantation, potentially reducing their overall Ig usage (which previously would be for long-term). A number of PID patients are also being treated alternatively including with antibiotic prophylaxis which reduces their need for Ig.
- The ability to transplant acquired hypogammaglobulinaemia or haematology oncology patients with haemopoietic stem cells, which typically carry greater risk of infection. For this patient cohort, Ig use is anticipated to grow.
- Over the COVID-19 period, a number of patients were transitioned to Subcutaneous Ig (instead of IvIg) to reduce their hospital visitation. However, this isn't considered to change the dosage rates particularly

The composition of the top 10 medical conditions remains relatively stable over the period analysed

Figure 9 shows the top ten medical conditions (in terms of total Ig dispensed per financial year) between 2009-10 to 2019-20.

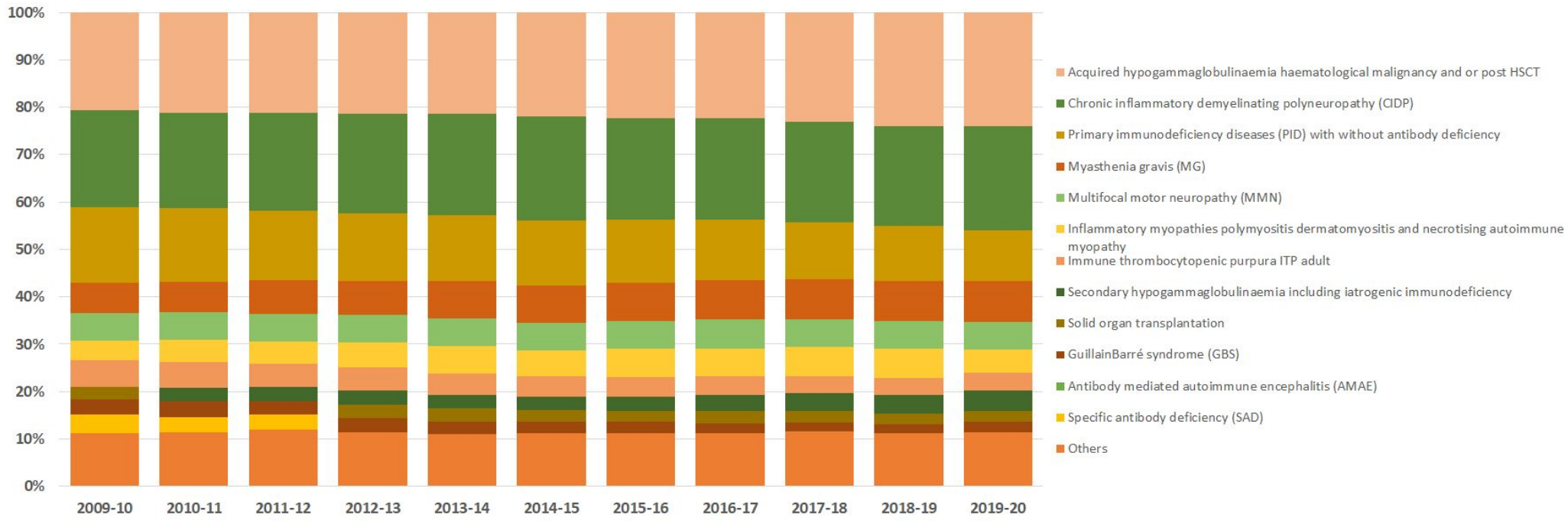
The top 5 medical conditions (acquired hypogammaglobulinaemia haematological malignancy, chronic inflammatory demyelinating polyneuropathy, primary immunodeficiency diseases, myasthenia gravis and multifocal motor neuropathy) account for around 70% of the total Ig dispensed and it has not changed with the Program.

Some variability is observed in the last 3 positions of the top 10 medical conditions. However, these only account for around 10% of the total Ig dispensed per year.

The top 10 medical conditions account for almost 90% of all Ig dispensed from July 2009 to December 2020.

Data from July to December 2020 were also analysed but is not included in the graph. The composition of the ten top medical conditions over these six months is very similar to the composition shown in Figure 9 for 2019-20.

Figure 9: Top 10 medical conditions in terms of total Ig dispensed in Australia from 2009-10 to 2019-20



Line of enquiry:
Is there any change in the top 10 conditions before and after the Program?

Average Ig dispensed per kilogram has increased across many conditions over time

We have assessed the average grams of Ig per kilogram dispensed to patients pre-, during and post-implementation of the Program for the top 10 medical conditions in 2019-20:

- Pre-implementation of the Program: from Jul-2009 to Dec-2013
- Implementation of the Program: from Jan-2014 to Oct-2019
- Post-implementation of Ig Governance Program: from Nov-2019 to Dec-2020

In the analysis of Ig grams per kilogram, blank records and negative values were excluded from our analysis.

Increase in Ig grams per kilogram post-implementation should be considered with recognition of the short period assessed (fourteen months).

Out of the top 10 medical conditions, the average Ig grams per kilogram for eight of them have increased, while the other two medical conditions have recorded a decrease in the Ig dispensed.

The average growth from pre- to post- implementation of the Program for those medical conditions with an increase, saw an average dosage increase of 25% and the two medical conditions with a decrease, saw an average decrease of 18%.

Table 22: Average Ig grams dispensed per kilogram pre, during and post implementation in the top 10 medical conditions in 2019-20 and 2020-21

Position	Medical condition	Pre-implementation of the Program	Implementation of the Program	Post-implementation of the Program	Difference pre- vs. post- Program
	Total dispensing activities	268,266	593,808	160,609	-
1	Acquired hypogammaglobulinaemia haematological malignancy and/or post HSCT	0.37	0.40	0.44	**18%**
2	Chronic inflammatory demyelinating polyneuropathy CIDP	0.58	0.64	0.80	**37%**
3	Primary immunodeficiency diseases PID with/without antibody deficiency	0.43	0.48	0.55	**28%**
4	Myasthenia gravis MG	0.58	0.62	0.70	**20%**
5	Multifocal motor neuropathy MMN	0.66	0.78	0.97	**48%**
6	Inflammatory myopathies polymyositis dermatomyositis & necrotising autoimmune myopathy	0.62	0.64	0.72	**16%**
7	Secondary hypogammaglobulinaemia including iatrogenic immunodeficiency	0.40	0.43	0.47	**16%**
8	Immune thrombocytopenic purpura ITP adult	1.07	1.20	1.23	**15%**
9	Solid organ transplantation	0.88	0.87	0.84	**-5%**
10	Antibody mediated autoimmune encephalitis AMAE	1.19	0.85	0.82	**-31%**

4.2 Immunoglobulin cost assessment

Estimated cost savings can be attributed to reductions in the total growth rate for Ig use

Table 23: Summary of evaluation question 5

	Pre-implementation of the Program	Implementation of the Program	Post-implementation of the Program
Observed cost saving	-	-	**$71m***

* The average Ig cost per gram depends on the distribution of intravenous and subcutaneous Ig, distribution of different Ig products and ration between domestic and imported Ig. For this calculation, it was assumed that all variables associated with the Ig cost per gram would be constant and the only difference being the total Ig dispensed per year.

To assess the **cost saving** of the Program, the observed Ig growth rate was compared to what it may have otherwise been over the past two financial years. This results in an estimated $71 million saved over the past two years based on the lower Ig growth rate of around 6% between 2018-19 and 2019-20. The main driver of change in Ig growth rate in the last two years is the decrease in growth rate in the number of patients.

While not key performance indicators of the Program, two further analyses were undertaken to understand how Ig use has and is changing:

- The first was the comparison of changes in Ig use per 1,000 population across a range of medical conditions and different Jurisdictions (per the 2012 Review of Authorisation and Clinical Governance Arrangements of IVIg).
- The second was the Ig accessed through Jurisdictional Direct Orders which are for medical conditions that are not funded under the Criteria, but which are accessed through jurisdictional arrangements.

An estimated $71 million in savings has been achieved through reduced Ig growth rates over the last two years

Table 24: Total Ig dispensed, total cost, Ig cost per gram and annual growth from 2009-10 to 2019-20

Financial year	Ig dispensed (tonnes)	Total cost ($million)	Ig cost per gram	Annual growth of total Ig dispensed
2009-10	2.7	273.8	$103	-
2010-11	3.0	296.1	$100	**11%**
2011-12	3.3	322.0	$98	**11%**
2012-13	3.6	347.6	$96	**11%**
2013-14	4.0	435.6	$108	**11%**
2014-15	4.4	498.9	$113	**10%**
2015-16	5.0	544.6	$109	**12%**
2016-17	5.5	532.3	$96	**11%**
2017-18	6.1	582.3	$95	**11%**
2018-19	6.6	615.9	$94	**7%**
2019-20	7.0	639.5	$91	**7%**
2020-21*	3.8	342.2	$91	**N/A**

* Financial year 2020-21 includes only 6 months of data, from July to December-2020.

In the two financial years after the implementation of the Program, the annual growth of total Ig dispensed was significantly lower than the previous years (average of 11% *versus* 7%, respectively) - see table 24.

In order to estimate the cost saving associated with the Program, the total Ig dispensed has been assumed to follow a 11% growth rate in the last two financial years after the implementation of the Program (table 25). The average Ig cost per grams (based on costs provided by NBA in each year) has been applied to this growth estimate. The total cost for 2018-19 and 2019-20 based on an 11% growth rate, as compared to the actual growth observed calculates a $71 million cost savings over the past two financial years; $22 million in 2018-19 and $49 million in 2019-20.

Table 25: Projected scenario of total Ig dispensed, total costs and savings with the Program

Financial year	Ig dispensed (tonnes)	Total cost ($million)	Ig cost per gram**	Annual growth	Savings ($million)
2018-19	6.7	632.1	$94	11%	$21.6
2019-20	7.5	682.5	$91	11%	$49.3
Total savings	-	-	-	-	**$70.9**

** The average Ig cost per gram depends on the distribution of intravenous and subcutaneous Ig, distribution of different Ig products and ration between domestic and imported Ig. For the no Program projected scenario (Ig annual growth of 11%), It was assumed that all variables associated with the Ig cost per gram would be constant and the only difference being the total Ig dispensed per year.

The indicative saving scenarios modelled as part of the 2012 Review have not been observed

Table 26: Potential saving scenarios (1-5 and 6) pre-, during and post-implementation of the Program*

	Pre-implementation					Implementation				Post-implementation	
	2009-10	2010-11	2011-12	2012-13	2013-14	2014-15	2015-16	2016-17	2017-18	2018-19	2019-20
Scenario 1: Idiopathic thrombocytopenic purpura: expected to be reduced to 6 grams per 1,000 population*											
NSW	7.8	8.9	7.4	7.8	8.4	8.0	9.1	9.8	10.7	11.0	10.0
NT	2.7	8.1	7.5	10.0	5.1	4.2	5.1	4.7	8.0	2.4	6.0
QLD	9.0	10.0	9.1	10.7	10.2	11.7	12.4	11.8	11.9	11.0	13.2
SA	9.5	9.2	9.9	10.5	12.3	11.5	12.7	14.1	11.9	15.0	18.0
Scenario 2: Acquired hypogammaglobulinemia: expected to be reduced to 20 grams per 1,000 population*											
NSW	25.5	29.2	32.3	35.5	38.6	43.6	50.6	55.8	62.5	67.4	25.5
QLD	43.0	48.7	52.9	57.8	63.0	69.1	76.1	83.5	89.2	92.5	43.0
TAS	43.8	54.2	53.7	53.2	57.5	63.6	62.7	55.6	70.1	77.8	43.8
VIC	18.3	21.2	22.3	24.5	28.6	32.7	34.1	36.3	42.1	47.8	18.3
Scenario 3: Primary immunodeficiency diseases: expected to be reduced to 20 grams per 1,000 population*											
NSW	24.8	27.3	27.4	29.2	32.5	35.7	37.6	40.7	42.6	42.6	39.9
Scenario 4: Inflammatory myopathies: expected to be reduced to 8 grams per 1,000 population*											
NSW	6.3	8.8	9.5	11.0	12.1	11.9	12.5	13.9	16.3	16.2	13.1
TAS	8.3	10.3	11.4	10.1	8.8	8.5	9.4	10.5	11.6	10.3	8.8
Scenario 6: GuillainBarré syndrome: expected to be reduced to 4 grams per 1,000 population*											
NSW	4.1	4.6	4.7	4.3	4.2	4.3	5.3	6.0	5.3	6.4	5.5
VIC	4.5	5.8	4.5	5.0	5.8	4.9	5.5	3.8	4.5	4.1	4.4

The 2012 Review of the Authorisation and Clinical Governance Framework for Intravenous Immunoglobulin highlighted significant variation in IVIg use, management and processes nationally.

Improvements were recommended as part of this review which later resulted in the Program in 2014.

In order to illustrate potential savings, a number of different scenarios were modelled using an analysis of the impact on individual jurisdictional prescribing rates applying conservative assumptions.

In total, six different indicative saving scenarios were modelled and five of them have been assessed as part of this review. As can be seen in table 26, none of the scenarios have been observed. Instead, different prescribing practices have been observed.

For scenario 5 “Chronic inflammatory demyelinating polyneuropathy: of the 20% of CIDP patients who are on long term therapy, 20% who are trialled off are assumed to remain off therapy and symptom free”, due to limitations of the data available, It was not possible to test this.

* For each scenario, the 2012 review have modelled reduction in Ig use per 1,000 population only for those jurisdictions considered to have a high Ig use.
** Population data were sourced from Australian Bureau of Statistics: ABS. Australian Bureau of Statistics. Population Projections, Australia. Available from: <https://www.abs.gov.au/statistics/people/population/population-projections-australia/latest-release#data-download>.

It is estimated that the Program could save on average $200 million/year out to 2030-31

Three different scenarios of Ig growth rate have been created to estimate cost savings associated with changes in demand (based on historical data) between 2020-21 to 2030-31. See Figure 10 for project annual Ig growth for the analysis period. These scenarios were compared with "no Program", which represents an annual Ig growth rate of 11%.

Table 27: Summary of evaluation question 6: difference from previous period

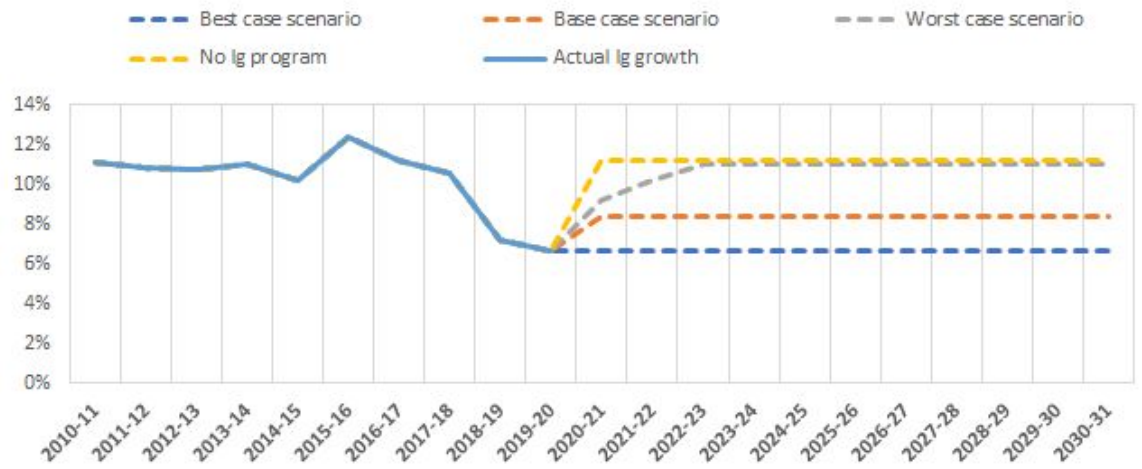
		from 2020-21 to 2030-31
Project cost saving	base-case scenario (Ig annual growth of 8.4%)	$2.2b
	best-case scenario (Ig annual growth of 6.7%)	$3.4b
	worst-case scenario (Variable Ig growth rate, with maximum of 11%)	$0.3b

For the base-case scenario, an estimated $2.2 billion in savings could be achieved from changes in Ig growth rate over the period 2020-31, which represents an average of around $200 million dollars per financial year. Total savings vary between $3.4 billion to $0.3 billion across best- and worst-case scenarios.

It is worth noting that the purpose of the analysis here considers historical data and the estimated Ig growth rate in the future. However, there are many factors that could drive changes in Ig growth rate in the future which can not be easily predicted. For instance, new treatments which could replace Ig and reduce its use, can have a significant impact on the estimated cost saving.

The analysis presented here focuses on what the future cost savings could be based on the annual growth rates in the last few years. Figures should be interpreted with full understanding/ acknowledgement of the assumptions or limitations.

Figure 10: Current Ig annual growth and projected growth for three different scenarios



A continued reduction in growth rates for Ig use will deliver savings over the next 11 years

Table 28: Total Ig dispensed and total costs projected to 2030-31 for four different scenarios*

Financial year	Scenario 1 (no Program)[1]		Scenario 2 (best-case)[2]		Scenario 3 (base-case)[3]		Scenario 4 (worst scenario)[4]		Cost savings (base-case minus no Program scenarios)
	Ig (tonnes)	Cost ($m)	Ig (tonnes)	Cost ($m)	Ig (tonnes)	Cost ($m)	Ig (tonnes)	Cost ($m)	Cost ($m)
2020-21	7.8	736	7.5	707	7.6	718	7.7	724	**-17**
2021-22	8.6	816	8.0	754	8.2	779	8.4	797	**-38**
2022-23	9.6	906	8.5	804	8.9	844	9.4	885	**-62**
2023-24	10.6	1,006	9.1	858	9.7	915	10.4	982	**-91**
2024-25	11.8	1,117	9.7	915	10.5	992	11.5	1,091	**-125**
2025-26	13.1	1,239	10.3	976	11.4	1,075	12.8	1,211	**-164**
2026-27	14.6	1,376	11.0	1,041	12.3	1,165	14.2	1,344	**-210**
2027-28	16.2	1,527	11.7	1,110	13.4	1,263	15.8	1,491	**-264**
2028-29	17.9	1,695	12.5	1,184	14.5	1,369	17.5	1,656	**-326**
2029-30	19.9	1,881	13.4	1,263	15.7	1,484	19.4	1,838	**-397**
2030-31	22.1	2,088	14.3	1,348	17.0	1,609	21.6	2,040	**-479**
Total	152.2	14,387	116.0	10,960	129.2	12,214	148.7	14,057	**-2,173**
Difference from no Program and Ig price sensitivity analysis									
Ig price: $94.5/g (base)			-36.3	-3,427	-23.0	-2,173	-3.5	-329	**-2,173**
Ig price: $113.4/g (+20%)			-36.3	-4,112	-23.0	-2,608	-3.5	-395	**-2,608**
Ig price: $75.6/g (-20%)			-36.3	-2,742	-23.0	-1,739	-3.5	-263	**-1,739**

To compare the potential future cost savings associated with Ig growth rate reductions, a number of scenarios have been modelled against a "no Program" scenario.

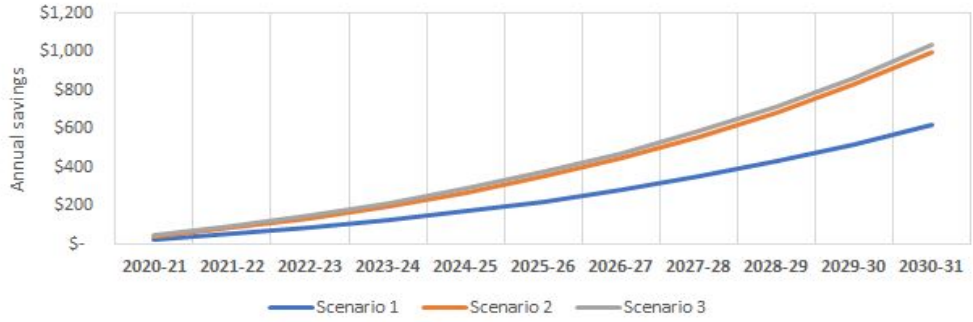
The total cost for the "no Program" has been estimated using an annual Ig growth rate of 11%, the average rate growth pre and during the implementation of the Program. The three additional scenarios use different Ig growth rates, defined as:

- Scenario 2: Ig annual growth rate of 6.7%, which is the annual growth rate of 2019-20 and reflects the best-case scenario. In this case, the lower growth rate is maintained for the next 11 years
- Scenario 3: Ig annual growth rate of 8.4%, which is the estimated annual growth rate from the last three quarters of data (Q4 2019-20, Q1 and Q2 2020-21 - see appendix B) and represents the base-case.
- Scenario 4: Ig annual growth rate increasing from 8.4% to a maximum of 11.0%, following the trajectory of the last three quarters of data only (Q4 2019-20, Q1 and Q2 2020-21). This is the worst-case scenario.

The predicted future cost saving for the base-case scenario is $2.2 billion for the next 11 years, varying from $3.4 billion to $0.3 billion for the best-case and worst-case scenario, respectively.

Sensitivity analysis was also applied to the Ig price per gram, considering a variation of plus and minus 20%.

Figure 11: Annual savings: difference between "No Program" and scenarios (1-3)



* Cost per gram of Ig is based on a national weighted average price adopted for HTA Review: Australian Government. Medical Service Advisory Committee. Review of immunoglobulin use for Acquired Hypogammaglobulinaemia Secondary to Haematological Malignancies and haemopoietic stem cell transplantation. November 2019. Available from: <http://www.msac.gov.au/internet/msac/publishing.nsf/Content/1565-public>.

4.3 Immunoglobulin Program implementation

Evaluation question 7 - Has the Program implemented/achieved what the 2012 Review of the Authorisation and Clinical Governance Framework recommended?

A series of questions relating to patient education, the approval process to access Ig, clinician participation in the IVIg framework and effectiveness of BloodSTAR and the Criteria were asked of stakeholders to this review and relate to the recommendations of the 2012 Review. Insights from the evaluation are explored below.

Awareness of the Program and its applicability has grown
While clinical stakeholders perceived that patient awareness of the impact of the Program on their treatment was limited, clinical awareness appears to have grown. The specific resources and Criteria embedded through BloodSTAR has guided clinical teams to better monitor patients, improved access and anecdotally, increased equity in Ig use among patients.

BloodSTAR's inbuilt guidance has driven standardisation
Clinical and jurisdictional stakeholders consider that BloodSTAR, in combination with the Criteria, has improved the use of Ig. The inbuilt guidance has driven improvements in prescription practices, including to 'force' clinicians to consider the evidence for prescriptions and dosage rates, as well as prompting review of patients with ongoing treatment. However, more opportunities exist to tighten the Criteria and to use BloodSTAR to drive common dosing practices. For example, the use of actual body weight instead of ideal body weight to derive a dosage amount is adopted by some clinicians in some jurisdictions, noting, however, that the evidence base is not yet well established and this is an area for exploration and further research.

Clinicians have greater opportunity to input to the Ig Governance framework
The Specialist Working Groups have increased the roles of clinicians in inputting into the Ig Governance framework. While the governance structure (committees and their roles and responsibilities) is outside the scope of this review, anecdotally, clinicians are supportive of the role and guidance of clinicians into the Criteria in particular.

Gain in efficiency with BloodSTAR, as it automates components of the approval process
Similarly, the introduction of BloodSTAR is well-recognised to require prescribers to standardise their prescribing practices in line with the Criteria. The BloodSTAR system partly automates this in that it provides clear indications to clinicians without the need to rely on phone support (although this is available if needed).

Further benefits are perceived to exist in that the system allows for improved data collection and auditing of prescription practices. However, the rigidity of the requirements was noted by some clinicians to restrict personalisation of treatments and the capacity to use Ig as a management tool (given the authorisation periods lapse). This is the case for rare diseases which don't categorise neatly in BloodSTAR.

Despite the benefits of BloodSTAR, some clinicians perceived that BloodSTAR presented more onerous requirements in entering patient details and undertaking patient reviews which can be time consuming and has the potential to be partly automated. This is particularly the case where patients are likely to receive Ig therapy for a longer period.

A number of emerging treatments and indications are likely to influence demand for Ig over time

The following observations were made by stakeholders to this review:

Haematology

- The introduction of anti-CD19 CAR-T cell therapy for B-cell leukaemia/lymphomas may increase usage as patients will develop an acquired hypogammaglobulinemia for a prolonged period
- Indications which do not yet have a strong evidence base may emerge in future demand; for example, haemolytic disease of the newborn

Neurology

- Autoimmune encephalitis and other antibody mediated neurological disorders may drive demand for Ig
- There remains a possibility that B cell manipulating therapies could replace Ig in some settings
- Alternative treatments, such as plasma exchange for neurology patients, may influence future demand for Ig
- Other emerging treatments such as FcRM inhibitors may influence demand for Ig in neurology patients over time

Transplant

- An increase in marginal renal transplant grafts and the age of suitable patients, which will in turn increase demand for Ig

Immunology

- Increasing prevalence of Paediatric Inflammatory Multisystem Syndrome Temporally associated with SARS-CoV-2 (PIMS-TS) or Multisystem inflammatory Syndrome in Children (MIS-C) and its associated need for Ig

Further advice regarding the extent of clinical changes and its impact on future demand should be informed by Specialist Working Groups.

5 Recommendations and opportunities

The Program is associated with a decrease in growth in Ig demand, but enhancement opportunities exist

Key insights from this evaluation:

- There is a **correlation between the Program components and decreasing use of Ig** (most notably following the introduction of Criteria Version 3 and BloodSTAR)
- While a **dip in Ig use is observed through 2018** - likely driven by a decrease in the number of patients - the past four quarters have recorded some growth.
- The observed growth in Ig use over the past four quarters appears to be related to the **age, weight, dosage rates of Ig among patients**, which in turn is driving an overall increase in Ig.
- **Other factors may have impacted Ig growth** (such as adoption of ideal body weight for dosing and other therapies that replaced Ig use), but these are difficult to attribute without robust data).
- Ig demand will continue to grow overall, and the Program provides an important function in ensuring these patients can access Ig
- In particular, there is a **continued and anticipated growing need for Ig** among haematology and neurology patients where an ongoing need and newer clinical treatments are emerging

Recommendations

1. Improving use of data	This review has identified that the reduced growth rate in the total number of Ig patients and slight increase in Ig dispensed per kilogram has driven some of the observed changes in Ig demand. Further analysis should be undertaken into the drivers for: • the reduced growth in patient numbers, accounting for both new and continuing patients, and analysing patient numbers by medical speciality • the slight increase in Ig dispensed per kilogram during and in post-implementation of the Program. Further opportunities exist, more generally, to improve the use of data collected through BloodSTAR to continuously improve and tailor the Program, and drive standardisation across jurisdictions. Examples include: • using data to regularly review the Ig use by speciality to understand how effectively the Criteria are being applied and any differences that exist, including changes in treatment duration for the top ten medical conditions • analysing the changes and associated drivers in Ig use by condition to anticipate changing clinical practice • ongoing monitoring and potentially, auditing, of patient reviews • using data to inform research into the evidence base for the use of ideal body weight for dosage and patient outcomes for 'trial offs' for particular indications. Areas of research could be defined by NBA's Specialist Working Groups to identify opportunities for enhancing the Ig evidence base.
2. Consider opportunities to streamline BloodSTAR	There may be opportunity to continue to enhance the user experience of BloodSTAR, such as pre-population of patient data (from medical records) and supporting specific customisation. Enhancements could continue to be informed by NBA's user groups as a way to improve data quality and reduce barriers to its effective use.
3. Enhance patient education	Improve patient education and awareness of Ig, including the development of patient resources in plain English and patient forums to promote patient engagement. Patients are largely reliant on their clinical team for information and limited understanding of alternatives, the value of 'trial offs' (for fear of placebo effect), and limited incorporation of clinical and patient user needs in the Program may constrain future efficiencies.

A Appendices

Appendix A: Stakeholders consulted

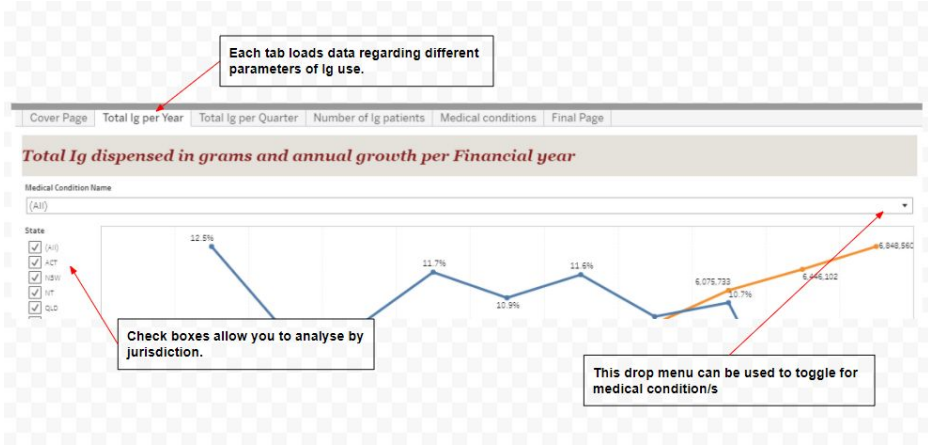
Stakeholders consulted

Online survey

In addition to workshops and consultations held, an online survey was circulated to elicit input from clinicians and user groups. The survey was complemented by an online dashboard to present the key data to support respondents to answer the evaluation questions from the perspective of clinical indications treated or jurisdiction of treatment:

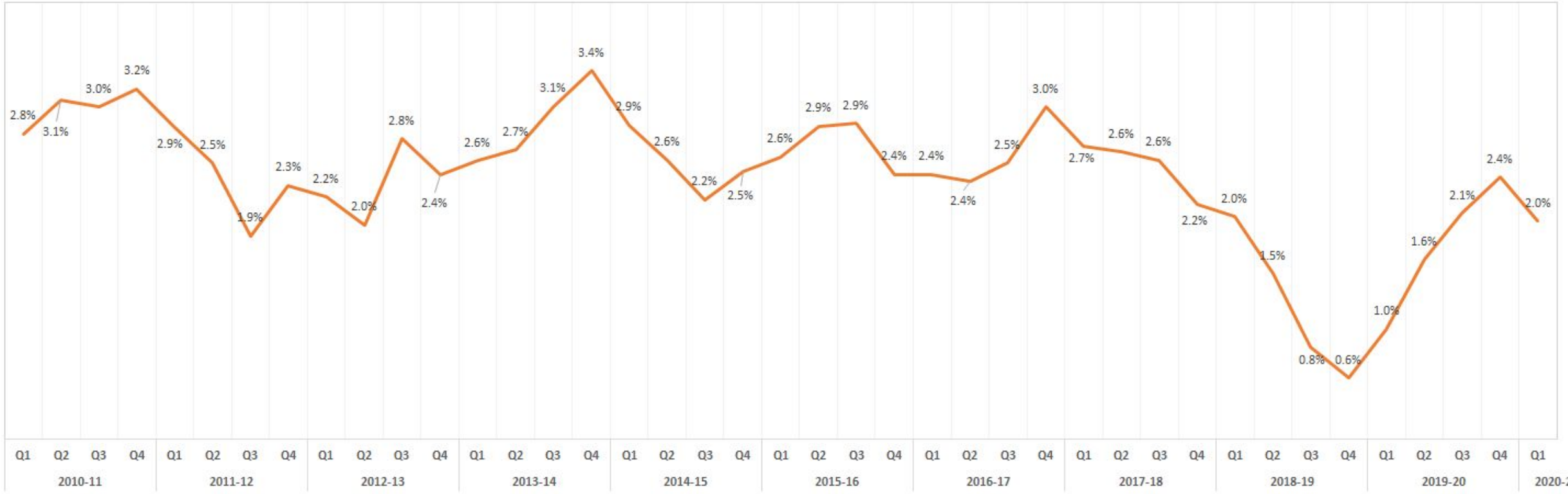
Method of consultation	Stakeholder group	Representation	Date
Workshop	Jurisdictional representatives	Commonwealth (2), ACT (1), NSW (2), VIC (2), NT (1), WA (1), TAS (1) and QLD (1)	22-Feb-2021
	Ig Prescribers	National Immunoglobulin Governance Advisory Committee - NIGAC (8), Neurology (0), Haematology (3), Immunology (1), Transplant (3)	22-Feb-2021
	Lifeblood	4 participants	18-Feb-2021
Online survey	Clinicians	NIGAC (2), Immunology (1), transplant (1), and neurology (1)	N/A
	Ig User group members	7 members, including representatives from each of the four specialties	N/A

Interactive dashboard

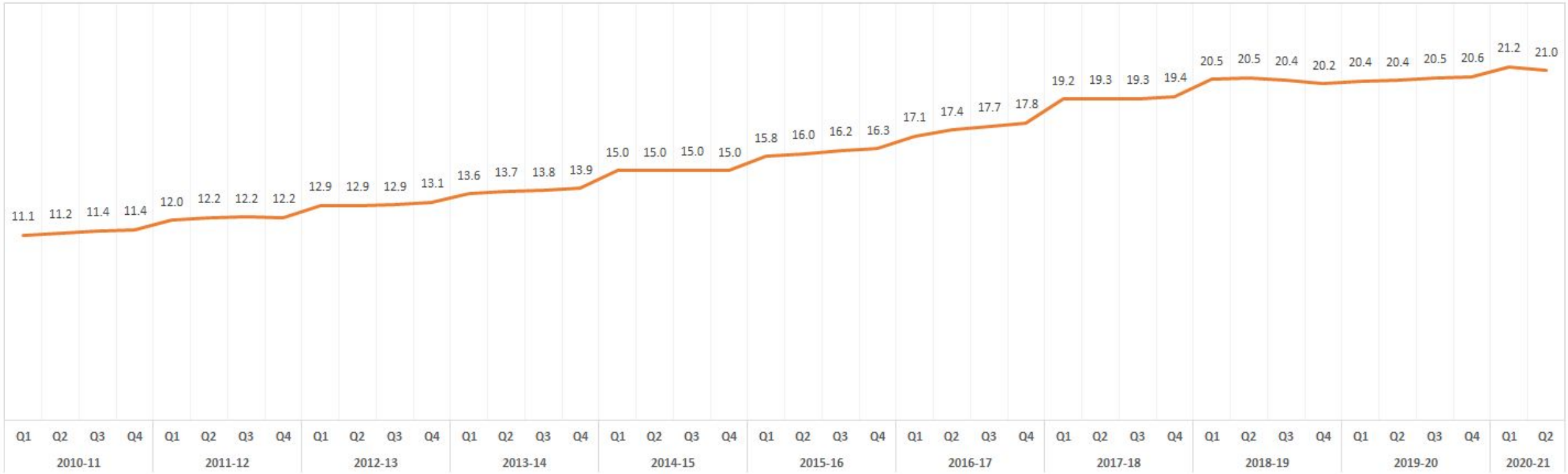


Appendix B: Quarter Ig growth rate, number of Ig patients and total Ig in Australia

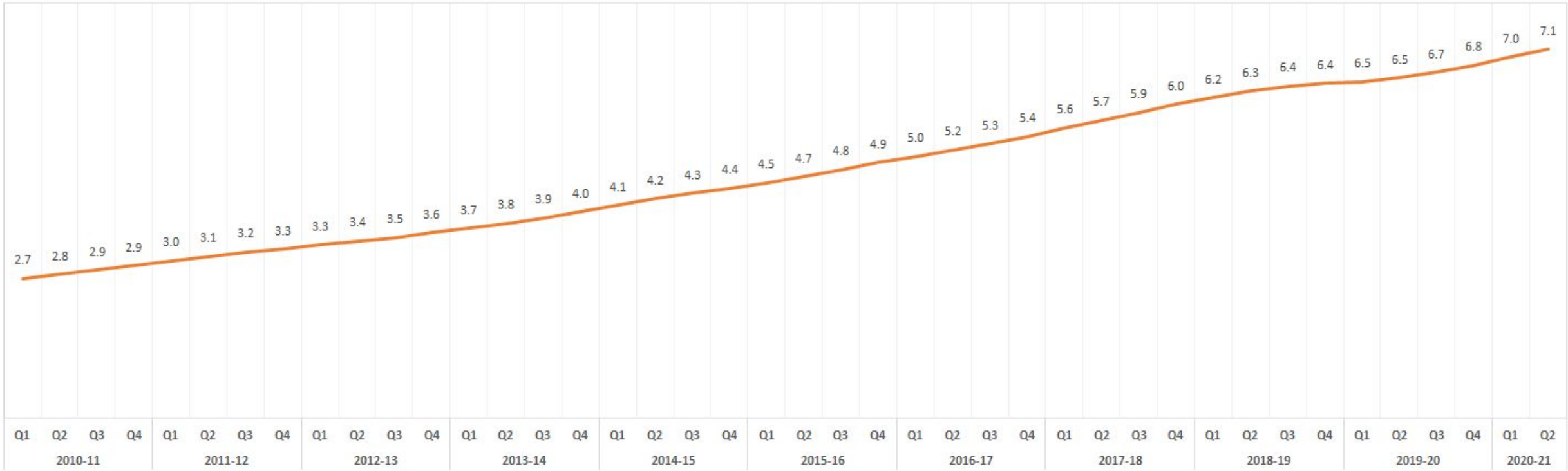
Ig 12-month growth rate, quarter by quarter, in Australia



Number of Ig patients in the last 12 months, reported in thousands, quarter by quarter, in Australia

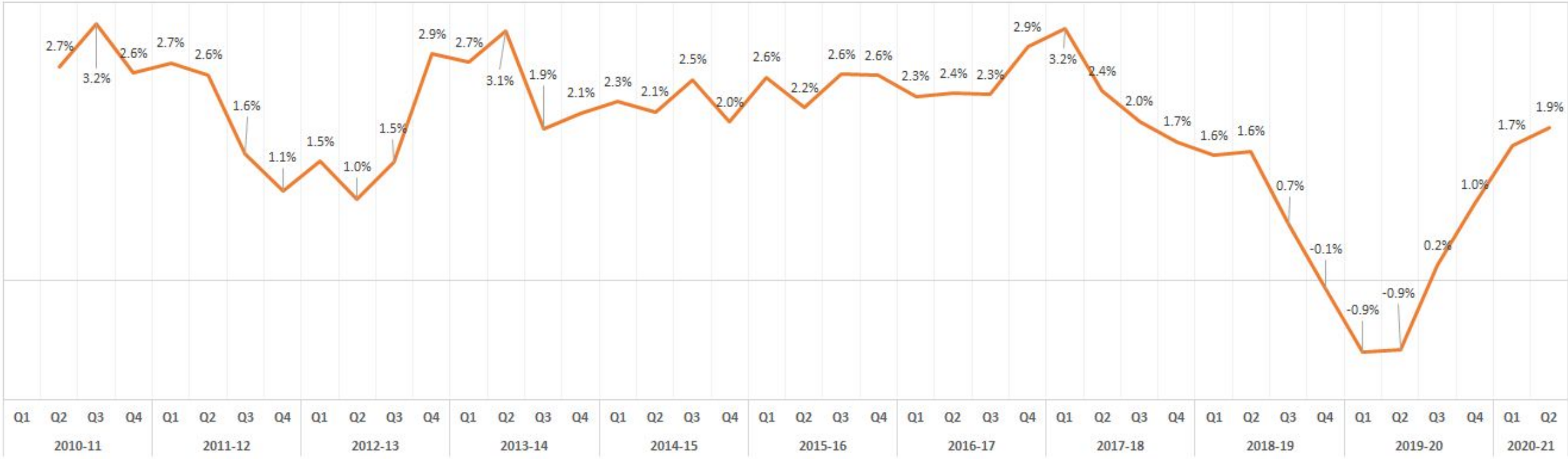


Total Ig dispensed in the last 12 months, reported in tonnes, quarter by quarter, in Australia



Appendix C: Twelve-month Ig growth by quarter of Ig per 1,000 population, adjusted by aging for each Jurisdiction

New South Wales



Australian Capital Territory

Northern Territory

Queensland


2.8%
3.1%
2.2%
2.6%
2.8%
3.2%
3.5%
3.4%
2.5%
1.1%
1.7%
1.0%
1.0%
2.4%
3.0%
3.3%
2.6%
1.9%
1.8%
2.2%
2.8%
2.9%
2.0%
1.5%
1.3%
1.0%
1.4%
2.0%
1.9%
2.1%
1.6%
0.8%
0.8%
0.5%
0.3%
0.4%
0.9%
1.1%
1.5%
1.5%
0.9%
Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2
2010-11
2011-12
2012-13
2013-14
2014-15
2015-16
2016-17
2017-18
2018-19
2019-20
2020-21

South Australia

Tasmania


3.4%
0.4%
0.8%
-0.5%
-1.5%
0.8%
0.6%
-0.9%
-1.0%
-2.3%
-2.7%
0.3%
2.5%
3.1%
3.8%
3.4%
1.3%
1.5%
0.6%
0.5%
-1.0%
-0.5%
1.8%
1.1%
2.6%
1.2%
-1.4%
0.8%
2.5%
5.1%
5.1%
4.1%
3.1%
0.7%
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-1.6%
0.9%
2.5%
3.6%
5.5%
2.3%
Q1 Q2 Q3 Q4
2010-11
2011-12
2012-13
2013-14
2014-15
2015-16
2016-17
2017-18
2018-19
2019-20
2020-21

Victoria


2.2%
2.2%
2.5%
3.2%
2.6%
1.2%
-0.3%
0.5%
1.6%
1.8%
2.6%
2.1%
1.5%
2.0%
2.2%
2.4%
2.0%
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Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2
2010-11
2011-12
2012-13
2013-14
2014-15
2015-16
2016-17
2017-18
2018-19
2019-20
2020-21

Western Australia

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