Demand for plasma-derived medicinal products in Australia

Dr Joanne Pink

Chief Medical Officer, Australian Red Cross Lifeblood

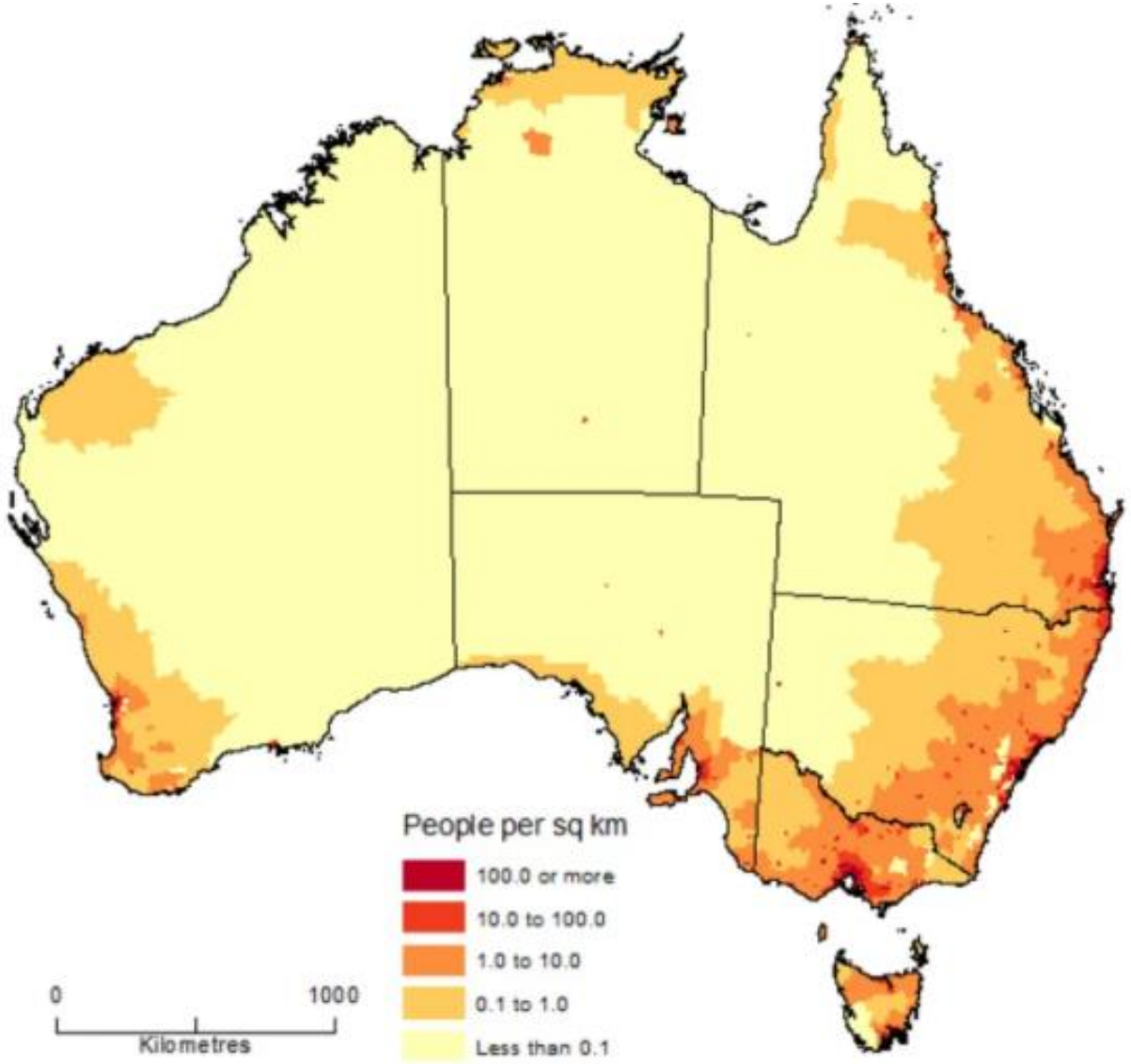
Centro nazionale sangue – CNS
International Federation of Blood Donor Organisations
(IFBDO – FIODS)
28-29 April 2022

Australian Red Cross Lifeblood®

Australia

- Australia is the 6th biggest county in the world – 7.7 million km^2
- 26 million people

- Lifeblood is funded by all Australian Governments
- Blood donation is voluntary and non-remunerated
- Blood and blood products are provided to Australian patients at no cost

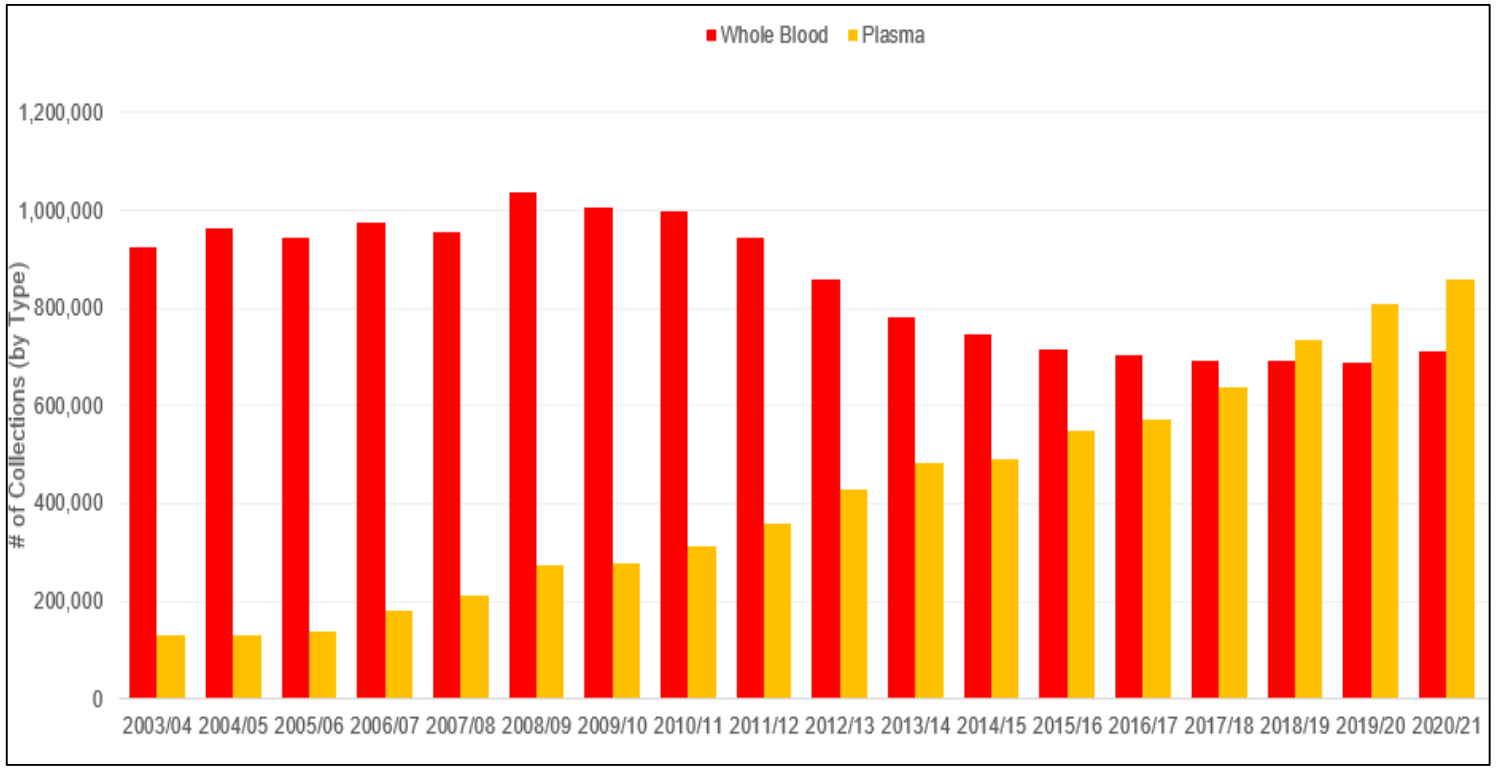


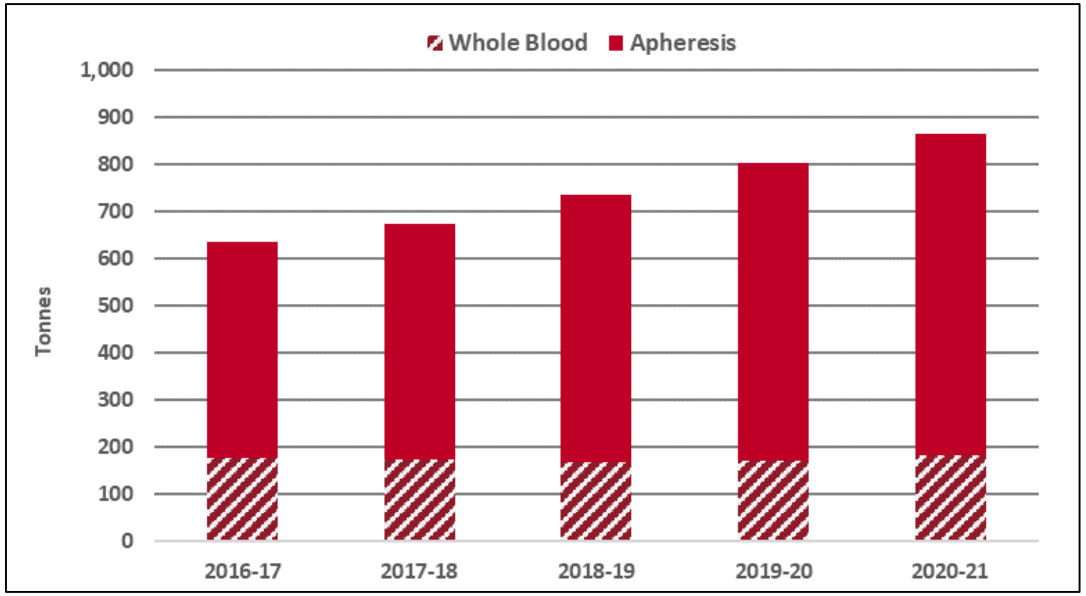
- 96 blood donor collection centres and mobiles
- 515,000 blood donors

- 4 major blood processing facilities
- 2 milk bank processing facilities
- 1 microbiome facility

Changing mix of donations

- 2018/19 was the first year that plasma donations outnumbered whole blood.
- Expect trend to continue (and widen)





Source of plasma for fractionation

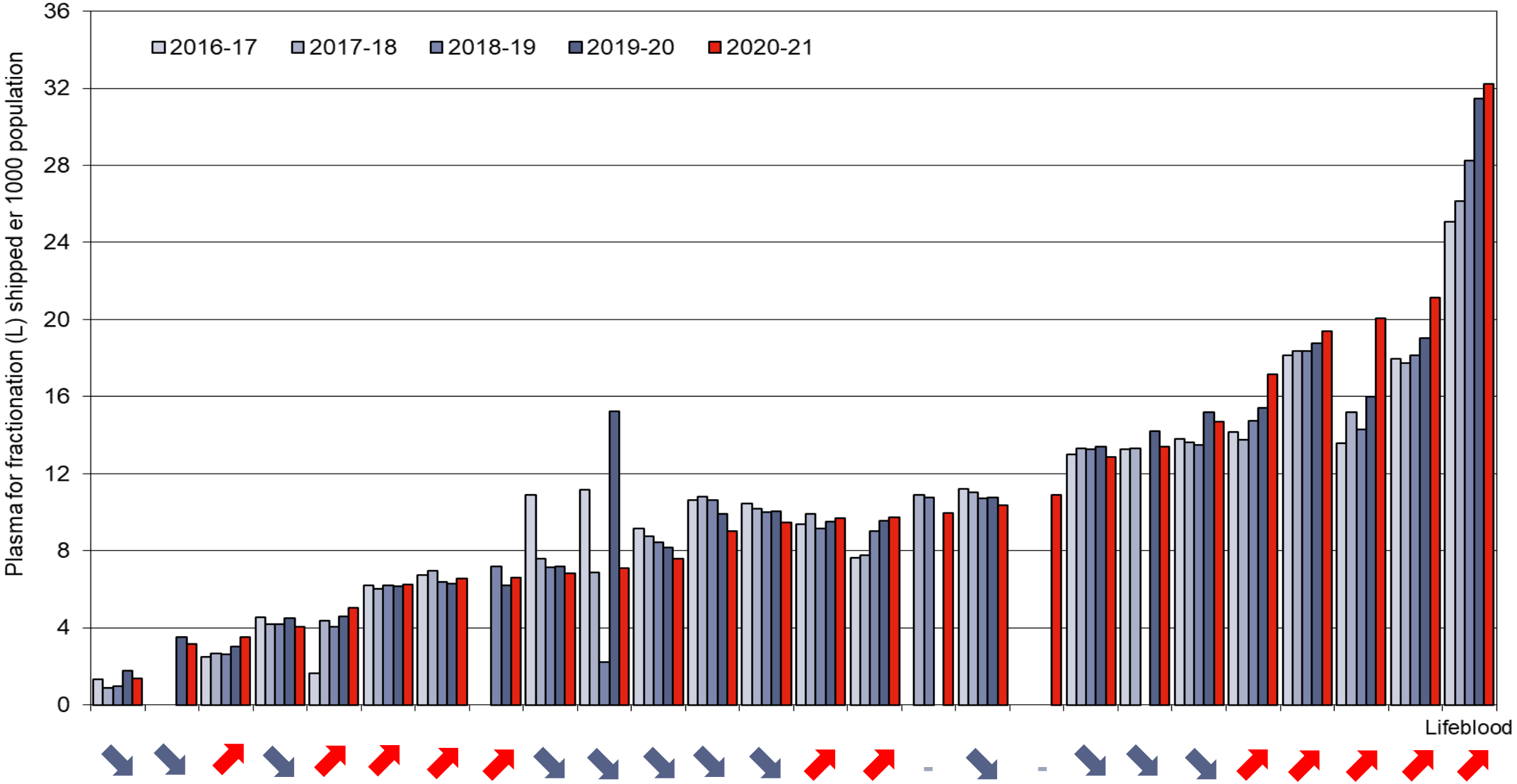
Plasmapheresis collection protocol

- Aurora – Fresenius Kabi Platform

- Comply with CoE Guidelines
- 2 weekly
- Maximum of 25 L per year
- First donation 13% TBV or maximum of 800mL (excluding anticoagulant)
- Second and subsequent 16% TBV or maximum of 800mL (excluding anticoagulant)
- 500mL end-saline wash-back
- 206,000 plasmapheresis panel
- Average donation frequency = 4.07

International benchmarking

Plasma for fractionation (L) per 1,000 population



Note: This information is confidential and reflects deidentified data provided from blood operators (with voluntary donor bases) within the United States of America, Canada, Europe and the Asia Pacific Region

Transforming the supply chain

Donor engagement

Regaining the panel:
- Year of the Blood Donor
- Plasma awareness campaign

Encouraging greater donation frequency:
- Personalisation through technology (Marketing Automation Platform)
- Customer Experience program

Collection sites

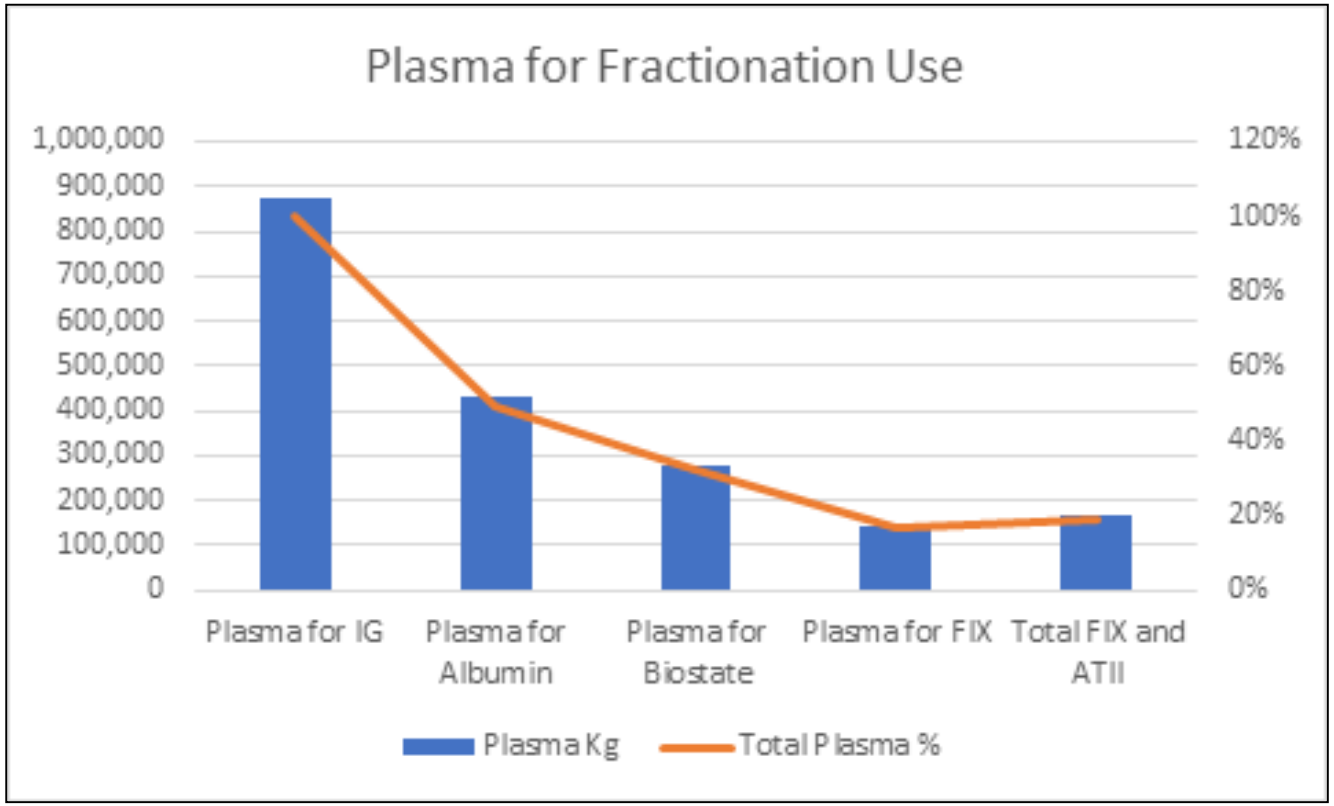
Releasing capacity within the donor centre network:
- Increased opening hours
- Staff roster adjustments
- Additional donor couches
- Additional plasma machines

Increasing efficiency:
- Electronic donor questionnaire
- Aurora

Manufacturing

Releasing capacity with existing Processing Centres:
- Re-configuring storage freezers
- New freezing methods (Blast Freezing) smoothing workflow
- Reviewing transport frequency
- Pooled testing of plasma for fractionation

Plasma for Ig is our plasma driver



FY21	Plasma for IG	Plasma for Albumin	Plasma for Biostate	Plasma for FIX	Total FIX and ATII
Plasma Kg	874,000	429,000	281,000	145,000	169,000
Total Plasma %	100%	49%	32%	17%	19%

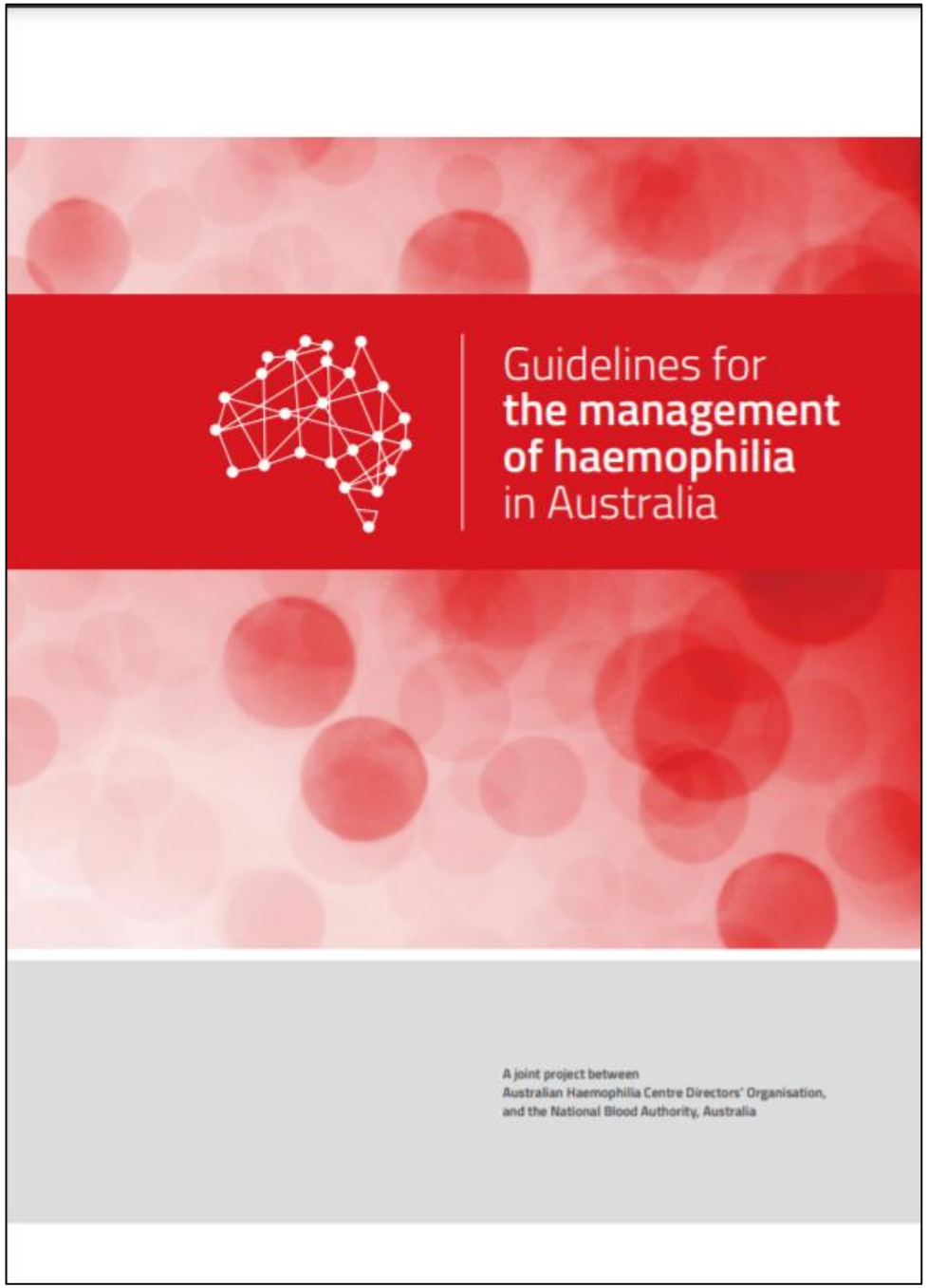
Demand for plasma-derived medicinal products in Australia

- Clotting factor concentrates
  - Factor IX (MonoFIX)
  - Factor VIII (Biostate)
  - Prothrombin complex (Prothrombinex)
- Albumin
- Immunoglobulin products

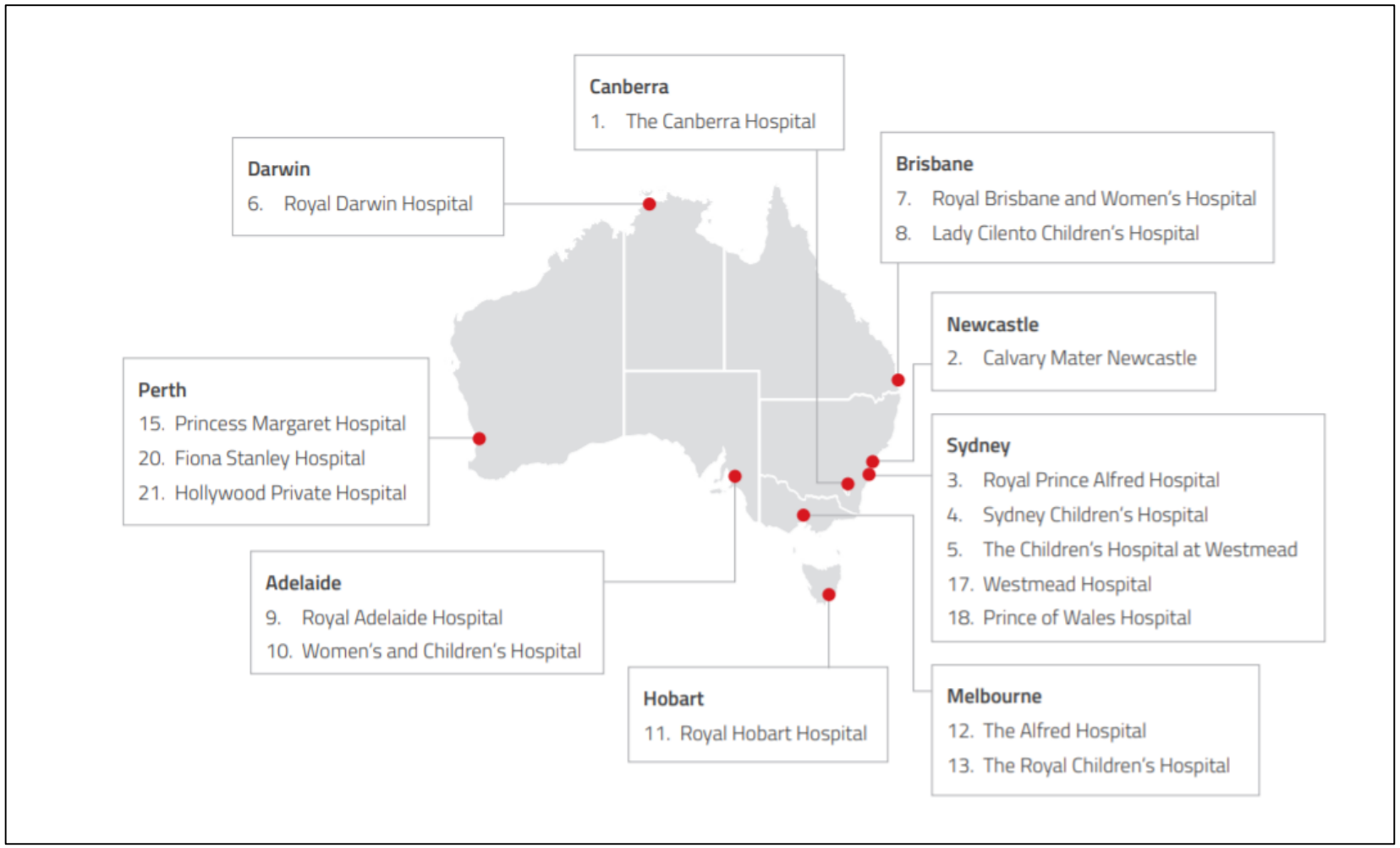
- Governance systems in place

Demand for clotting factor products

- In Australia, recombinant clotting factor concentrates are available for the treatment of haemophilia A and haemophilia B.
- Hemlibra (emicizumab) was introduced in Nov 2020 – a humanized recombinant monoclonal antibody that mimics the function of coagulation factor VIII.
- Plasma-derived products are only used in these patient groups for urgent treatment in cases where recombinant products are not available.
- Plasma derived factor VIII is used for patients with vWD and in patients with factor VIII inhibitors undergoing tolerisation.



Haemophilia Treatment Centres



- Coordinate and, where possible, integrate patient care, research and education to provide the optimal use of expertise and resources within hospitals and the community.

Australian Bleeding Disorders Registry

Database that is designed to collect clinical information related to the treatment of people with inherited bleeding disorders and is used by clinicians to manage the treatment of people with bleeding disorders.

Includes information about:

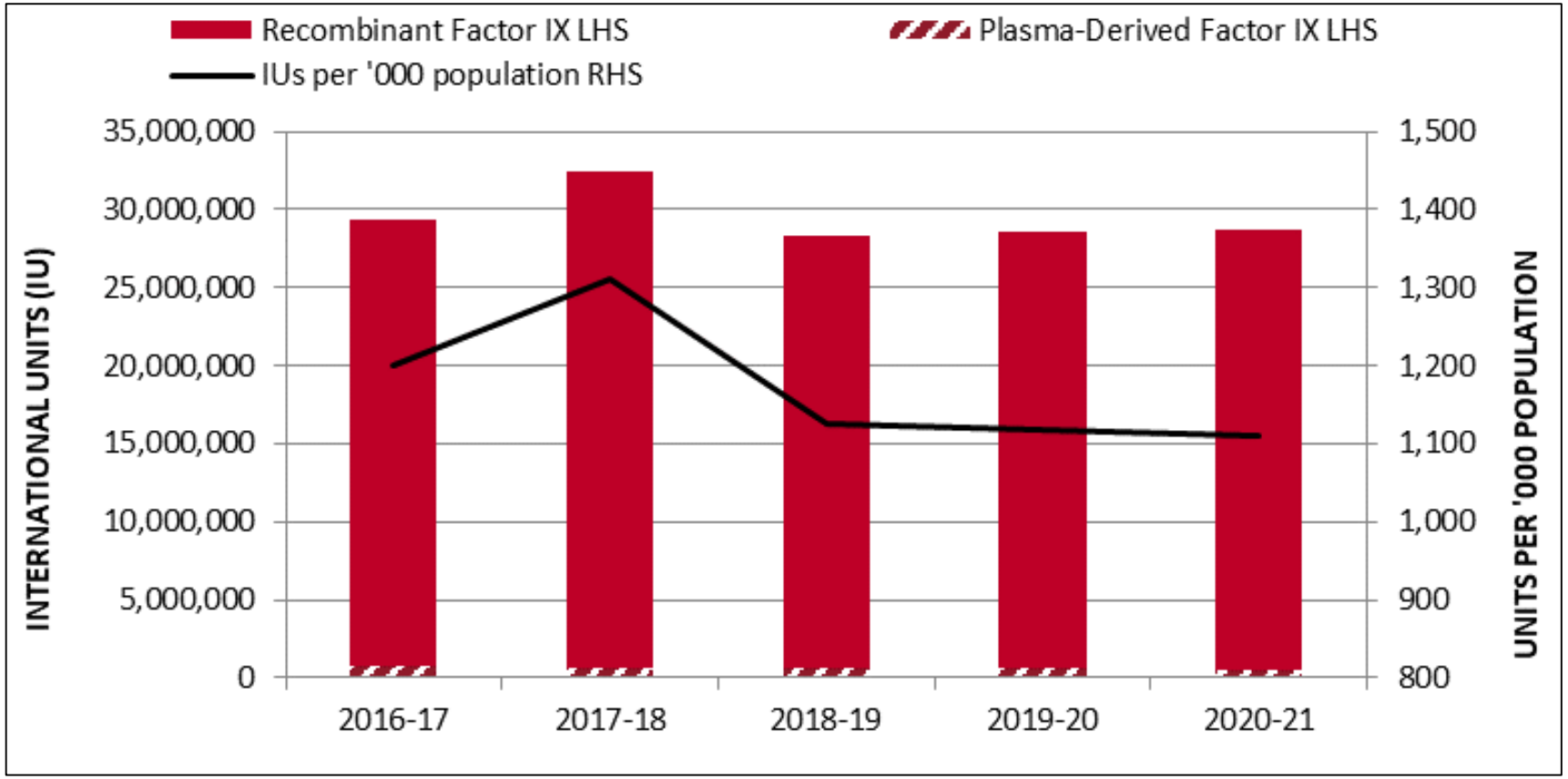
- Patient diagnosis
- Viral status
- Treatment details
- Hospital admissions
- Administration information
- Ordering, supply and use of clotting factor products

In 2019/20:

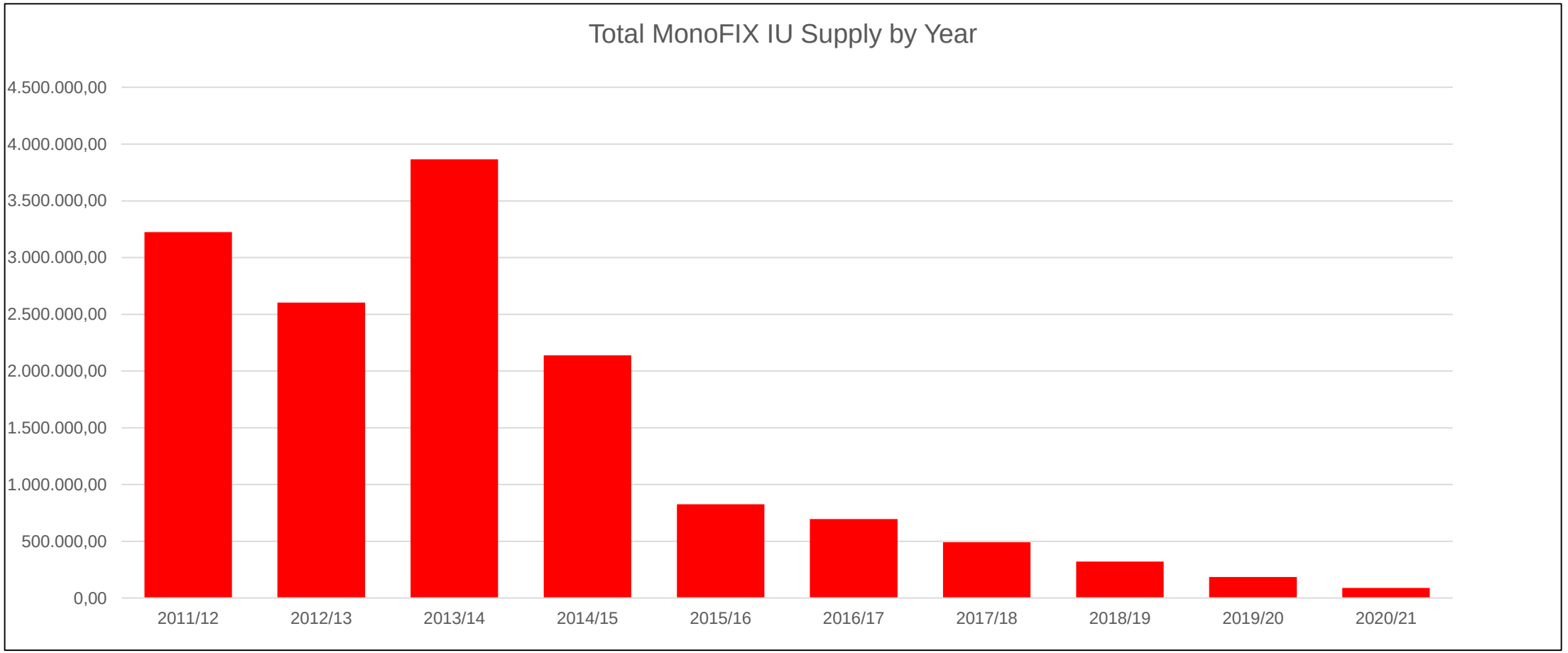
- 6,686 patients
- 5,358 with either Haemophilia A, Haemophilia B or von Willebrand Disease
- 127 with acquired bleeding
- 1201 with other bleeding disorders

Supply of Factor IX products

- Supply about 1,100 units Factor IX per 1,000 population
- Vast proportion is recombinant product

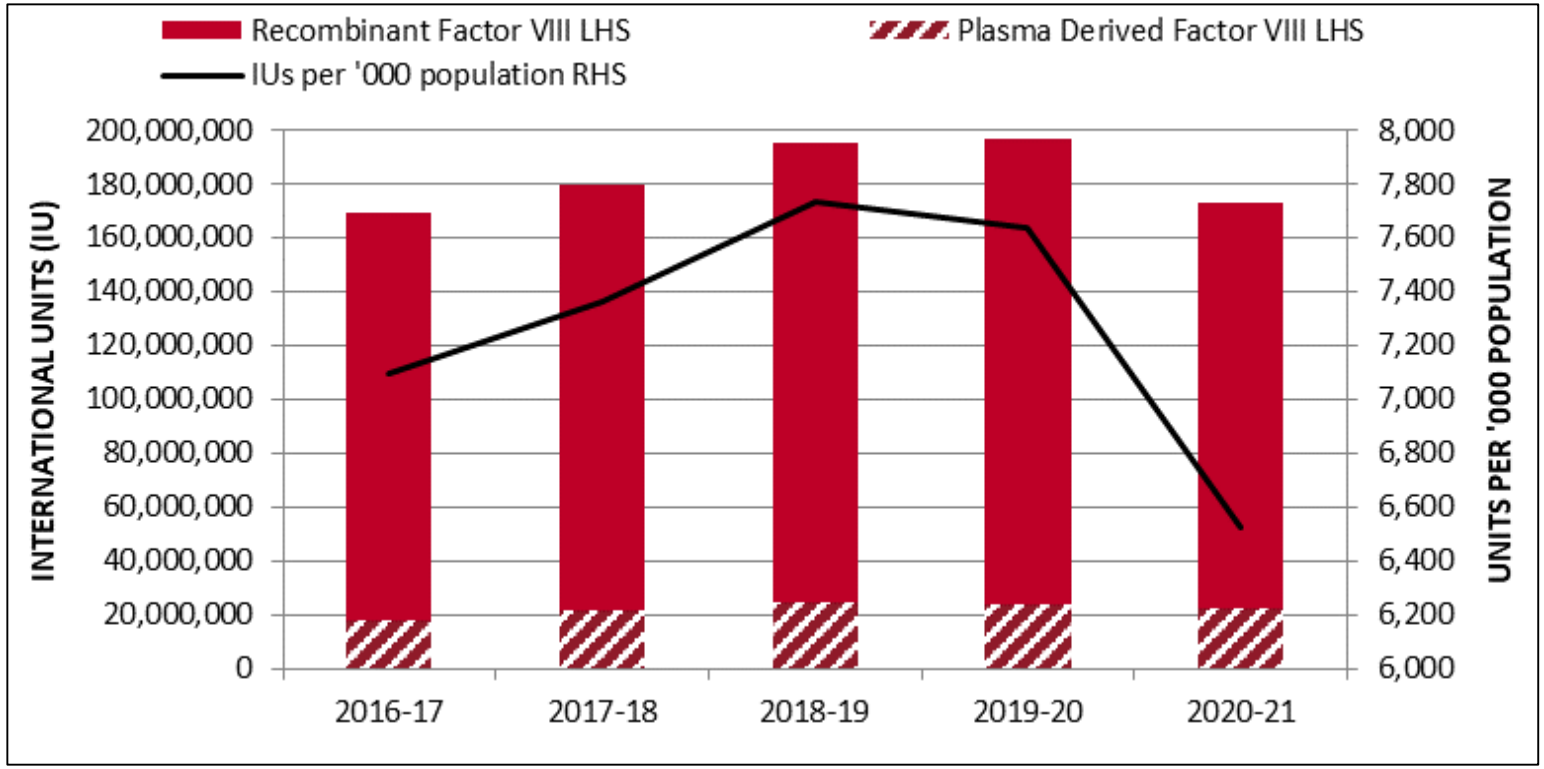


Supply of Plasma-derived factor IX (MonoFIX)

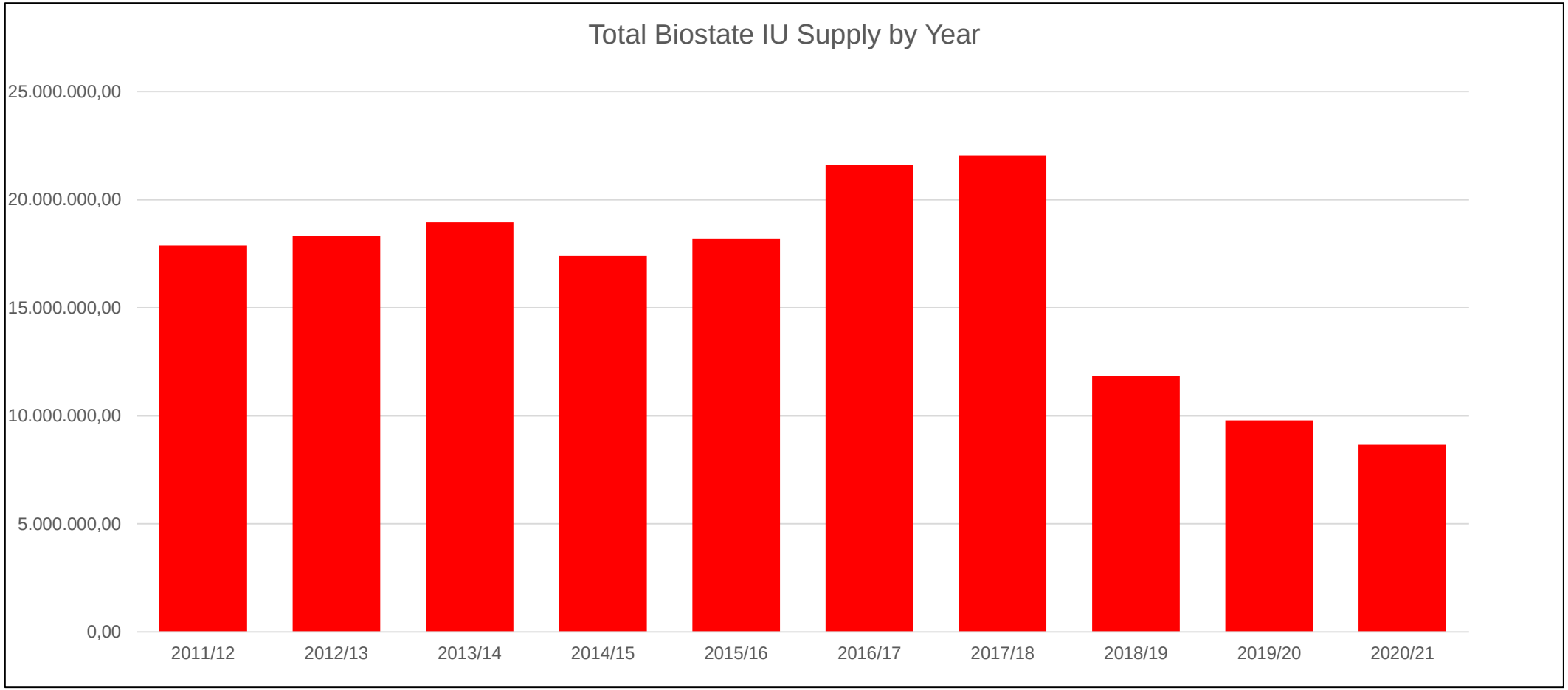


Supply of Factor VIII products

- About 6,500 total units FVIII issued per 1,000 population in 20/21, reduced from 7,650 in 19/20.
- Decrease due to the introduction of Hemlibra.
- Vast proportion is recombinant product
- Demand for PD FVIII reduced by 15.7% compared with last year.
- Used for patients with vWD and in patients with factor VIII inhibitors undergoing tolerisation.



Supply of Plasma-derived factor VIII (Biostate)



5 Management of patients on warfarin therapy with bleeding*

Clinical setting	Recommendations and levels of evidence†
INR ≥ 1.5 with life-threatening‡ (critical organ) bleeding	**Cease warfarin therapy and administer:** • vitamin K_1 5.0–10.0 mg IV **(2C)** • *and* Prothrombinex-VF 50.0 IU/kg§ IV **(GPP)** • *and* fresh frozen plasma 150–300 mL **(GPP)** • If Prothrombinex-VF is unavailable, administer fresh frozen plasma 15 mL/kg **(GPP)**
INR ≥ 2.0 with clinically significant bleeding (not life-threatening)	• Cease warfarin therapy and administer: • vitamin K_1 5.0–10.0 mg IV **(2C)** • *and* Prothrombinex-VF 35.0–50.0 IU/kg IV **(GPP)** according to INR (see Box 4) • If Prothrombinex-VF is unavailable, administer fresh frozen plasma 15 mL/kg **(GPP)**
Any INR with minor bleeding	• Omit warfarin, repeat INR the following day and adjust warfarin dose to maintain INR in the target therapeutic range **(2C)** • If bleeding risk is high¶ or INR > 4.5, consider vitamin K_1, 1.0–2.0 mg orally or 0.5–1.0 mg IV **(GPP)**

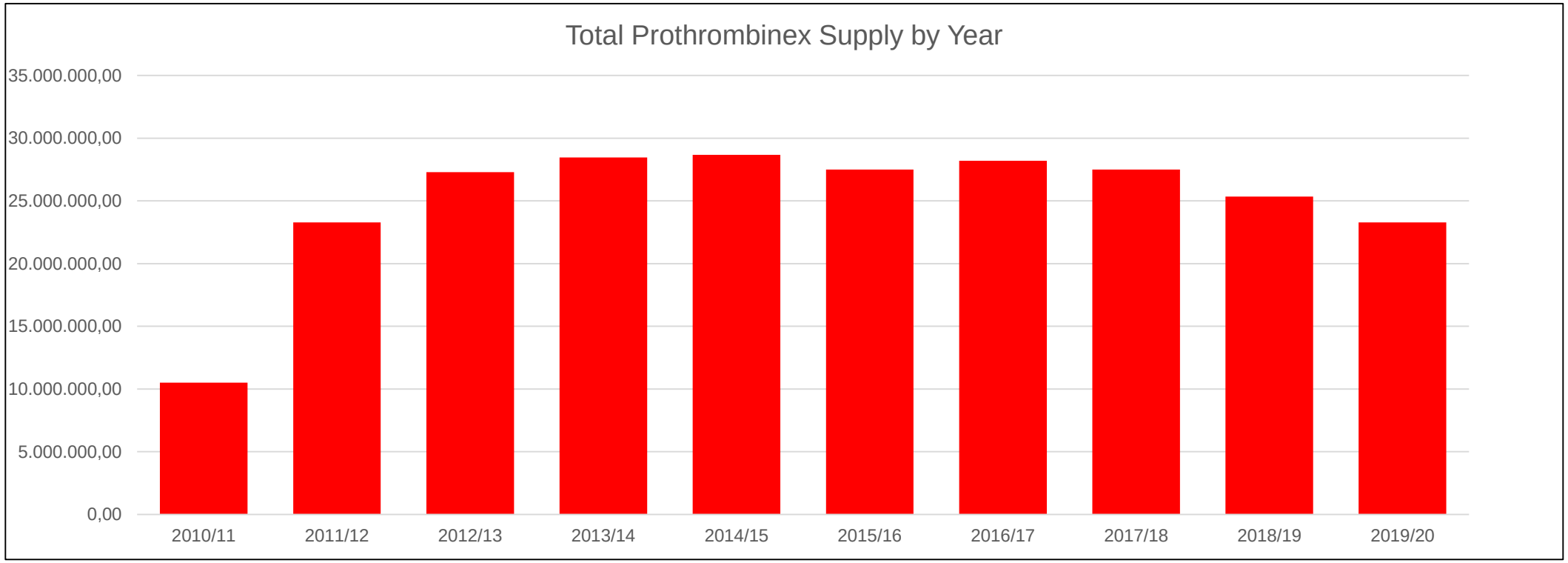
INR = international normalised ratio. IV = intravenously. * Indication for warfarin therapy should be reviewed; if clinically appropriate, consider permanent cessation. † Level of evidence in parentheses in **bold**. Details, Box 1. ‡ Includes intracranial bleeding. § Consider administering a Prothrombinex-VF dose less than 50.0 IU/kg when INR 1.5–1.9. ¶ Recent major bleed (within previous 4 weeks) or major surgery (within previous 2 weeks), thrombocytopenia (platelet count, < 50×10^9/L), known liver disease or concurrent antiplatelet therapy. ◆

An update of consensus guidelines for warfarin reversal. HA Tran et al. MJA 198 (4) 2013

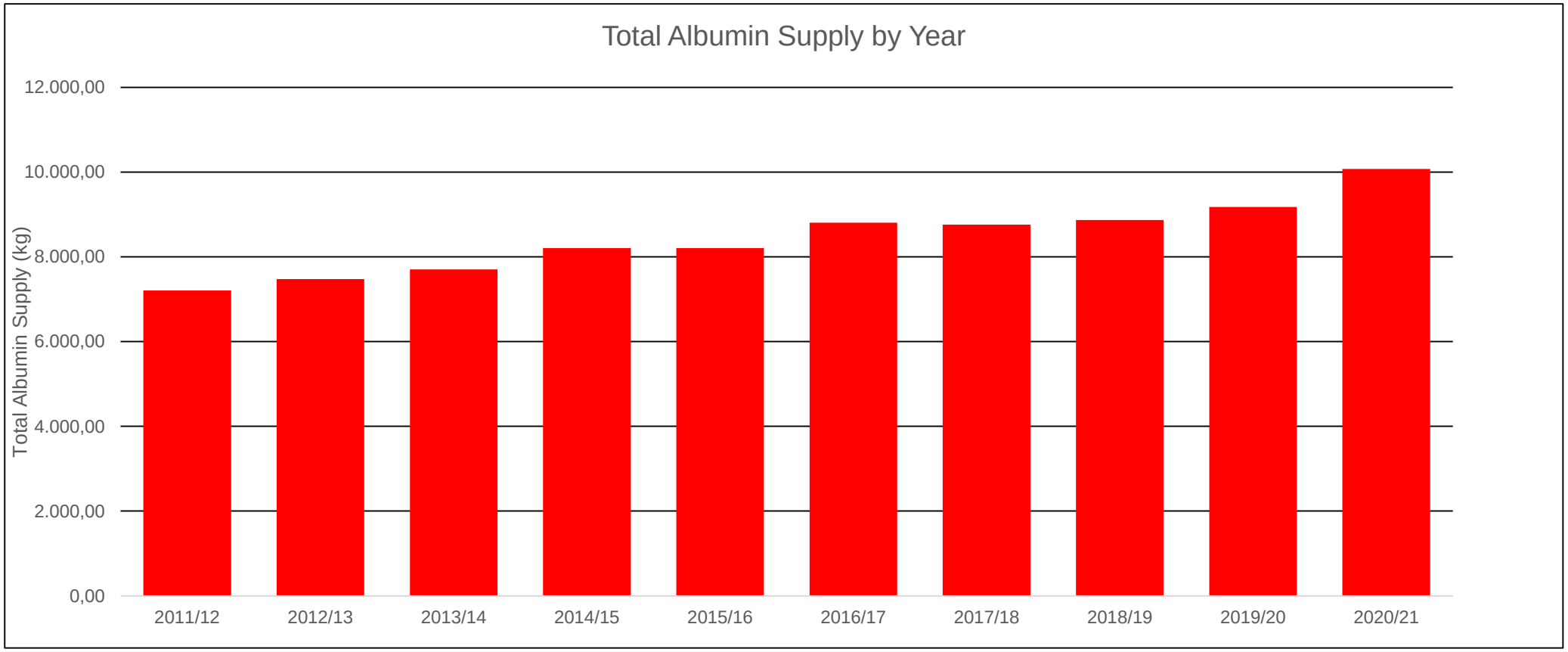
Prothrombinex - VF

- Human prothrombin complex containing Factors II, IX and X and low levels of factors V and VII
- Indicated for life-threatening or clinically significant bleeding with a prolonged INR, and when the INR >10 if the bleeding risk is high.
- Congenital deficiencies of factors II, IX and X

Prothrombinex supply



Demand for Albumin (Albumex)



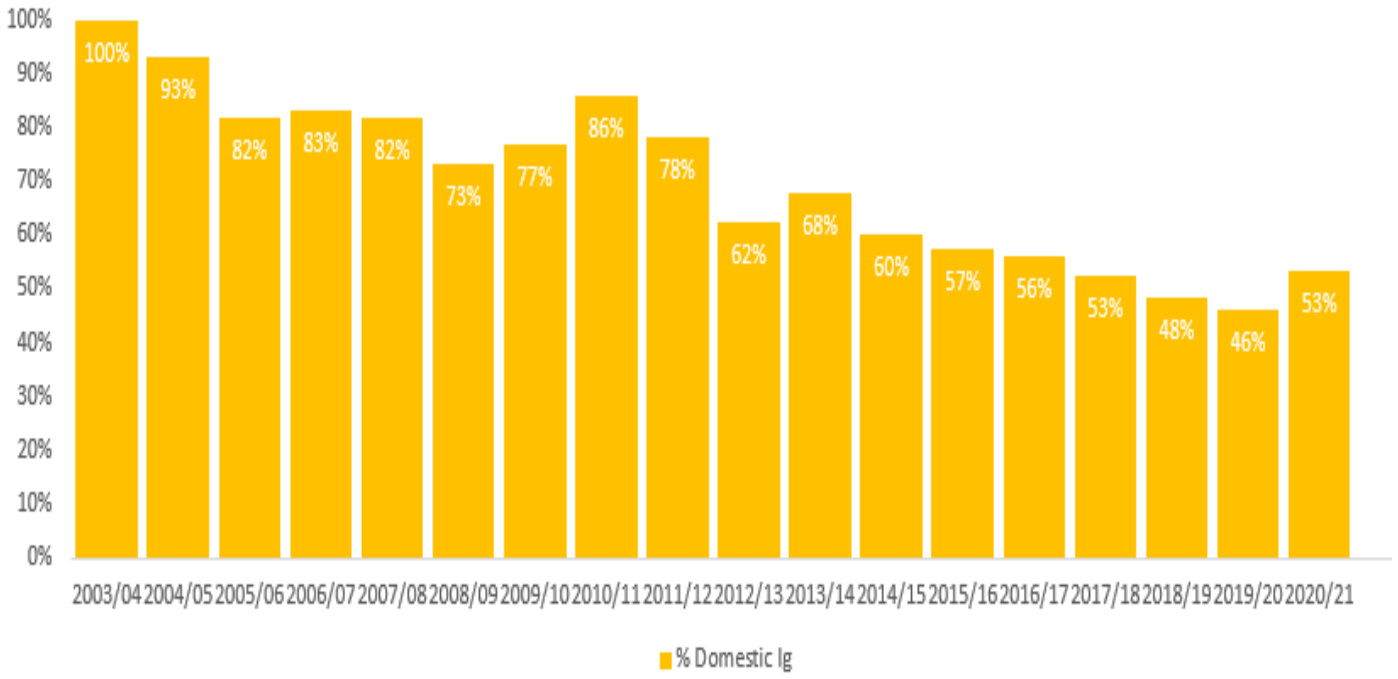
Supply is about 392 gm per 1,000 population

Immunoglobulin products

The following immunoglobulin products are manufactured from Australian domestic plasma:

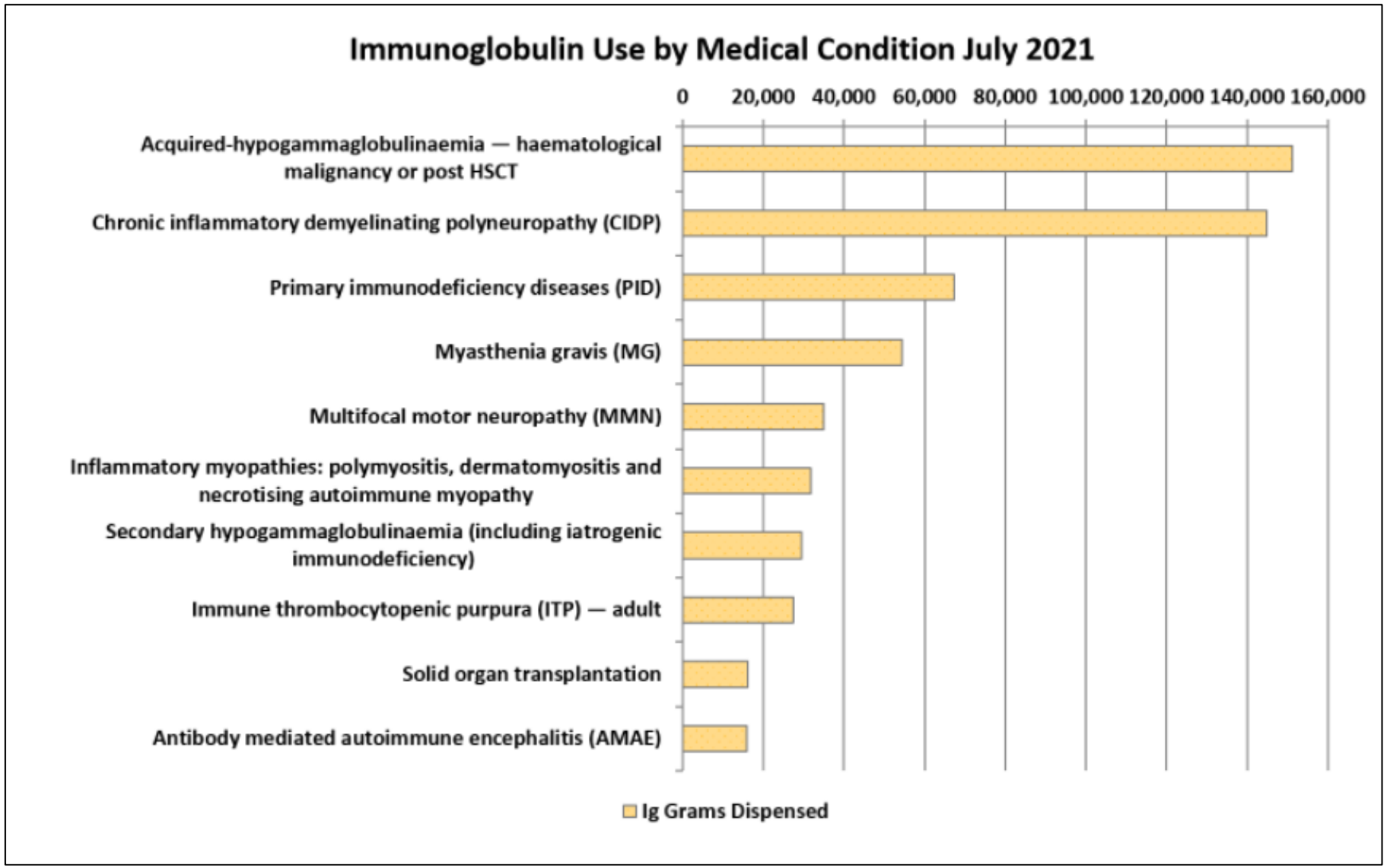
- Intravenous immunoglobulin
- Subcutaneous immunoglobulin
- Normal Immunoglobulin
- Hyperimmune immunoglobulins:
  - CMV
  - Hepatitis B
  - RhD
  - Tetanus
  - Zoster

Australian Ig demand met through domestic plasma supply

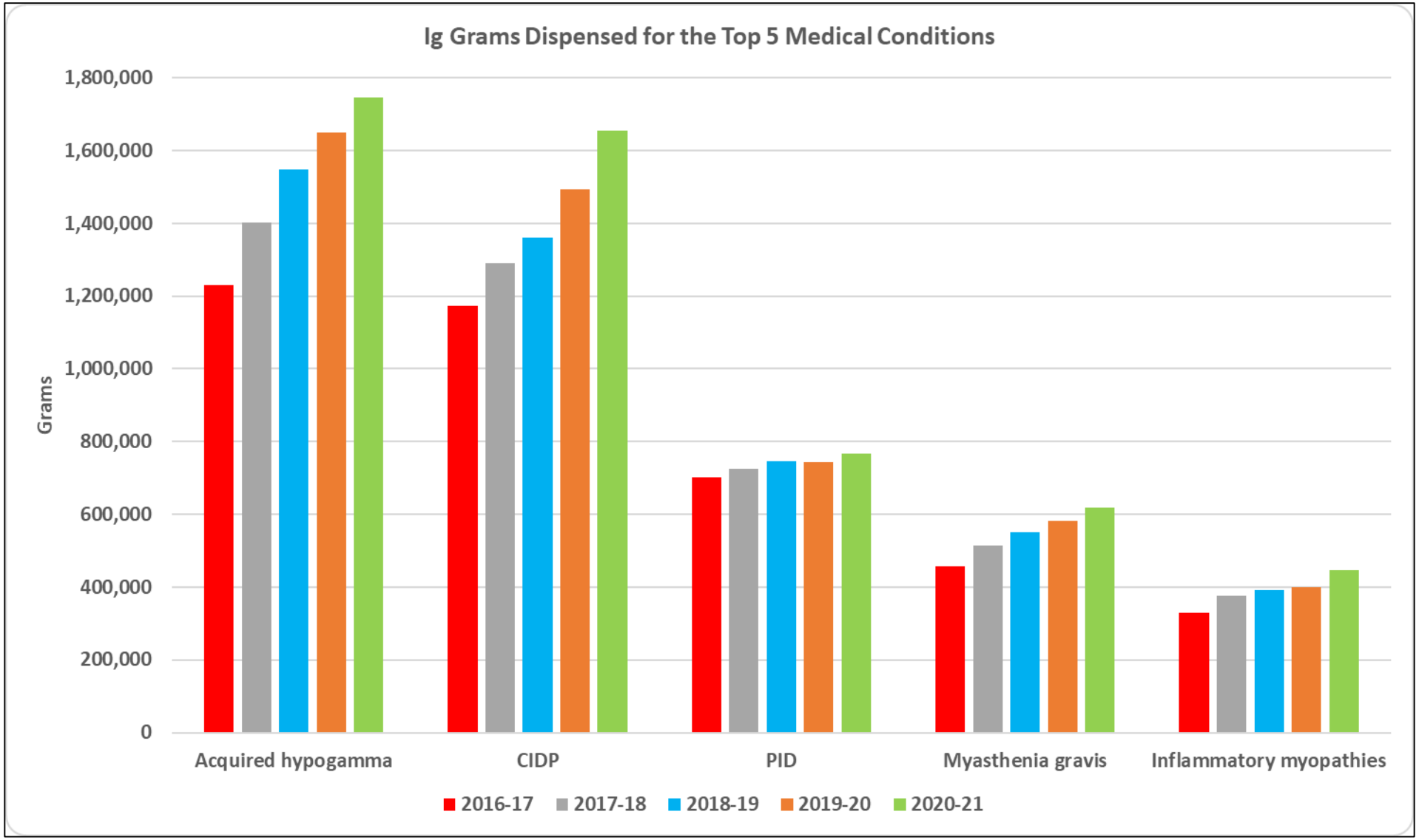


- 100% of patient demand was met through products made from domestically donated plasma in 2003/4
- Despite continuing increases in the volume of plasma donated in Australia, demand has outstripped supply
- Importing IVIg ensures patients have continuing access to life-changing products

Ig use by medical condition in July 2021



Changes in demand for Ig by medical condition

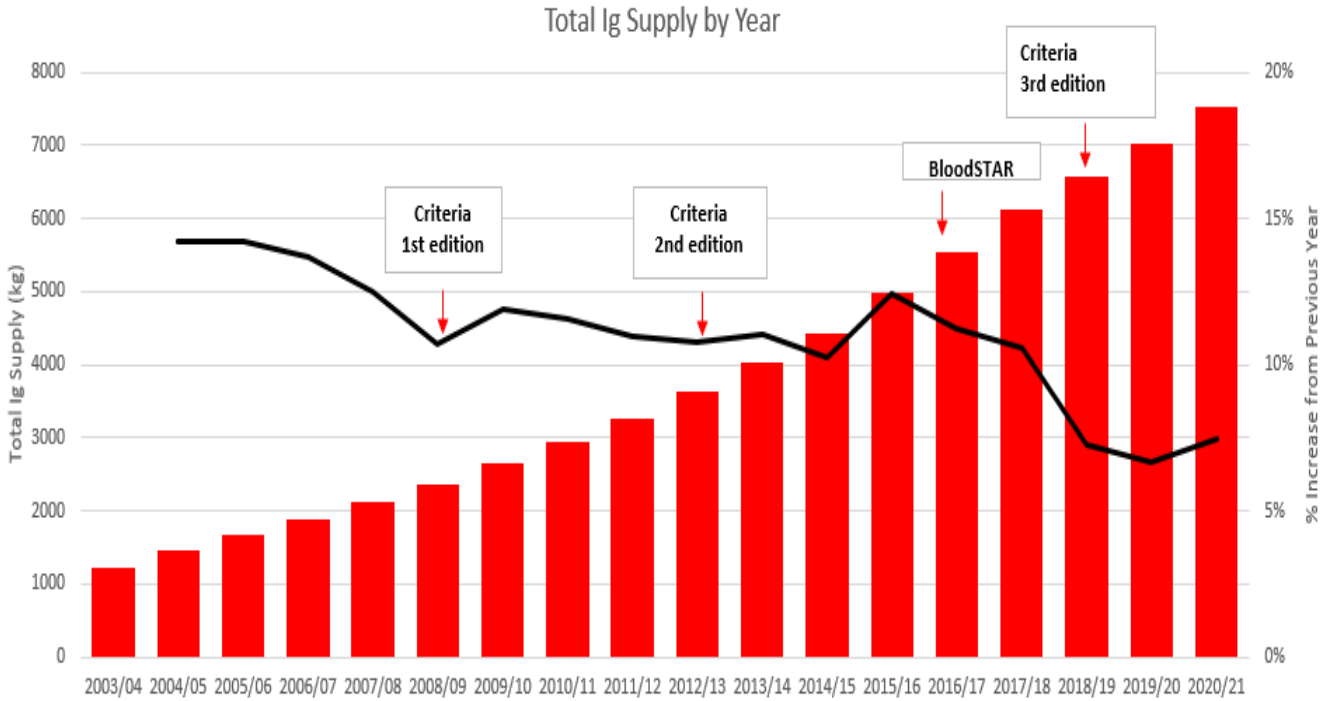


Australian demand for immunoglobulin

- Domestic demand for IVIg has been growing annually over a decade or more at a rate of approximately 11% per year

- Recent slowing of demand to around 7% over the last 3 years.

2011/12	2012/13	2013/14	2014/15	2015/16	2016/17	2017/18	2018/19	2019/20	2020/21
11.6%	10.8%	11.0%	10.2%	12.4%	11.2%	10.6%	7.2%	6.7%	7.4%



Why has the demand increase slowed?

- Since the program was implemented there have been no major changes in use observed in the 10 most commonly treated medical conditions, and no reduction in doses administered.
- An external evaluation of the Ig Governance Program undertaken by the National Blood Authority has found that the Program is effective in helping ensure that Ig products are available to the right patients.
- The Program has been effective in reducing the growth in demand for Ig, with effectiveness linked to the key program elements:
  - the National Policy on Access to Government-funded Immunoglobulin Products in Australia
  - the Criteria for the Clinical Use of Immunoglobulin in Australia
  - BloodSTAR - the Blood System for Tracking Authorisations and Reviews

National Blood Authority Immunoglobulin Governance Program

The National Blood Authority (NBA) is a statutory agency within the Australian Government Health portfolio that manages and coordinates arrangements for the supply of blood and blood products and services on behalf of the Australian Government and state and territory governments.

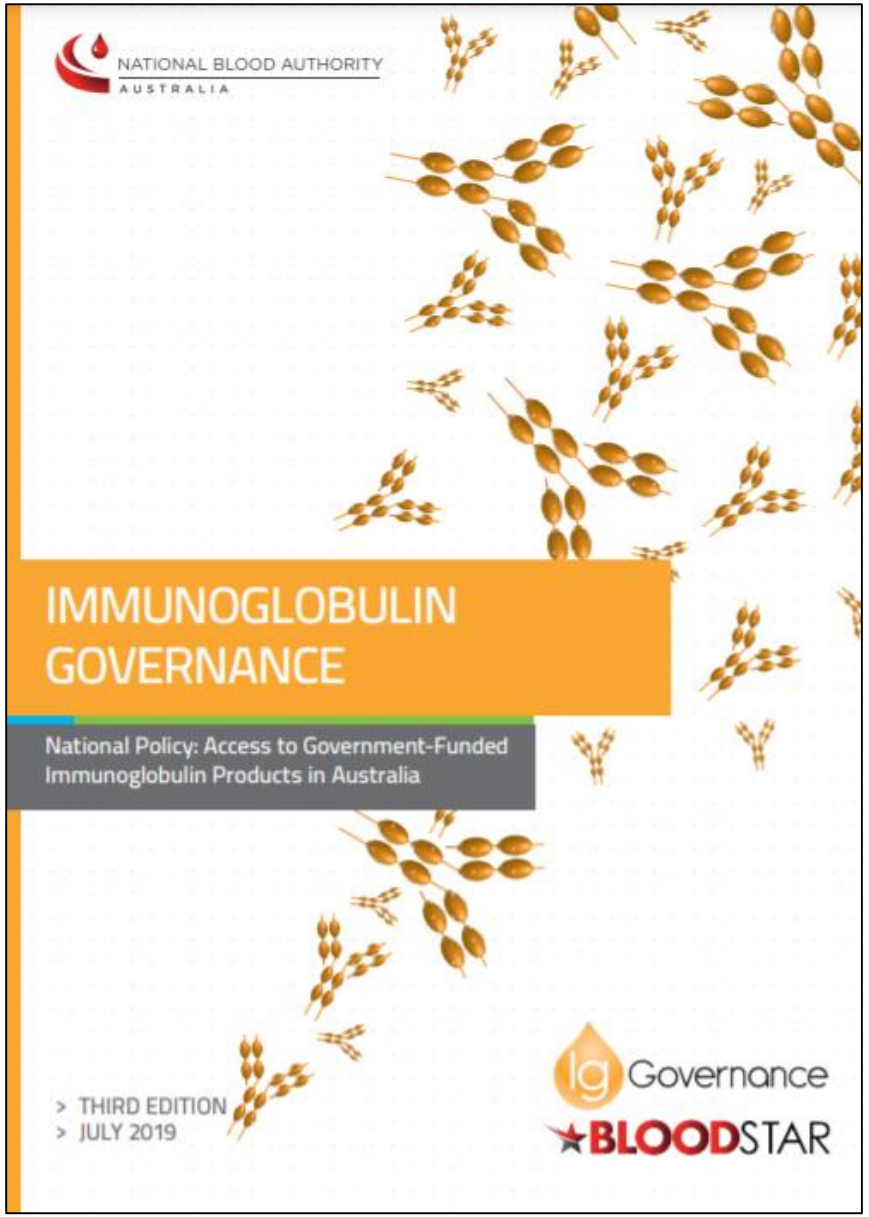
The Ig Governance program aims to improve the governance and management of publicly funded Ig to ensure that:

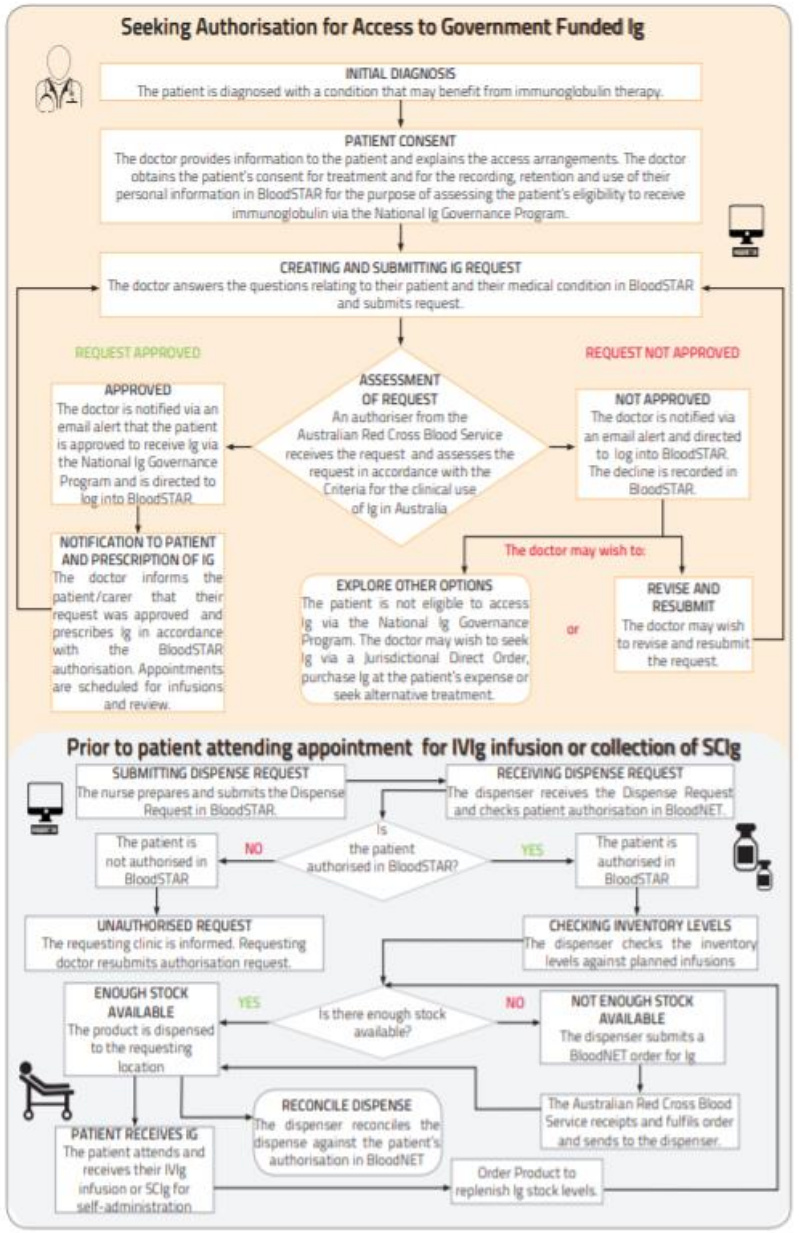
- product use and management reflects appropriate clinical practice and
- represents efficient, effective and ethical expenditure of government funds
- in accordance with relevant national safety and quality standards for health care.

Governance

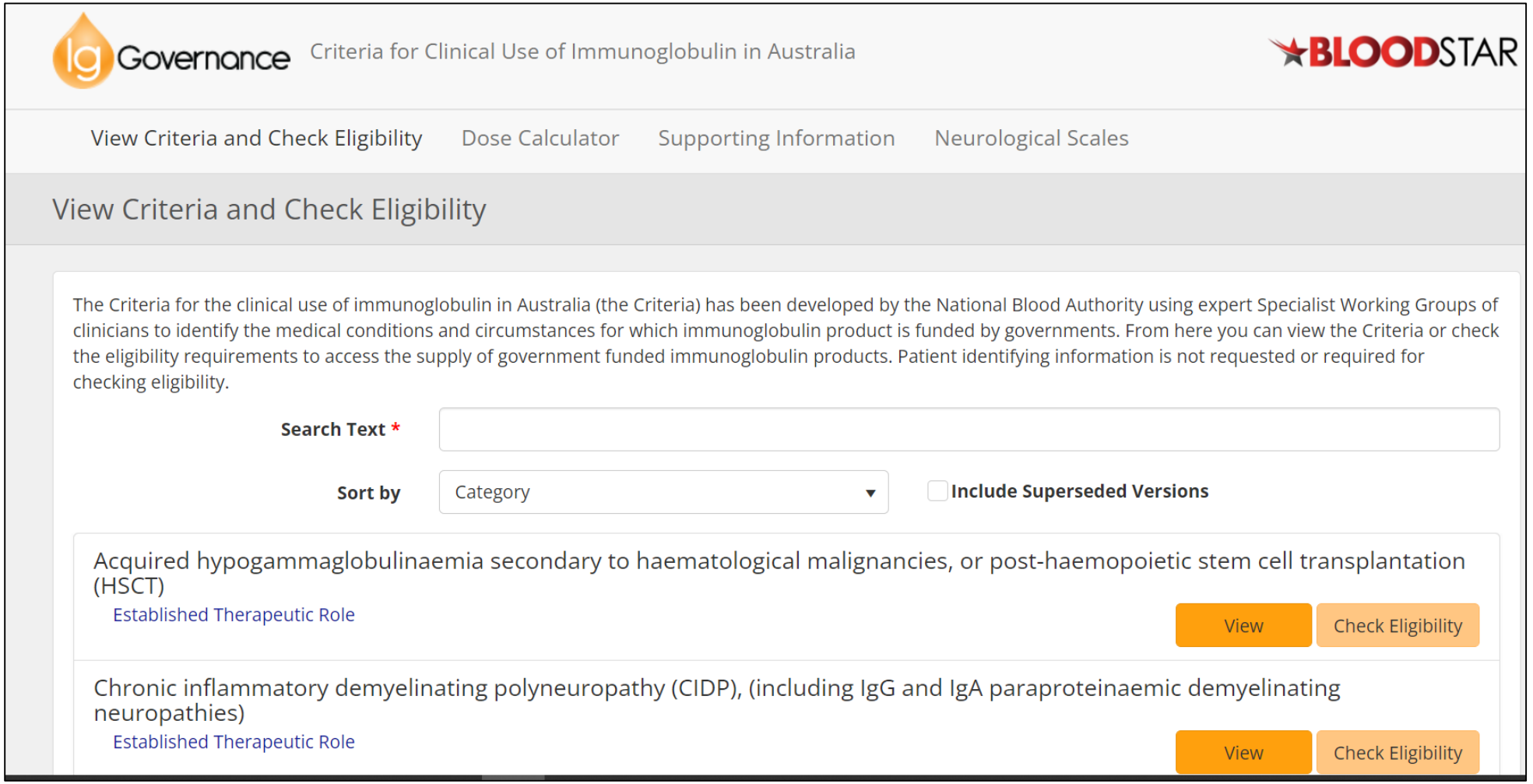
- This document covers the process that must be followed and the rules and requirements that must be complied with to access government-funded Ig

- Funding is provided for conditions which have an established therapeutic role, emerging therapeutic role and for exemptional circumstances.





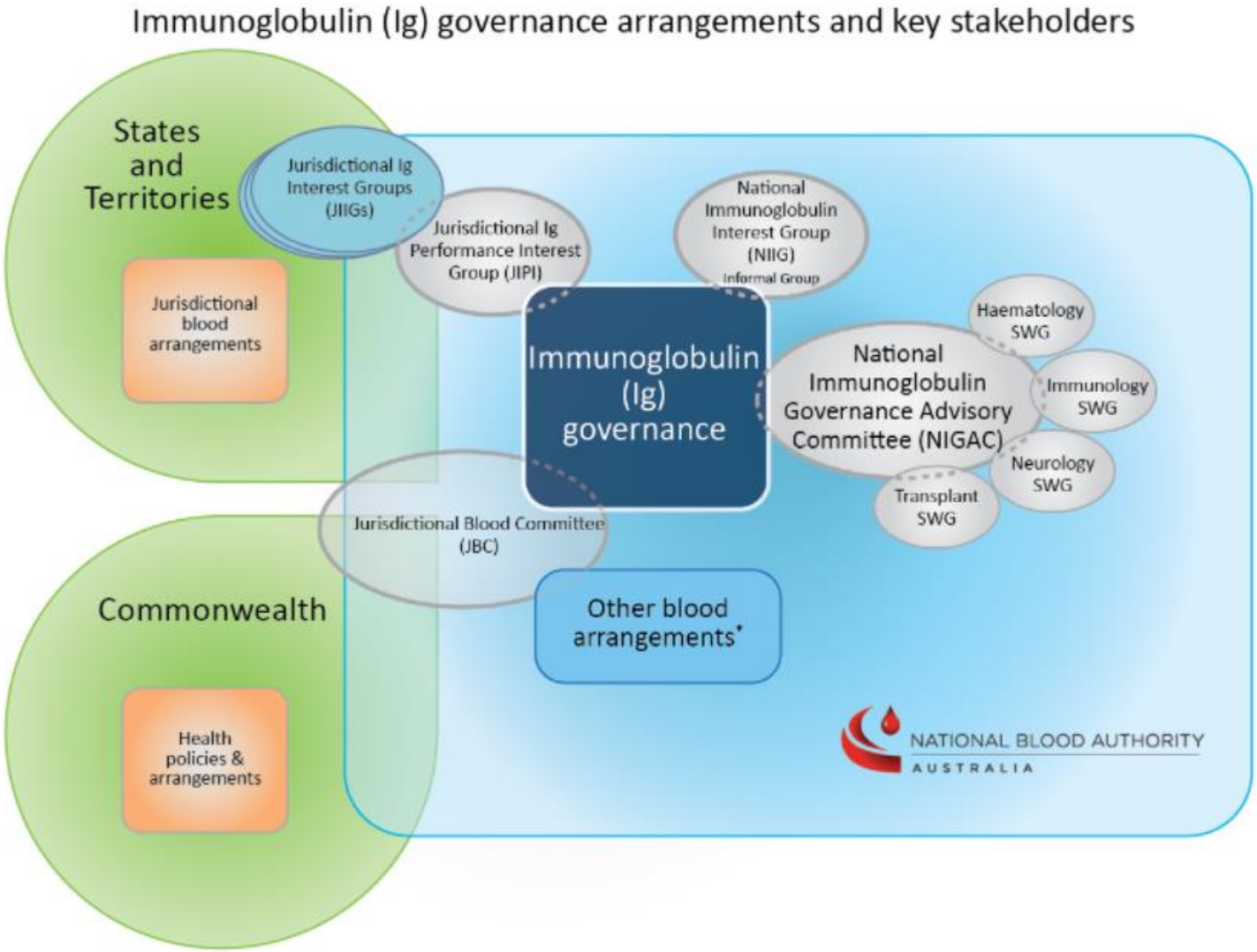
Criteria for the clinical use of immunoglobulin in Australia



Example: ITP - adult

- Specific conditions - eg newly diagnosed, persistent, chronic, Evans
- Indication for Ig use – eg newly diagnosed ITP, initial Ig therapy
- Level of evidence
- Description and diagnostic criteria
- Justification for evidence category
- Diagnosis requirements – eg which type of physician, haematologist
- Qualifying criteria for Ig therapy – eg platelet count <30 $X10^9$/L, AND evidence or risk of clinically significant bleeding AND no improvement with 14 days of steroids or steroids contraindicated
- Exclusion criteria
- Review criteria for assessing the effectiveness of Ig use – eg doubling of the platelet count to more than 30 within 7 days
- Dose

National network of committees



National ordering and outcomes database

- BloodSTAR is an online system used across Australia to manage access to government funded immunoglobulin products.
- The system manages the authorisation request and review process for the treatment of conditions identified in the *Criteria for the clinical use of intravenous immunoglobulin in Australia*.
- Specific medical conditions, eligibility requirements, and a dose calculator can all be found within the criteria.
- A resource outlining what BloodSTAR is, why it was developed, its key benefits, and its target users, is available.

In conclusion

- The National Blood Authority (NBA) manages and coordinates arrangements for the supply of blood and blood products and services on behalf of Australian Governments
- Lifeblood has a mature and expanding voluntary, non-remunerated plasmapheresis program, collecting about 32L of plasma for fractionation per 1,000 population.
- The driver for domestic plasma collection is immunoglobulin, Australia has surplus fractions for other plasma-derived products.
- Immunoglobulin demand continues to increase annually, with more recent slowing to about 7%.
- Australia has a strong Ig governance program to ensure product use reflects appropriate clinical practice and usage represents efficient, effective and ethical expenditure of government funds
- Recombinant clotting factor concentrates are available for the treatment of haemophilia A and haemophilia B, with more recent introduction of Hemlibra – both have resulted in limited demand for plasma-derived clotting factors.

Thank you!

Questions?

Australian governments fund Australian Red Cross Lifeblood to provide blood, blood products and services to the Australian community.

Data provided for this presentation was sourced from the National Blood Authority Annual Report 2020-21 and from Lifeblood internal data.