NATIONAL BLOOD AUTHORITY
AUSTRALIA

AUSTRALIAN BLEEDING DISORDERS REGISTRY

Annual Report 2016-17

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Table of Contents

LIST OF TABLES

LIST OF FIGURES

Purpose of this document

The intention of this document is to present the reader with an integrated view of current clinical and demographic information on people with inherited bleeding disorders in Australia and the resultant demand for clotting factor products. It draws on data from the Australian Bleeding Disorders Registry (ABDR) and other National Blood Authority (NBA) supply and contract sources. Some international data comparisons have also, where meaningful, been included.

The Australian Bleeding Disorders Registry (ABDR) is a clinical registry for patients in Australia with bleeding disorders. It is used on a daily basis by clinicians in all Australian Haemophilia Treatment Centres (HTCs) to assist in managing the treatment of people with bleeding disorders and to gain a better understanding of the incidence and prevalence of bleeding disorders. This information will also be used by the NBA to understand demand for, and to facilitate ordering of, clotting factor product.

This document will be used by people involved in providing care for patients with bleeding disorders, and may also be useful for patient advocacy groups and those in administrative and government positions.

Key findings

The data contained in this reports shows:

- There were 6,155 patients in the Australian Bleeding Disorders Registry (ABDR) in 2016-17
- Of these patients 5,070 were recorded as having common hereditary bleeding disorders
    - 2,365 patients with Haemophilia A (666 patients with severe Haemophilia A)
    - 564 patients with Haemophilia B (106 patients with severe Haemophilia B)
    - 2,141 patients with von Willebrand Disease
- A total of 94 patients were registered as acquired Haemophilia A, Haemophilia B or von Willebrand bleeding disorders
- 1,590 patients with hereditary bleeding disorders received product in 2016-17, 1,009 Haemophilia A patients, 218 Haemophilia B patients, 248 von Willebrand Disease patients and 94 patients with other diagnoses. Of these, 21 patients had acquired bleeding disorders
- 160,598,764 IU of Factor VIII products were used by hereditary Haemophilia A patients in 2016-17
    - Prophylactic use by Haemophilia A patients accounted for 129,124,996 IU, or 80.4 per cent of the volume issued
- 26,632,580 IU of Factor IX products were used by hereditary Haemophilia B patients in 2016-17
    - Prophylactic use by Haemophilia B patients accounted for 18,326,000 IU, or 68.8 per cent of the volume issued
- Demand for Factor VIII products increased by 1.5 per cent when compared to 2015-16 (NBA Annual Report)
    - Recombinant FVIII decreased by 0.5 per cent (NBA Annual Report)
    - Plasma derived FVIII increased by 18.9 per cent (NBA Annual Report)
- Demand for Factor IX increased by 1.6 per cent compared to 2015-16 (NBA Annual Report)
    - Plasma derived FIX decreased by 15.6 per cent due to a reduction in specific patient requirements
    - Recombinant FIX increased 1.6 per cent compared to 2015-16 (NBA Annual Report)
- Clotting factors comprise 14.4 per cent of total blood and blood product expenditure by cost and by product category in 2016-17 (NBA Annual Report)

Background

The information in this section has been drawn from the materials and websites of two peak bodies for haemophilia; the World Federation of Hemophilia (www.wfh.org) and the Haemophilia Foundation of Australia (www.haemophilia.org.au).

WHAT ARE BLEEDING DISORDERS?

In people with bleeding disorders, the clotting process doesn't work properly. As a result, people with bleeding disorders can bleed for longer than normal, and some may experience spontaneous bleeding into joints, muscles, or other parts of their bodies.

BLEEDING DISORDERS ARE INHERITED OR ACQUIRED

Bleeding disorders are almost always inherited or passed through families; they have a genetic basis and the genes responsible for the disorders are passed from parents to children. However, a person can also spontaneously develop a bleeding disorder, although this is rare.

Acquired bleeding disorders are not inherited or passed through families. Most acquired bleeding disorders have an identifiable root cause. Men and women are equally likely to be affected by an acquired bleeding disorder, and the potential for problems is high.

TABLE 1 - MAJOR BLEEDING DISORDERS AND THEIR CAUSE

Disorder group	Cause
Haemophilia A	Deficiency of Factor VIII
Haemophilia B	Deficiency of Factor IX
von Willebrand Disease	Deficiency, or dysfunction, of von Willebrand Factor
Other Factor deficiencies	Deficiency of other coagulation factors
Platelet Disorder	Inherited deficiency of effective platelet function

HAEMOPHILIA

Haemophilia causes excessive bleeding following trauma or surgery and can be related to spontaneous haemorrhages into muscles and joints. People with haemophilia do not bleed any faster than normal, but they can bleed for a longer time.

Haemophilia is an X-linked disorder that typically affects males, whereas females are normally classified as carriers. However, affected males will pass on the haemophilia gene to their daughters, and women carrying a F8 or F9 gene mutation may have reduced factor levels and should therefore be classified as having haemophilia. Most carriers are asymptomatic. Carriers with clotting factor levels in the haemophilia range may be symptomatic, with bleeding manifestations commensurate with their degree of clotting factor deficiency, particularly during trauma and surgery. Symptomatic carriers are classified as haemophilia in line with the World Federation of Haemophilia (www.wfh.org) guidelines.

TYPES OF HAEMOPHILIA

- The most common type of haemophilia is called Haemophilia A. This means the person does not have enough clotting Factor VIII (factor eight).
- Haemophilia B is less common. A person with Haemophilia B does not have enough Factor IX (factor nine). The symptoms are the same for people with Haemophilia A and B; that is, they bleed for a longer time than normal.

HAEMOPHILIA FAST FACTS

- Haemophilia occurs in 1 in 6,000-10,000 males internationally.
- Currently in Australia there are 2,998 people with Haemophilia A and B, (including 69 with Acquired Haemophilia) with varied degrees of severity, in the Australian Bleeding Disorders Registry (ABDR).
- Bleeding is most commonly internal into the joints and/or muscles. Less commonly, bleeding into internal organs can also occur. It can happen without an obvious cause (sometimes called 'spontaneous'), or as a result of injury.
- Over time this internal bleeding into joints ('bleeds') can cause severe arthritis, chronic pain and disability.
- Specialised treatment is needed to help blood clot normally. With appropriate treatment haemophilia can be managed effectively.
- Haemophilia is an inherited condition and occurs in families; however in 1/3 of cases it appears in families with no previous history of the disorder. The haemophilia gene is passed down from parent to child through generations. Men with haemophilia will pass the gene on to their daughters but not their sons. Women who carry the haemophilia gene can pass the haemophilia gene on to their sons and daughters. Sons with the gene will have haemophilia. Some women and girls who carry the gene may also experience bleeding problems.

VON WILLEBRAND DISORDER/DISEASE (VWD)

Von Willebrand disease (VWD) is the most common type of bleeding disorder. People with VWD have a problem with von Willebrand Factor (VWF), a protein in their blood that would normally help control bleeding. When a blood vessel is injured and bleeding occurs, VWF helps cells in the blood, called platelets, adhere to damaged blood vessels and mesh together and form a clot to stop the bleeding. People with VWD do not have enough VWF, or it does not work the way it should. It takes longer for blood to clot and for bleeding to stop.

VWD is generally less severe than other bleeding disorders. Many people with VWD may not know that they have the disorder because their bleeding symptoms are very mild. For most people with VWD, the disorder causes little or no disruption to their lives except when there is a serious injury or need for surgery. However, with all forms of VWD, there can be bleeding problems. VWD is difficult to accurately diagnose as laboratory values can fluctuate and values in those with mild bleeding symptoms can overlap with normal laboratory values.

From some studies, it is estimated that up to 1% of the world's population has VWD, but because many people have only very mild symptoms, only a small number of them are diagnosed. Research has shown that as many as 9 out of 10 people with VWD have not been diagnosed. It is estimated that VWD affects approximately 200,000 people in Australia, but symptomatic individuals possibly less. Currently there are 2,166 people with VWD in the ABDR including 25 with acquired VWD.

TYPES OF VWD

There are three main types of VWD. Within each type, the disorder can be mild, moderate, or severe. Bleeding symptoms can be quite variable within each type depending in part on the VWF activity. It is important to know which type of VWD a person has, because treatment is different for each type.

- Type 1 VWD is the most common form. People with Type 1 VWD have lower than normal levels of VWF. Symptoms are usually mild. Still, it is possible for someone with Type 1 VWD to have serious bleeding.
- Type 2 VWD involves a defect in the VWF structure. The VWF protein does not work properly, causing lower than normal VWF activity. There are different Type 2 VWD defects. Severity of symptoms can vary.
- Type 3 VWD is usually the most serious form. People with Type 3 VWD have very little or no VWF. Symptoms are more severe. People with Type 3 VWD can have bleeding into muscles and joints, sometimes without injury.

RARE CLOTTING FACTOR DEFICIENCIES

Rare clotting factor deficiencies are a group of inherited bleeding disorders caused by a problem with one of several clotting factors. Clotting factors are proteins in the blood that control bleeding. Many different clotting factors work together in a series of chemical reactions to stop bleeding. This is called the clotting process.

Problems with Factor VIII and Factor IX are known as Haemophilia A and B, respectively. Rare clotting factor deficiencies are bleeding disorders in which one of the other clotting factors (i.e. factors I, II, V, V+VIII, VII, X, XI, or XIII) is missing or not working properly. The World Federation of Haemophilia produced a summary (Table 25 of the characteristics of rare clotting factor deficiencies, the severity of bleeds associated with them, and the treatment typically required.

SPECIAL ISSUES FOR GIRLS AND WOMEN

Women with clotting factor deficiencies may have additional symptoms because of menstruation and childbirth. Girls may have especially heavy bleeding when they begin to menstruate. Women with clotting factor deficiencies may have heavier and/or longer menstrual flow, which can cause anaemia (with low levels of iron, which results in weakness and fatigue). Women with clotting factor deficiencies should receive genetic counselling about the risks of having an affected child well in advance of any planned pregnancies and should see an obstetrician as soon as they suspect they are pregnant. The obstetrician should work closely with the staff of the haemophilia/bleeding disorder treatment centre in order to provide the best care during pregnancy and childbirth and to minimize the potential complications for both the mother and the newborn child.

Women with certain rare factor deficiencies (such as Factor XIII deficiency and afibrinogenemia) may be at greater risk of miscarriage and placental abruption (a premature separation of the placenta from the uterus that disrupts the flow of blood and oxygen to the foetus). Therefore, these women require treatment throughout the pregnancy to prevent these complications.

The main risk related to pregnancy is postpartum haemorrhage. All bleeding disorders are associated with a greater risk of increased bleeding after delivery. The risk and the severity of the bleeding can be reduced with appropriate treatment. This treatment is different for each woman and depends on her personal and family history of bleeding symptoms, the severity of the factor deficiency, and the mode of delivery (vaginal birth vs. caesarean section). Factor replacement may be necessary in some cases.

INHERITED PLATELET DISORDERS

Platelets are small parts of cells that circulate in the blood. They are involved in the formation of blood clots and the repair of damaged blood vessels.

When a blood vessel is injured, platelets stick to the damaged area and spread along the surface to stop the bleeding (this process is called adhesion). At the same time, chemical signals are released from small sacks inside the platelets called granules (this process is called secretion). These chemicals attract other platelets to the site of injury and make them clump together to form what is called a platelet plug (this process is called aggregation).

Sometimes the platelet plug is enough to stop the bleeding. However if the wound is large, other proteins called clotting factors are recruited to the site of injury. These clotting factors work together on the surface of the platelets to form and strengthen the blood clot.

WHAT ARE PLATELET FUNCTION DISORDERS?

Platelet function disorders are conditions in which platelets don't work the way they should, resulting in a tendency to bleed or bruise. Since the platelet plug does not form properly, bleeding can continue for longer than normal. Since platelets have many roles in blood clotting, platelet function disorders can lead to bleeding disorders of various intensities.

SEVERITY

Haemophilia A and B are classified according to their severity, as this informs the treatment regimens required. The definitions of severity that are applied within the ABDR are listed in Table 2. Definition of severity of VWD and other coagulation factor deficiencies is not standardised but variable.

TABLE 2 - SEVERITIES AND THE CONCENTRATION OF CLOTTING FACTORS[1]

Severity	Concentration of Clotting Factor	Typical Bleeding Picture
Severe	<0.01 IU/ml (<1% of normal†)	Frequent bleeding episodes common, predominantly into joints & muscles. Bleeding can occur spontaneously or after minor injury.
Moderate	0.01 – 0.05 IU/ml (1–5% of normal)	Can bleed after minor injury. May have joint bleeding. Severe bleeding with trauma, surgery, invasive procedures.
Mild	>0.05 – 0.40 IU/ml (5-40% of normal)‡	Spontaneous bleeding does not occur. Bleeding with major trauma, surgery, invasive procedures.

Notes † Normal concentration of Factor VIII or IX is defined as 100% or one unit of Factor VIII activity per ml of plasma - 100 U/dL (Kasper, CK 2004, Hereditary plasma clotting factor disorders and their management. Treatment of Hemophilia Monograph Series, No. 4, World Federation of Hemophilia, Montreal, Canada)
‡ Levels of FVIII above 40% are usually considered sufficient for normal haemostasis

[1] Modified from Srivastava A, Brewer AK, Mauser-Bunschoten EP, Key NS, Kitchen S, Llinas A, Ludlam CA, Mahlangu JN, Mulder K, Poon MC, Street A; Treatment Guidelines Working Group on Behalf of The World Federation Of Hemophilia (2013). Guidelines for the management of hemophilia, Haemophilia 19(1):e1-47.

TREATMENT OF BLEEDING DISORDERS

Mild conditions may require no treatment or treatment only under special circumstances, such as surgery. More severe conditions may require regular interventions. Treatment may occur in hospital or other medical facilities, or at home. The treatments may be regular and preventative (prophylaxis), or on demand (when a bleed occurs). In some patients, therapy is complicated when their body develops inhibitors that destroy the replacement clotting factors and other treatment is necessary.

Often the treatments involve providing replacement for the missing or defective clotting factors. Products used include plasma derived and recombinant clotting factors, cryoprecipitate and Desmopressin (1-desamino-8-D-arginine vasopressin; DDAVP) which can stimulate the release of Factor VIII and VWF from stores in the body (this is not used in Haemophilia B or Factor IX deficiency).

Treatment of bleeding disorders in Australia

The majority of people with these conditions are treated at HTCs which are specialist centres that provide comprehensive care to people with haemophilia and other bleeding disorders. The comprehensive care model ensures that preventative and general treatment on the complex aspects of haemophilia are given in a co-ordinated way by a multi-disciplinary team with specialised expertise within the one centre.

HTCs were established following a decision by Australian Health Ministers Advisory Council (AHMAC) in 1998, to provide a leadership role within their hospital, city and outlying areas to ensure optimal care and an equitable distribution of professional and therapeutic resources, together with responsible record-keeping. The roles, aims and governance of these Centres are defined in Appendix B. The locations of the HTCs in Australia are shown in Figure 1.

FIGURE 1 - LOCATION OF HAEMOPHILIA TREATMENT CENTRES

The model for HTCs varies between jurisdictions in relation to centralisation of services, size and age of patient population.

There are also some patients whose treatment is managed by clinicians who are not associated with a HTC. The proportion of product that is used in these circumstances varies across jurisdictions and there is some variability in the data capture for this activity between jurisdictions. Accordingly, data on total volume of products recorded from the ABDR may not be consistent with data from other sources.

The Australian Bleeding Disorders Registry (ABDR)

The Australian Bleeding Disorders Registry (ABDR) is a database that is designed to collect all clinical information related to the treatment of people with inherited bleeding disorders. This includes information about patient diagnosis, viral status, treatment details, hospital admissions and administrative information as well as details on ordering, supply and use of clotting factor products. Information is entered into the ABDR web enabled software by staff at HTCs. The current version of the ABDR has been in existence since December 2008 and background on the development of the system is at Appendix D History of the ABDR. In August 2012 the 4th generation ABDR was implemented.

The ABDR provides health care teams and support staff with a record enabling them to monitor and manage treatment over time to improve patients' quality of life. De-identified information from the ABDR may be used for research purposes by authorised organisations to understand and improve treatment for bleeding disorders. Considerations for the release of any information for research are made under specific governance arrangements. The ABDR also provides governments with information on total clotting factor product requirements to inform supply planning to meet the needs of all Australians with bleeding disorders.

The ABDR has evolved and improved with improvements in technology and feedback from stakeholders. In 2014 the ABDR entered a new phase with MyABDR - a secure app for smartphones (Android and iOS) and a web site for people with bleeding disorders or parents/caregivers to record home treatments and bleeds. It is an internet-based online system that gives patients a quick, easy and reliable way to:

- Record treatments and bleeds
- Manage treatment product stock
- Share the information with a Haemophilia Treatment Centre through the Australian Bleeding Disorders Registry (ABDR)
- Update contact and personal details.

ABDR MANAGEMENT AND GOVERNANCE

The ABDR is managed on a day to day basis by the National Blood Authority (NBA) in accordance with the guidance and policy oversight provided by the ABDR Steering Committee. The Committee consists of representatives of the key stakeholders involved in the clinical management, advocacy and funding of treatment for people with bleeding disorders.

Endorsement from Haemophilia Foundation Australia

Haemophilia Foundation Australia supports the ABDR. It helps doctors and other treating health professionals to understand more about the care and treatment needs of people affected by bleeding disorders. The ABDR will assist and guide planning to ensure treatment product is available when it is needed. We are confident the steps in place will mean accurate, reliable and confidential data is available and that no patient details can be identified outside haemophilia centres.

www.haemophilia.org.au

Endorsement from Australian Haemophilia Centre Directors' Organisation

The ABDR is a valuable tool that provides a summary of those affected with haemophilia and other bleeding disorders in Australia. Data from the ABDR is the best information available for clinicians to advise governments making policy decisions regarding treatment needs and product availability.

National statistics available through the ABDR will give AHCDO an overview of practice and allow opportunities for improvement. This data can be pooled to compare Australian treatment standards with international benchmarks. The ABDR will continue to provide the ability to assess quality of life and other important clinical questions arising across Australia.

AHCDO's partnership on this initiative with the National Blood Authority, Haemophilia Foundation Australia and other specialist health professional groups is vital to the pursuit of excellence in clinical treatment practices.

www.ahcdo.org.au

In 2016-17 the Steering Committee representatives were:

- Dr John Rowell (Chair) – Australian Haemophilia Centre Directors' Organisation
- Dr Simon McRae – Chair of Australian Haemophilia Centre Directors' Organisation
- Ms Sharon Caris – Executive Director, The Haemophilia Foundation Australia
- Mr Michael Furey, VIC Health – Jurisdictional Blood Committee nominee
- Mr Ian Kemp – National Blood Authority

PATIENT PRIVACY IN ABDR AND MYABDR

The ABDR and MyABDR are provided by the National Blood Authority (NBA). The NBA is required to ensure that patient information in ABDR and MyABDR is collected and managed in a way which complies with the Commonwealth *Privacy Act 1988*. There are also parallel requirements which may apply under state and territory laws. Privacy requirements under the *Privacy Act* were tightened in 2014, and a new Privacy Policy for these systems was implemented from 26 January 2015.

More information about the management of patient privacy in ABDR and MyABDR can be found at http://www.blood.gov.au/privacy-info-abdr-myabdr, including a copy of the ABDR/MyABDR Privacy Policy together with further information, forms and other implementation resources.

In order to maintain the anonymity of individual patients and health providers, small cell data published or released, showing less than five (5) may be suppressed or aggregated if there is a potential to re-identify or exceptions are agreed between national and state/territory data custodians.

DATA GOVERNANCE

There is an extremely robust governance framework that oversees the management and operation of the ABDR. An AHCDO member chairs the Steering Committee tasked with these responsibilities. The Steering Committee also includes the Executive Director of Haemophilia Foundation Australia to ensure patient needs are met. Patient privacy and confidentiality are paramount to these arrangements.

In addition, there is stringent security protocols embedded into the technical architecture of the ABDR. These effectively control access to personal data ensuring this information is only accessible to treating health professionals and authorised support staff.

The database provides a capability for all HTC staff to enter data on the interactions with patients to provide treating clinicians with a comprehensive picture of the health and wellbeing of patients. The database provides for both real time ordering of product and retrospective collection of data to provide national clotting factor usage data to inform and assist planning and funding. The system also provides for inclusion of information on physiotherapy and social work interactions with patients.

To ensure appropriate management of the information, the NBA has instigated a detailed governance framework for data use and release.

DATA QUALITY ISSUES

There are a number of data quality issues in the ABDR. These include incomplete records with empty fields or entries. The data entered into some fields has also been characterised by a lack of consistency. This issue in the interpretation of specific fields has been addressed with the development of data standards for users. Application of the data standards will improve data quality. The ABDR Steering Committee has initiated strategies to improve the data quality and over time the reporting from the ABDR has become more robust. However, there is still some data quality issues that impact the data presented in this report and review of these issues continues to be addressed.

ABDR SYSTEM

The 4th Generation ABDR was successfully implemented on 13 August 2012. System enhancements are ongoing and approved by the ABDR Steering Group to enhance performance and ease of use.

COMPARING DATA FROM PREVIOUS ABDR ANNUAL REPORTS

Comprehensive automated and manual data cleansing and validation processes (that occurred as part of the implementation of the new system) enhanced the ABDR data accuracy and consistency presented in this report. This will make it difficult to undertake comparisons with data published in previous reports particularly in regards to multiple diagnoses, treatment plans, ages and dates of death. In 2014-15 historical data was refreshed for the four previous years. Continued work on the data integrity of the registry has been undertaken in 2016-17.

CONSISTENT APPLICATION OF DIAGNOSES AND DEFINITIONS

The application of definitions for bleeding disorders (e.g. VWD subtypes) varies between HTCs, and work will continue to ensure consistent approaches are used, including alignment of the severity ratings and treatment regimens for some patient records.

Commencing 2014-15 the data has been categorised by hereditary and acquired.

VON WILLEBRAND DISEASE

Not all patients with VWD are treated through HTCs and the figures in this report do not represent the total number of VWD patients in Australia.

The diagnosis of VWD subtypes and the assignment of a severity rating to the disorder can vary between HTCs. Often the treatments for VWD involve providing replacement for the missing or defective clotting factors, and use of these products is included in this report.

TREATMENTS NOT INCLUDED IN THE ABDR

The treatments for bleeding disorders often involve providing replacement for the missing or defective clotting factors. The use of commercially produced clotting factors is the subject of this report.

However, there are other clinically appropriate treatments for bleeding disorders which are not counted in this report. Other products used include cryoprecipitate (a fresh blood product), platelets (a fresh blood product) and Desmopressin (1-desamino-8-D-arginine vasopressin, abbreviated as DDAVP).

Mild cases of HMA, HMB and VWD are often treated with DDAVP. Platelet disorders may be treated with DDAVP, platelet infusion or FVIIa.

CONSENT

Patient information in the Australian Bleeding Disorders Registry (ABDR) and MyABDR is collected and managed in a way which complies with the Commonwealth *Privacy Act 1988* and parallel requirements under state and territory laws. Privacy requirements under the *Privacy Act* were tightened in 2014, and a new ABDR/MyABDR Privacy Policy applied from 26 January 2015.

A patient's personal information may be entered into the ABDR, either at a Haemophilia Treatment Centre (HTC) or when a patient enters data directly via MyABDR, and becomes part of an electronic record about the patient's bleeding disorder condition.

In accordance with the ABDR/MyABDR Privacy Policy, a patient's consent is required for the recording of their data in ABDR (consent may be given by a parent, guardian or authorised representative where relevant). Where a patient does not consent then details will not be aggregated in this report, and therefore patient numbers and product use may be understated.

Supply of products for treatment

A key element in ensuring security of supply of products for the treatment of bleeding disorders is the NBA's role in developing, coordinating and monitoring the annual national supply plan and budget, including obtaining annual approval from health ministers. Further details on national supply and demand trends can be found in Appendix C.

The range of products available to clinicians has changed over the years. Figure 2 shows the total issues and market shares for recombinant products from 2012-13 to 2016-17.

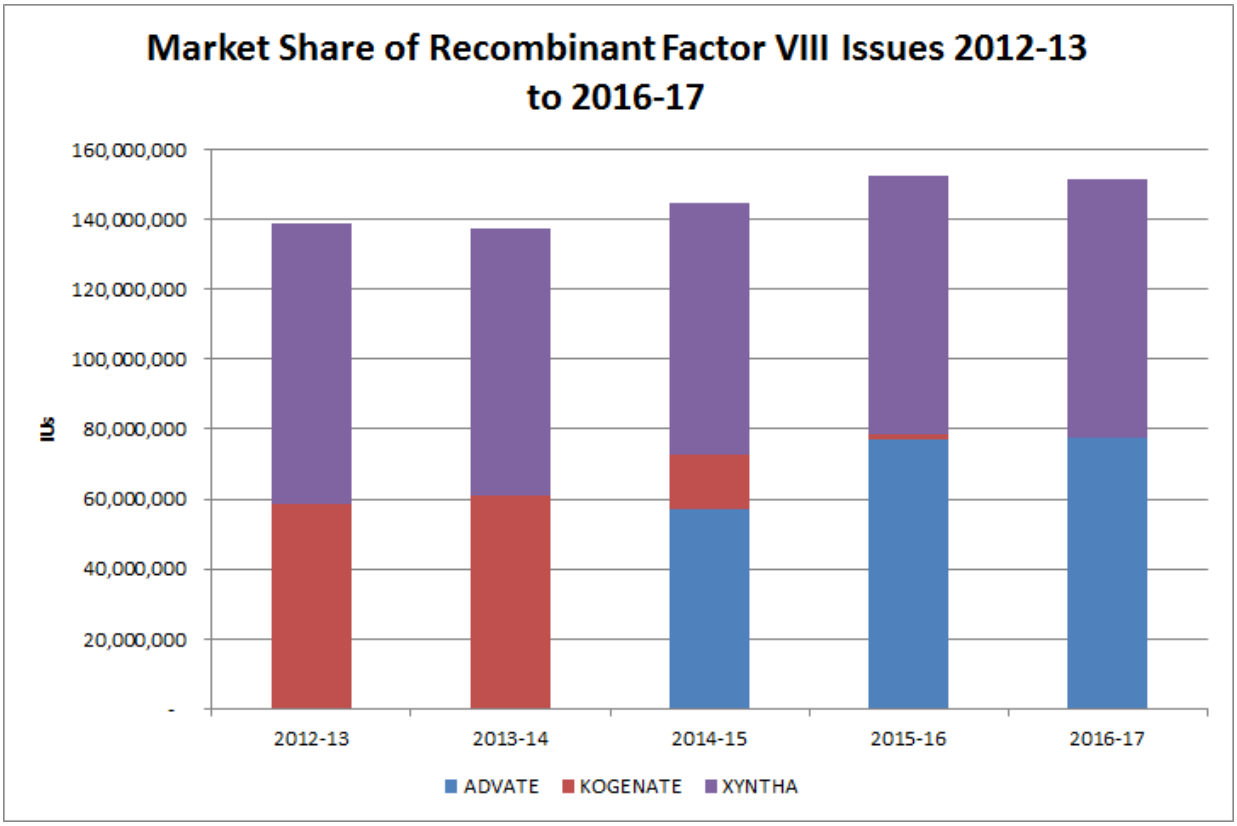

FIGURE 2 - MARKET SHARE OF RECOMBINANT FVIII ISSUES 2012-13 TO 2016-17

Figure 2 illustrates the changes that occurred during 2012 to 2017, brought about by new national supply arrangements, with a transition away from Kogenate and Recombinate, an increase in the issue of Xyntha and the introduction of Advate. In 2014-15 the NBA implemented new contracts for the supply of Recombinant Factor VIII and IX. The new supply arrangements have provided high level national efficiencies without detriment to the patient population. Advate accounted for approximately 51 per cent and Xyntha for 49 per cent of the market share of Recombinant FVIII issues during 2016-17.

The most challenging aspect of HMA management is the development of FVIII inhibitors; previously untreated patients are at the highest risk for inhibitor formation.

Patient participation in company clinical trials for Extended Half Life recombinant Factor VIII and Factor IX products continues to contribute to the variability of year-to-year product growth.

ABDR patient demographics

This section of the report presents the key patient demographic data collected in the ABDR.

DIAGNOSES

The following tables present the numbers of patients in the ABDR and the numbers of patients who received therapeutic products during the years 2012-13 to 2016-17. As noted in the section on *Data quality issues* (page 16) comprehensive automated and manual data cleansing and validation processes that occurred as part of the 4th Generation ABDR Redevelopment project released in August 2012 and the continuation in 2016-17 enhanced the ABDR data accuracy and consistency presented in this report. This may make it difficult to undertake comparisons with data published in previous reports.

Table 3 shows the number of people in the registry and the number treated by latest broad diagnosis for the years 2012-13 to 2016-17. Table 5 expands the data in Table 3 to show the number of people in the registry and the number treated by detailed diagnosis for the years 2012-13 to 2016-17.

TABLE 3 - NUMBER OF PEOPLE IN THE REGISTRY AND TREATED BY BROAD DIAGNOSIS

Diagnosis	Number in ABDR Registry*					Number who Received Product during the year				
	2012-13	2013-14	2014-15	2015-16	2016-17	2012-13	2013-14	2014-15	2015-16	2016-17
Hereditary										
HMA	2,091	2,155	2,158	2,301	2,365	984	964	992	1,022	1,009
HMB	517	532	530	548	564	206	205	218	219	218
VWD	1,921	2,013	2,012	2,092	2,141	222	249	255	287	248
Acquired										
HMA	40	49	59	74	68	10	9	23	13	11
HMB					<5				<5	
VWD	13	18	19	22	25	5	5	<5	8	10
Other Diagnoses										
Other‡	191	201	193	179	193	7	13	11	15	14
Other Factor Deficiency	295	328	344	391	427	36	46	36	52	50
Platelet Disorder	225	245	255	271	288	15	18	15	19	10
Vascular	7	7	7	7	9					
Fibrinogen Disorder	34	41	49	62	74	8	7	10	11	20
Total	**5,334**	**5,589**	**5,626**	**5,947**	**6,155**	**1,493**	**1,516**	**1,563**	**1,647**	**1,590**

Note: Includes asymptomatic carriers in Hereditary

* As noted in the section *Data quality issues* (p15) the data has improved since previous ABDR Annual Reports. The figures presented here represent the most accurate data currently available. The census date for number of people in the registry is 30 June, the last day of the financial year.

‡The ABDR allows for a diagnosis of 'Other' to be recorded for patients with rare and less prevalent disorders or difficult to classify disorders eg mild VWD

PATIENTS WITH MULTIPLE BLEEDING DISORDERS

Individual patients may have more than one bleeding disorder, and will be registered with more than one diagnosis. There are patients with multiple diagnoses in the registry for 2016-17. In these cases, a patient may be counted more than once in the data in this report (e.g. if a patient has two bleeding disorders, that patient may be counted in the totals for each disorder).

In 2016-17 there were 98 patients with two diagnoses and <5 patients with three diagnoses. Of the patients with more than one diagnosis 24 patients received product.

TABLE 4 - NUMBER OF PEOPLE IN THE REGISTRY WITH MULTIPLE BLEEDING DISORDERS

Diagnosis	Patients Numbers in ABDR Registry*			Number of Patient with Multiple Disorders who Received Product during the year
	Bleeding Disorder 1	Bleeding Disorder 2	Bleeding Disorder 3	
HMA	2,433	44	<5	17
HMB	565	<5		
VWD	2,166	18	<5	<5
Other‡	193	<5		<5
Other Factor Deficiency	427	19		
Platelet Disorder	288	11		<5
Vascular	9	<5		
Fibrinogen Disorders	74			
Total	**6,155**	**98**	**<5**	**24**

Note: Includes Acquired and Hereditary disorders

* As noted in the section *Data quality issues* (p15) the data has improved since previous ABDR Annual Reports. The figures presented here represent the most accurate data currently available. The census date for number of people in the registry is 30 June, the last day of the financial year.

‡The ABDR allows for a diagnosis of 'Other' to be recorded for patients with rare and less prevalent disorders or difficult to classify disorders eg mild VWD

TABLE 5 - NUMBER OF PEOPLE IN THE REGISTRY AND TREATED BY DETAILED DIAGNOSIS

	Number in ABDR Registry*					Number who Received Product during the year				
	2012-13	2013-14	2014-15	2015-16	2016-17	2012-13	2013-14	2014-15	2015-16	2016-17
Hereditary										
HMA										
Asymptomatic Carrier Factor VIII Deficiency (HmA)	218	241	190	226	235	7	<5	6	<5	<5
Factor VIII Deficiency (HmA)	1,723	1,752	1,793	1,972	2,085	962	942	972	1,011	1,005
Symptomatic Carrier Factor VIII Deficiency (HmA)	150	162	175	103	45	15	18	14	9	<5
HMB										
Asymptomatic Carrier Factor IX Deficiency (HmB)	49	54	47	47	53				<5	
Factor IX Deficiency (HmB)	418	424	426	471	489	197	199	209	213	216
Symptomatic Carrier Factor IX Deficiency (HmB)	50	54	57	30	22	9	6	9	5	<5
VWD										
von Willebrand Disease – Uncharacterised	313	318	279	219	180	10	14	13	8	9
von Willebrand Disease Type 1	1,175	1,236	1,233	1,328	1,387	113	130	127	137	115
von Willebrand Disease Type 2	392	417	459	502	533	69	73	84	108	94
von Willebrand Disease Type 3	41	42	41	43	41	30	32	31	34	30
Hereditary Total	**4,530**	**4,701**	**4,700**	**4,941**	**5,070**	**1,412**	**1,418**	**1,465**	**1,528**	**1,475**
Acquired										
HMA	40	49	59	74	68	10	9	23	13	11
HMB					<5				<5	
VWD	13	18	19	22	25	5	5	<5	8	10
Acquired Total	**52**	**66**	**78**	**96**	**<97**	**15**	**14**	**<27**	**<25**	**21**
Other Factor Deficiency										
Factor V Deficiency	11	10	11	17	15	<5	<5	<5	<5	<5
Factor VII Deficiency	53	54	61	67	73	10	9	8	7	9

	Number in ABDR Registry*					Number who Received Product during the year				
	2012-13	2013-14	2014-15	2015-16	2016-17	2012-13	2013-14	2014-15	2015-16	2016-17
Factor X Deficiency	17	17	17	20	19	5	<5	5	<5	6
Factor XI Deficiency	178	206	217	249	273	12	20	14	24	18
Factor XII Deficiency†	20	16	17	17	18	<5	<5	<5	<5	
Factor XIII Deficiency	15	18	19	21	24	9	10	6	11	14
Platelet Disorder										
Platelet - Bernard-Soulier	5	5	5	5	7				<5	
Platelet - Glanzmann's Thrombasthenia	16	17	18	21	22	<5	<5	<5	8	6
Platelet - Macrothrombocytopenias	10	10	12	13	13	<5				
Platelet - May Hegglin	<5	<5	<5	<5	<5	<5			<5	
Platelet - Primary Secretion Defect	7	9	10	10	9	<5	<5	<5		<5
Platelet - Storage Pool (Dense Granule) Deficiency	31	37	43	46	52	<5	<5		<5	<5
Platelet – Uncharacterised	153	164	164	173	182	8	10	10	7	<5
Vascular										
Vascular Disorders - Ehlers Danlos Syndrome	7	7	7	7	9					
Fibrinogen										
Fibrinogen – Afibrinogenemia	6	7	7	7	7	<5	5	5	<5	5
Fibrinogen – Dysfibrinogenemia	22	24	29	36	45	<5	<5	<5	<5	9
Fibrinogen – Hypofibrinogenemia	5	9	12	17	19			<5	<5	6
Fibrinogen Dysfunction - Uncharacterised	<5	<5	<5	<5	<5					
Other (Including Unclassified)	191	201	193	179	198	7	13	11	15	14
Other Diagnoses Total	**752**	**822**	**848**	**910**	**991**	**66**	**84**	**72**	**97**	**94**
Total	**5,334**	**5,589**	**5,626**	**5,947**	**6,155**	**1,493**	**1,516**	**1,563**	**1,647**	**1,590**

* As noted in the section *Data quality issues* (p15) the data has been improved since previous ABDR Annual Reports. The figures presented here represent the most accurate data currently available. The census date for number of people in the registry is 30 June, the last day of the financial year.

†Factor XII Deficiency does not require treatment with products, but is included as a diagnostic category.

AGE, DIAGNOSIS AND SEVERITY

In the following tables patients are categorised as either Adult (aged 18 years and over) or Paediatric and Adolescent (aged under 18 years).[2]

Table 6 and Table 7 detail the numbers of patients in the registry who received product (therapeutic treatment) during the period 2012-13 to 2016-17; by age group, broad diagnosis and by severity.

Table 8 and Table 9 set out age group and detailed diagnosis for patients with HMA, HMB and VWD.

The majority of patients receiving treatment for bleeding disorders have HMA, specifically those patients with severe HMA.

There are some discrepancies in the data regarding the coding of severity when a patient receives treatment, and data cleansing and patient record updates are continuing. This will improve the forecasting for the national supply plan and budget for future years. It should be noted that the national forecasting and supply management process continue to perform very well.

Whilst the data discrepancies affect the analysis for this annual report, there is minimal impact on patient care as Haemophilia Treatment Centre staff have full access to their patient records for the provision of care and treatment.

In 2016-17 the results show variations. The patterns indicate that the implemented strategies are improving data quality, completeness and accuracy. This will make it difficult to undertake comparisons with data published in previous reports particularly in regards to multiple diagnoses. Continued work on the data integrity of the registry has been undertaken again in 2016-17.

[2] In ABDR Annual Reports prior to 2011-12 the threshold age between paediatric and adult patients was 20 years of age. This threshold has been adjusted in subsequent reports to better reflect the manner in which patients are treated in HTCs.

TABLE 6 - NUMBER OF ADULT PATIENTS IN THE REGISTRY AND TREATED BY BROAD DIAGNOSIS AND SEVERITY FOR HMA, HMB

	Number in ABDR Registry*					Number who Received Product during the year				
Adult (aged 18 years and over)	**2012-13**	**2013-14**	**2014-15**	**2015-16**	**2016-17**	**2012-13**	**2013-14**	**2014-15**	**2015-16**	**2016-17**
Hereditary										
HMA										
Mild	939	961	996	1,040	1,007	220	205	208	227	220
Moderate	151	148	145	159	157	85	78	94	99	88
Severe	348	364	374	385	392	316	327	327	340	355
HMB										
Mild	229	234	235	240	227	53	41	55	53	54
Moderate	92	93	97	96	98	46	49	49	54	52
Severe	56	58	56	60	63	45	49	47	50	51
Total Hereditary	**1,815**	**1,858**	**1,903**	**1,980**	**1,944**	**765**	**749**	**780**	**823**	**820**
Total Acquired HMA	32	40	44	23	22	7	6	13	<5	<5
Total	**1,847**	**1,898**	**1,947**	**2,003**	**1,966**	**772**	**755**	**793**	**<828**	**<825**

* As noted in the section *Data quality issues* (p15) the data has been improved since previous ABDR Annual Reports. The figures presented here represent the most accurate data currently available. The census date for number of people in the registry is 30 June, the last day of the financial year. Patients can have their severity categorised as 'unknown' or 'not applicable' during the initial diagnosis procedures, and these figures are not shown in this table. Excludes those severities recorded as *Unknown, Not Applicable and Blank*.

TABLE 7 - NUMBER OF PAEDIATRIC AND ADOLESCENT PATIENTS IN THE REGISTRY AND TREATED BY BROAD DIAGNOSIS AND SEVERITY FOR HMA, HMB

	Number in ABDR Registry*					Number who Received Product*				
Paediatric and Adolescent (aged less than 18 years)	**2012-13**	**2013-14**	**2014-15**	**2015-16**	**2016-17**	**2012-13**	**2013-14**	**2014-15**	**2015-16**	**2016-17**
Hereditary										
HMA										
Mild	169	171	183	205	206	54	50	54	56	49
Moderate	67	69	68	66	70	55	50	56	52	48
Severe	263	265	266	275	274	250	252	249	247	246
HMB										
Mild	47	52	51	54	47	9	17	14	13	12
Moderate	19	20	21	21	19	14	14	16	13	15
Severe	40	39	41	42	43	39	35	37	35	34
Total Hereditary	**605**	**616**	**630**	**663**	**659**	**421**	**418**	**426**	**416**	**404**
Total Acquired HMA	**<5**	**<5**	**<5**	**<5**	**<5**		**<5**	**<5**		

* As noted in the section *Data quality issues* (p15) the data has been improved since previous ABDR Annual Reports. Patients can have their severity categorised as 'unknown' or 'not applicable' during the initial diagnosis procedures, and these figures are not shown in this table. The figures presented here represent the most accurate data currently available. The census date for number of people in the registry is 30 June, the last day of the financial year. Excludes those severities recorded as *Unknown, Not Applicable and Blank*.

BY AGE GROUP AND DETAILED DIAGNOSIS

TABLE 8 - NUMBER OF PEOPLE IN THE REGISTRY DIAGNOSED WITH HMA OR HMB BY AGE GROUP AND DISEASE CLASSIFICATION

	Number in ABDR Registry*					Number who Received Product during the year				
	2012-13	2013-14	2014-15	2015-16	2016-17	2012-13	2013-14	2014-15	2015-16	2016-17
Hereditary										
HMA – Adult (aged 18 years and over)										
Asymptomatic Carrier Factor VIII Deficiency	211	232	181	216	223	7	<5	6	<5	
Factor VIII Deficiency	1,239	1,264	1,293	1,441	1,536	604	592	615	658	662
Symptomatic Carrier Factor VIII Deficiency **	133	141	154	86	38	13	16	11	7	<5
HMA – Paediatric (aged less than 18 years)										
Asymptomatic Carrier Factor VIII Deficiency	7	9	9	10	12					<5
Factor VIII Deficiency	484	488	500	531	549	358	350	357	353	343
Symptomatic Carrier Factor VIII Deficiency	17	21	21	17	7	<5	<5	<5	<5	
HMB – Adult (aged 18 years and over)										
Asymptomatic Carrier Factor IX Deficiency	46	49	42	44	48				<5	
Factor IX Deficiency	319	322	321	360	382	136	133	142	152	155
Symptomatic Carrier Factor IX Deficiency	43	47	51	25	18	8	6	9	5	<5
HMB – Paediatric (aged less than 18 years)										
Asymptomatic Carrier Factor IX Deficiency	<5	5	5	<5	5					
Factor IX Deficiency	99	102	105	111	107	61	66	67	61	61
Symptomatic Carrier Factor IX Deficiency	7	7	6	5	<5	<5				
Acquired										
HMA – Adult (aged 18 years and over)	39	47	57	73	67	10	7	22	13	11
HMA – Paediatric (aged less than 18 years)	<5	<5	<5	<5	<5		<5	<5		
HMB – Adult (aged 18 years and over)					<5				<5	

* As noted in the section *Data quality issues* (p15) the data has been improved since previous ABDR Annual Reports. The figures presented here represent the most accurate data currently available. The census date for number of people in the registry is 30 June, the last day of the financial year.

** Symptomatic carriers transitioned to asymptomatic carriers and Haemophilia Factor VIII Deficiency patients, accounts for ongoing data quality changes in patient counts in 2016-17.

TABLE 9 - NUMBER OF PEOPLE IN THE REGISTRY DIAGNOSED WITH VWD BY AGE GROUP AND DISEASE CLASSIFICATION

	Number in ABDR Registry*					Number who Received Product during the year				
	2012-13	2013-14	2014-15	2015-16	2016-17	2012-13	2013-14	2014-15	2015-16	2016-17
Hereditary										
VWD – Adult (aged 18 years and over)										
von Willebrand Disease - Uncharacterised	255	263	231	176	149	6	11	9	6	9
von Willebrand Disease Type 1	958	1,016	1,023	1,123	1,184	96	108	107	116	99
von Willebrand Disease Type 2	296	320	354	394	427	56	60	68	86	75
von Willebrand Disease Type 3	32	34	35	35	32	24	24	26	27	24
VWD – Paediatric (aged less than 18 years)										
von Willebrand Disease - Uncharacterised	58	55	48	43	31	<5	<5	<5	<5	
von Willebrand Disease Type 1	217	220	210	205	203	17	22	20	21	16
von Willebrand Disease Type 2	96	97	105	108	106	13	13	16	22	19
von Willebrand Disease Type 3	9	8	6	8	9	6	8	5	7	6
Acquired										
VWD – Adult (aged 18 years and over)	12	17	19	22	25	5	5	<5	8	10
VWD – Paediatric (aged less than 18 years)	<5	<5								

* As noted in the section *Data quality issues* (p15) the data has been improved since previous ABDR Annual Reports. The figures presented here represent the most accurate data currently available. The census date for number of people in the registry is 30 June, the last day of the financial year.

BY LOCATION

Figure 3 depicts the geographic distribution of patients in the ABDR. Patient distribution is largely in line with the distribution of the general population. However, a more detailed analysis of geographic distribution could be expected to reveal the clustering effects often associated with the distribution of genetic disorder. Excluded from Figure 3 are 15 patients that have unknown locations (down from 33 in 2015-16).

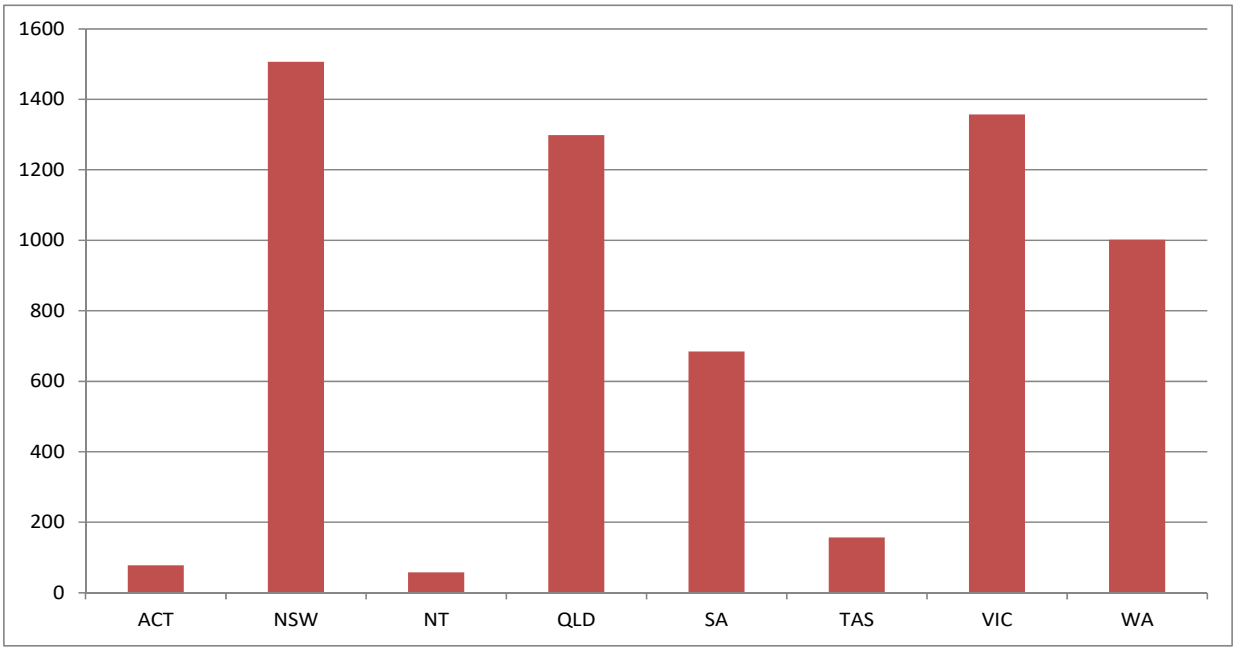

FIGURE 3 - NUMBERS OF ACTIVE PATIENTS IN THE REGISTRY AS AT 30 JUNE 2017

Table 10 shows the numbers of patients with severe hereditary HMA and HMB, acquired HMA and the numbers of male patients with severe HMA and HMB by state and territory.

TABLE 10 - NUMBERS OF PATIENTS WITH SEVERE HMA AND HMB BY LOCATION

	HMA			HMB	
State/Territory	Severe Hereditary	Severe Hereditary Males	Severe Acquired	Severe Hereditary	Severe Hereditary Males
ACT	13	13		<5	<5
NSW	197	195	8	36	36
NT	<5	<5	<5		
QLD	150	149		21	21
SA	51	51	<5	<5	<5
TAS	17	17		<5	<5
VIC	164	164		32	32
WA	71	71	<5	9	8
Total	**<668**	**<665**	**<20**	**106**	**105**

As noted in the section *Data quality issues* (p15) the data has been improved since previous ABDR Annual Reports. The figures presented here represent the most accurate data currently available. The census date for number of people in the registry is 30 June, the last day of the financial year. This table excludes patients with an unknown location.

BY GENDER AND AGE DISTRIBUTION

The figures in this section present the gender and age distribution of patients in the ABDR in 2016-17, compared to the general Australian population[3].

Figure 4 and Figure 5 chart the distribution of all female hereditary HMA and HMB patients against the female population. The tables next to each figure show the numbers and percentages used in the charts.

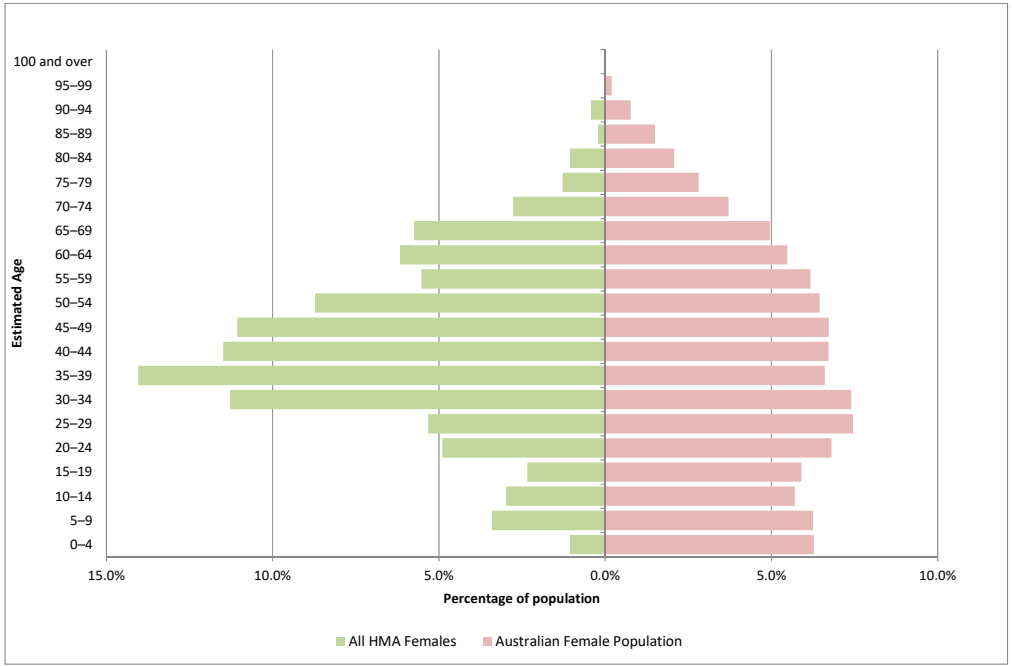

FIGURE 4 - DISTRIBUTION OF HEREDITARY FEMALE HMA PATIENTS BY AGE IN 2016-17

TABLE (FIG 4) – DISTRIBUTION OF HEREDITARY FEMALE HMA PATIENTS BY AGE IN 2016-17

Age group	2016 Australian Female Population	% 2016 Australian Female Population	HMA female patients	% HMA female patients
0–4	765,994	6.3%	5	1.1%
5–9	762,928	6.3%	16	3.4%
10–14	696,325	5.7%	14	3.0%
15–19	720,085	5.9%	11	2.3%
20–24	830,358	6.8%	23	4.9%
25–29	908,879	7.5%	25	5.3%
30–34	903,259	7.4%	53	11.3%
35–39	806,038	6.6%	66	14.0%
40–44	820,061	6.7%	54	11.5%
45–49	820,203	6.7%	52	11.1%
50–54	787,079	6.5%	41	8.7%
55–59	753,160	6.2%	26	5.5%
60–64	667,824	5.5%	29	6.2%
65–69	604,480	5.0%	27	5.7%
70+	1,352,290	11.1%	28	5.7%
All ages	**12,198,963**		**470**	

[3] Australian Bureau of Statistics, Australian Demographic Statistics, Cat. No. 3101.0 Released March 2017 (Table 59)

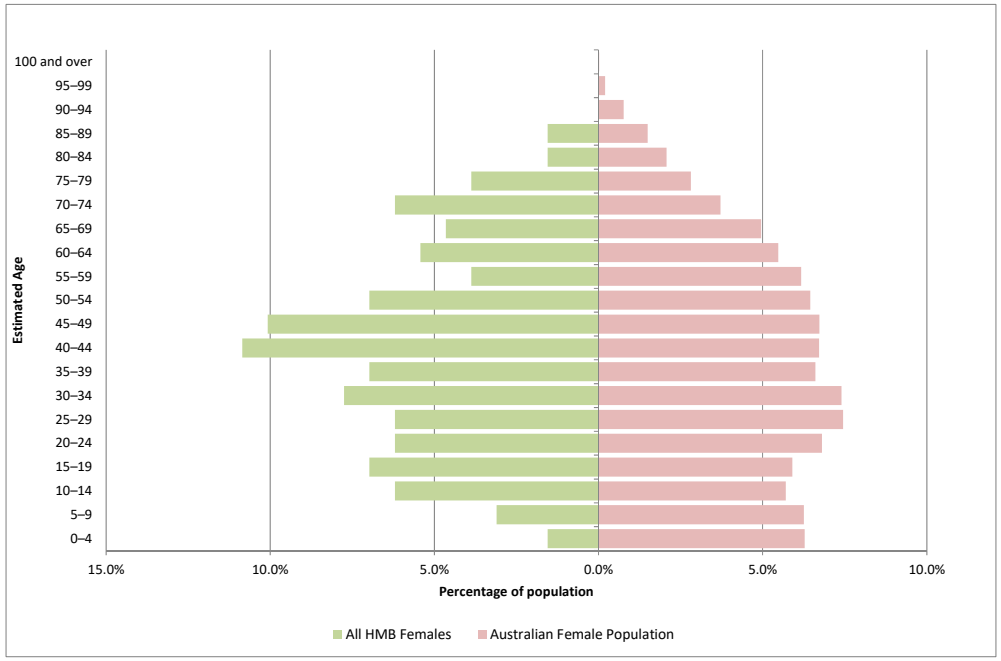

FIGURE 5 - DISTRIBUTION OF HEREDITARY FEMALE HMB PATIENTS BY AGE IN 2016-17

Age group	2016 Australian Female Population	% 2016 Australian Female Population	HMB female patients	% HMB female patients
0–4	765,994	6.3%	<5	<5
5–9	762,928	6.3%	<5	<5
10–14	696,325	5.7%	8	6.2%
15–19	720,085	5.9%	9	7.0%
20–24	830,358	6.8%	8	6.2%
25–29	908,879	7.5%	8	6.2%
30–34	903,259	7.4%	10	7.8%
35–39	806,038	6.6%	9	7.0%
40–44	820,061	6.7%	14	10.9%
45–49	820,203	6.7%	13	10.1%
50–54	787,079	6.5%	9	7.0%
55–59	753,160	6.2%	5	3.9%
60–64	667,824	5.5%	7	5.4%
65–69	604,480	5.0%	6	4.7%
70+	1,352,290	11.1%	17	13.2%
All ages	**12,198,963**		**129**	

TABLE (FIG 5) – DISTRIBUTION OF HEREDITARY FEMALE HMB PATIENTS BY AGE IN 2016-17

Figure 6 and 6.1 chart the distribution of all male hereditary HMA patients and all male severe hereditary HMA patients against the male population. The disorder is genetically linked to a patient's gender, and usually affects males. There are a relatively lower number of older patients (from the age grouping of 75-79 years onwards). The life expectancy of HMA patients has improved dramatically[4] in recent decades. The younger cohorts can expect to survive longer, which will increase the overall patient population and the demand for product in the future.

The number of acquired HMA severe male patients totalled 9.

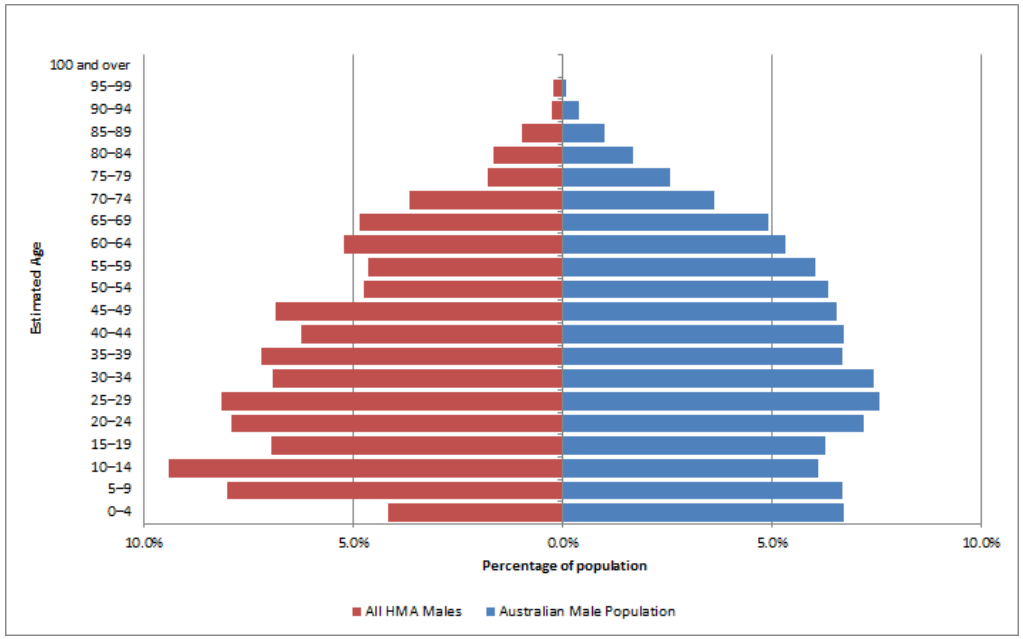

FIGURE 6 - DISTRIBUTION OF HEREDITARY MALE HMA PATIENTS BY AGE IN 2016-17

TABLE (FIG 6) – DISTRIBUTION OF HEREDITARY MALE HMA PATIENTS BY AGE IN 2016-17

Age group	2016 Australian Male Population	% 2016 Australian Male Population	HMA male patients	% HMA male patients
0–4	808,109	6.7%	79	4.2%
5–9	804,159	6.7%	152	8.0%
10–14	735,400	6.1%	178	9.4%
15–19	755,917	6.3%	132	7.0%
20–24	866,128	7.2%	150	7.9%
25–29	909,656	7.6%	154	8.1%
30–34	892,953	7.4%	131	6.9%
35–39	802,100	6.7%	136	7.2%
40–44	808,149	6.7%	118	6.2%
45–49	786,139	6.5%	130	6.9%
50–54	763,717	6.4%	90	4.7%
55–59	724,403	6.0%	88	4.6%
60–64	638,275	5.3%	99	5.2%
65–69	589,768	4.9%	92	4.9%
70+	1,126,973	9.4%	166	8.5%
All ages	**12,011,846**		**1,895**	

[4] Oldenburg J, Dolan G, Lemm G (2009).Haemophilia care then, now and in the future. Haemophilia 15, S1: 2-7.

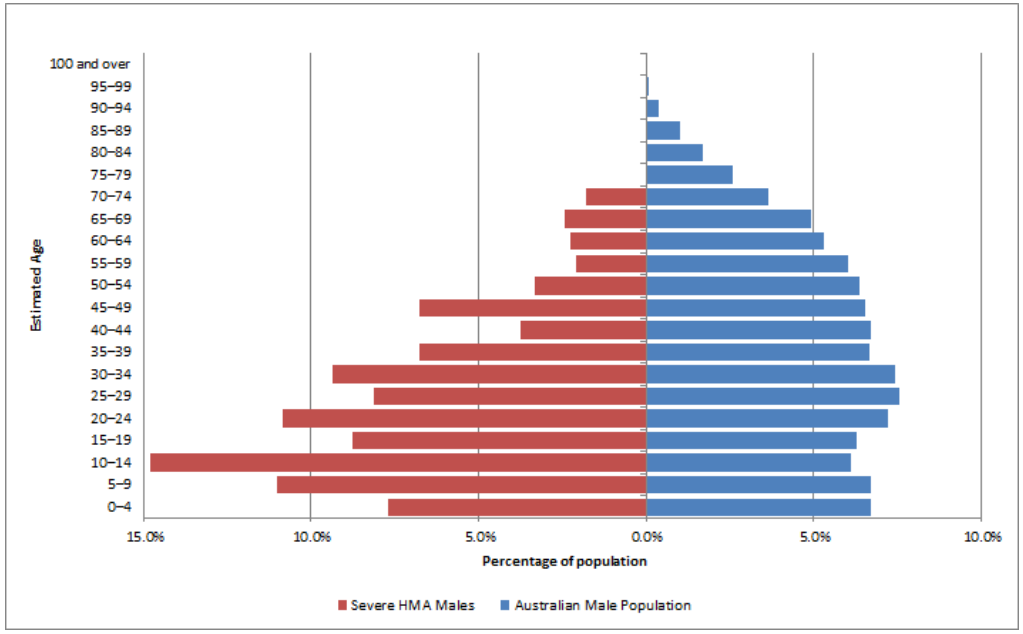

FIGURE 6.1 - DISTRIBUTION OF HEREDITARY MALE HMA SEVERE PATIENTS BY AGE IN 2016-17

Age group	2016 Australian Male Population	% 2016 Australian Male Population	HMA severe male patients	% HMA severe male patients
0–4	808,109	6.7%	51	7.7%
5–9	804,159	6.7%	73	11.0%
10–14	735,400	6.1%	98	14.8%
15–19	755,917	6.3%	58	8.7%
20–24	866,128	7.2%	72	10.9%
25–29	909,656	7.6%	54	8.1%
30–34	892,953	7.4%	62	9.4%
35–39	802,100	6.7%	45	6.8%
40–44	808,149	6.7%	25	3.8%
45–49	786,139	6.5%	45	6.8%
50–54	763,717	6.4%	22	3.3%
55–59	724,403	6.0%	14	2.1%
60–64	638,275	5.3%	15	2.3%
65–69	589,768	4.9%	16	2.4%
70+	1,126,973	9.4%	13	1.8%
All ages	**12,011,846**		**663**	

TABLE (FIG 6.1) – DISTRIBUTION OF HEREDITARY MALE HMA SEVERE PATIENTS BY AGE IN 2016-17

Figure 7 and Figure 7.1 chart the distribution of all male hereditary HMB patients and all male severe hereditary HMB patients against the male population. As with HMA, HMB is also genetically linked to a patient's gender, and usually affects males. The observed male severe HMB population does not conform to the same pattern as the general male population, however there are low patient numbers (n=105) in this group and no conclusions should be drawn.

There were no acquired HMB severe male patients.

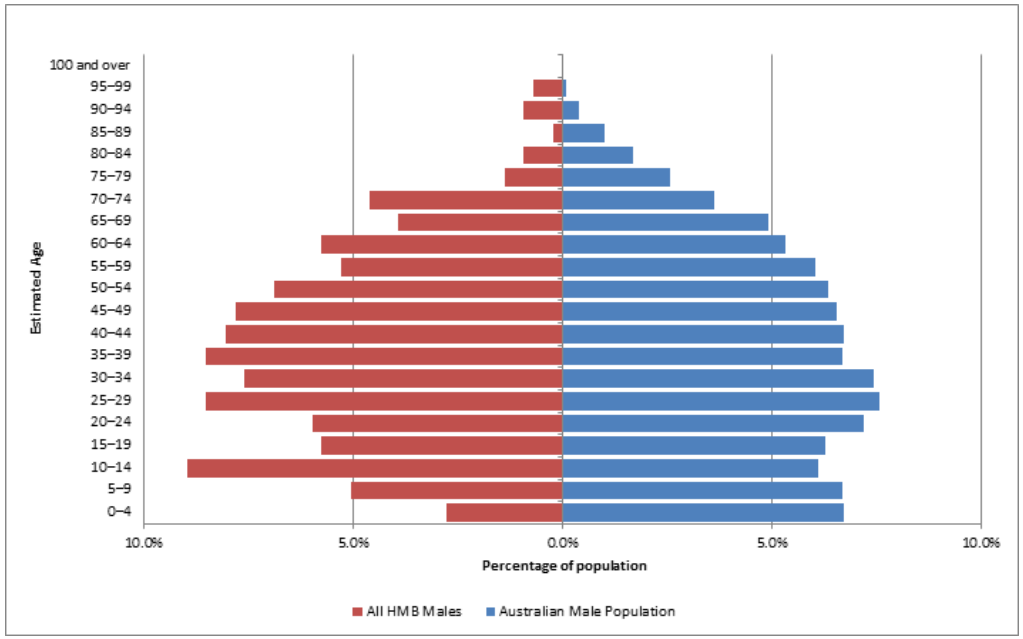

FIGURE 7 - DISTRIBUTION OF HEREDITARY MALE HMB PATIENTS BY AGE IN 2016-17

Age group	2016 Australian Male Population	% 2016 Australian Male Population	HMB male patients	% HMB male patients
0–4	808,109	6.3%	12	2.8%
5–9	804,159	6.3%	22	5.1%
10–14	735,400	5.7%	39	9.0%
15–19	755,917	5.9%	25	5.7%
20–24	866,128	6.8%	26	6.0%
25–29	909,656	7.5%	37	8.5%
30–34	892,953	7.4%	33	7.6%
35–39	802,100	6.6%	37	8.5%
40–44	808,149	6.7%	35	8.0%
45–49	786,139	6.7%	34	7.8%
50–54	763,717	6.5%	30	6.9%
55–59	724,403	6.2%	23	5.3%
60–64	638,275	5.5%	25	5.7%
65–69	589,768	5.0%	17	3.9%
70+	1,126,973	9.4%	40	8.7%
All ages	**12,011,846**		**435**	

TABLE (FIG 7) – DISTRIBUTION OF HEREDITARY MALE HMB PATIENTS BY AGE IN 2016-17

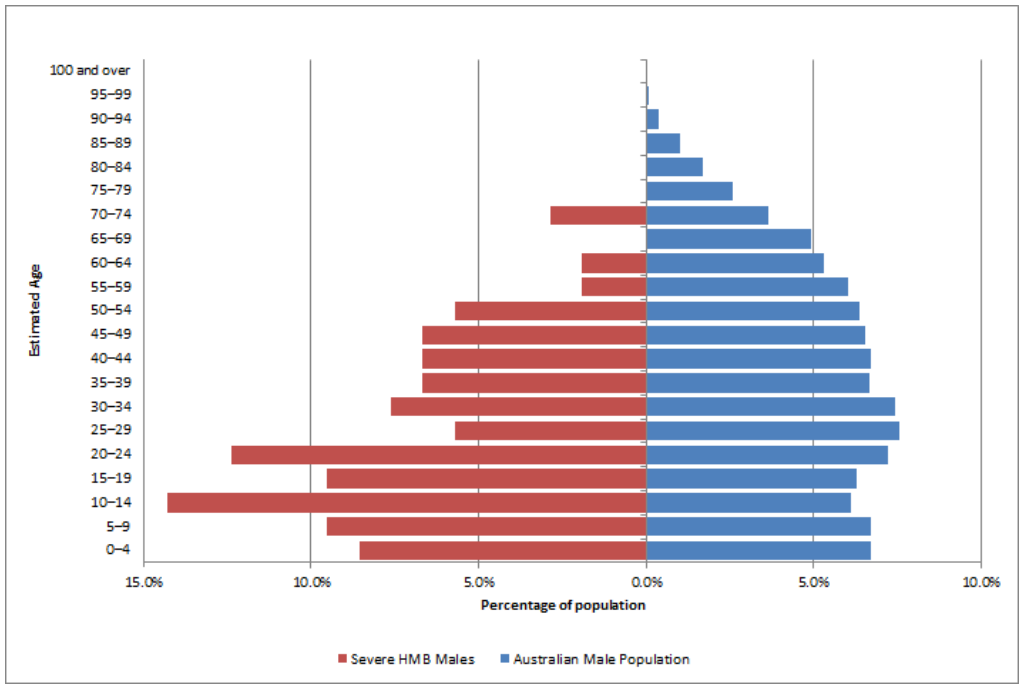

FIGURE 7.1 - DISTRIBUTION OF HEREDITARY MALE HMB SEVERE PATIENTS BY AGE IN 2016-17

TABLE (FIG 7.1) – DISTRIBUTION OF HEREDITARY MALE HMB SEVERE PATIENTS BY AGE IN 2016-17

Age group	2016 Australian Male Population	% 2016 Australian Male Population	HMB severe male patients	% HMB severe male patients
0–4	808,109	6.3%	9	8.6%
5–9	804,159	6.3%	10	9.5%
10–14	735,400	5.7%	15	14.3%
15–19	755,917	5.9%	10	9.5%
20–24	866,128	6.8%	13	12.4%
25–29	909,656	7.5%	6	5.7%
30–34	892,953	7.4%	8	7.6%
35–39	802,100	6.6%	7	6.7%
40–44	808,149	6.7%	7	6.7%
45–49	786,139	6.7%	7	6.7%
50–54	763,717	6.5%	6	5.7%
55–59	724,403	6.2%	<5	<5
60–64	638,275	5.5%	<5	<5
65–69	589,768	5.0%		0.0%
70+	1,126,973	9.4%	<5	<5
All ages	**12,011,846**		**105**	

Figure 8, Figure 8.1, Figure 9 and Figure 9.1 chart the distribution of all female and male VWD patients and female and male severe VWD patients against the female and male populations.

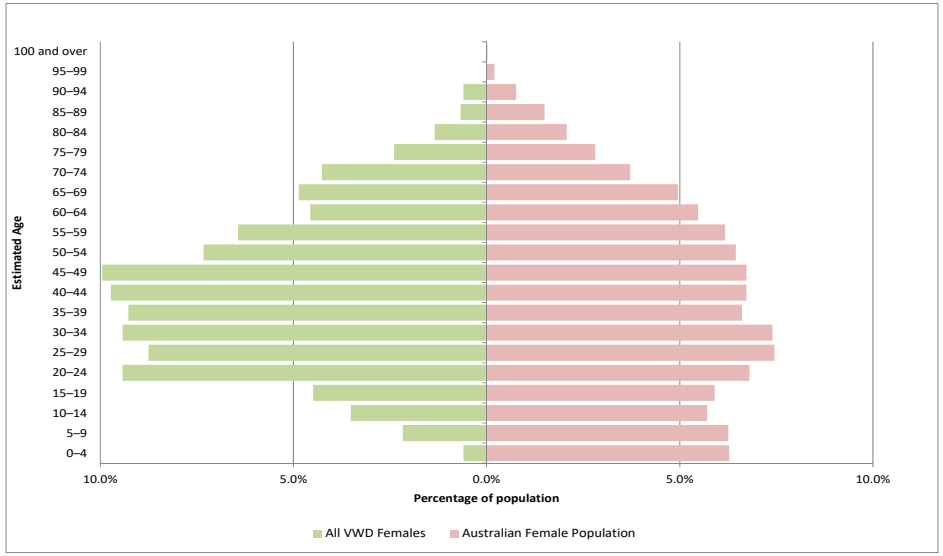

FIGURE 8 - DISTRIBUTION OF HEREDITARY FEMALE VWD PATIENTS BY AGE IN 2016-17

TABLE (FIG 8) – DISTRIBUTION OF HEREDITARY FEMALE VWD PATIENTS BY AGE IN 2016-17

Age group	2016 Australian Female Population	% 2016 Australian Female Population	VWD female patients	% VWD female patients
0–4	765,994	6.3%	8	0.6%
5–9	762,928	6.3%	29	2.2%
10–14	696,325	5.7%	47	3.5%
15–19	720,085	5.9%	60	4.5%
20–24	830,358	6.8%	126	9.4%
25–29	908,879	7.5%	117	8.8%
30–34	903,259	7.4%	126	9.4%
35–39	806,038	6.6%	124	9.3%
40–44	820,061	6.7%	130	9.7%
45–49	820,203	6.7%	133	9.9%
50–54	787,079	6.5%	98	7.3%
55–59	753,160	6.2%	86	6.4%
60–64	667,824	5.5%	61	4.6%
65–69	604,480	5.0%	65	4.9%
70+	1,352,290	11.1%	127	9.3%
All ages	**12,198,963**		**1,337**	

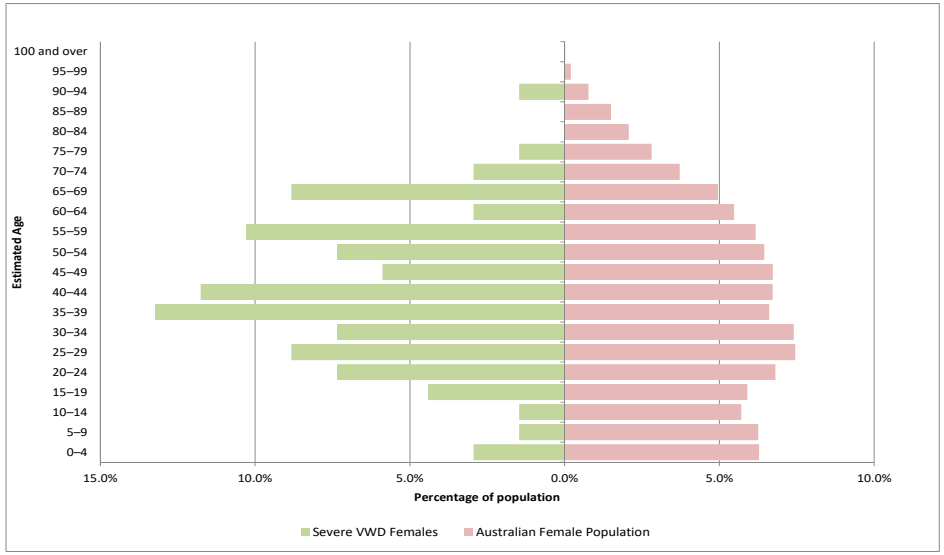

FIGURE 8.1 - DISTRIBUTION OF HEREDITARY FEMALE VWD SEVERE PATIENTS BY AGE IN 2016-17

TABLE (FIG 8.1) – DISTRIBUTION OF HEREDITARY FEMALE VWD SEVERE PATIENTS BY AGE IN 2016-17

Age group	2016 Australian Female Population	% 2016 Australian Female Population	VWD severe female patients	% VWD severe female patients
0–4	765,994	6.3%	<5	<5
5–9	762,928	6.3%	<5	<5
10–14	696,325	5.7%	<5	<5
15–19	720,085	5.9%	<5	<5
20–24	830,358	6.8%	5	7.4%
25–29	908,879	7.5%	6	8.8%
30–34	903,259	7.4%	5	7.4%
35–39	806,038	6.6%	9	13.2%
40–44	820,061	6.7%	8	11.8%
45–49	820,203	6.7%	<5	<5
50–54	787,079	6.5%	5	7.4%
55–59	753,160	6.2%	7	10.3%
60–64	667,824	5.5%	<5	<5
65–69	604,480	5.0%	6	8.8%
70+	1,352,290	11.1%	<5	<5
All ages	**12,198,963**		**68**	

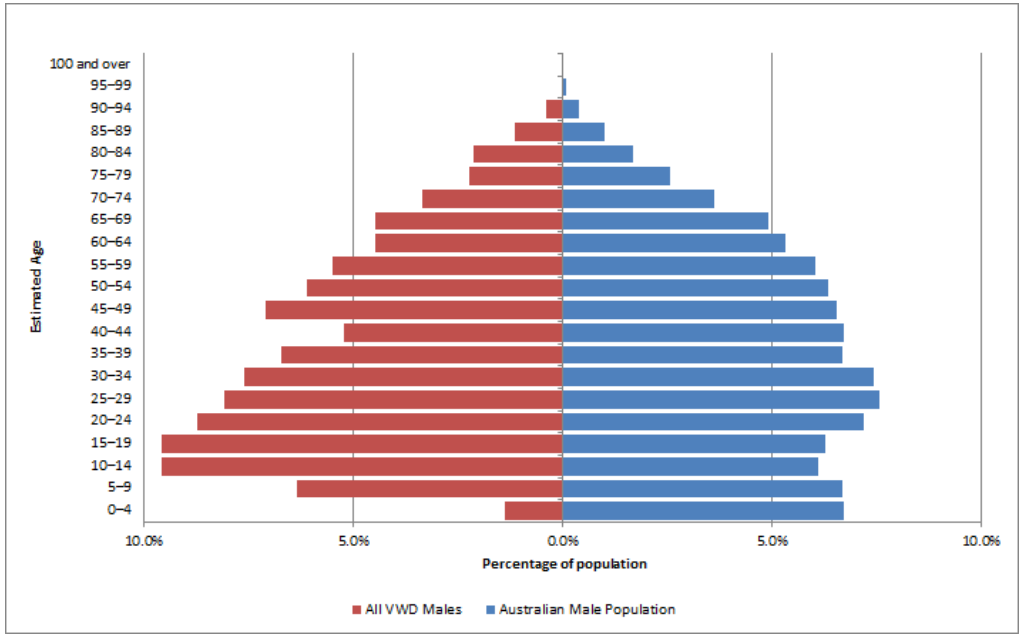

FIGURE 9 - DISTRIBUTION OF HEREDITARY MALE VWD PATIENTS BY AGE IN 2016-17

TABLE (FIG 9) – DISTRIBUTION OF HEREDITARY MALE VWD PATIENTS BY AGE IN 2016-17

Age group	2016 Australian Male Population	% 2016 Australian Male Population	VWD male patients	% VWD male patients
0–4	808,109	6.3%	11	1.4%
5–9	804,159	6.3%	51	6.3%
10–14	735,400	5.7%	77	9.6%
15–19	755,917	5.9%	77	9.6%
20–24	866,128	6.8%	70	8.7%
25–29	909,656	7.5%	65	8.1%
30–34	892,953	7.4%	61	7.6%
35–39	802,100	6.6%	54	6.7%
40–44	808,149	6.7%	42	5.2%
45–49	786,139	6.7%	57	7.1%
50–54	763,717	6.5%	49	6.1%
55–59	724,403	6.2%	44	5.5%
60–64	638,275	5.5%	36	4.5%
65–69	589,768	5.0%	36	4.5%
70+	1,126,973	9.4%	74	9.2%
All ages	**12,011,846**		**804**	

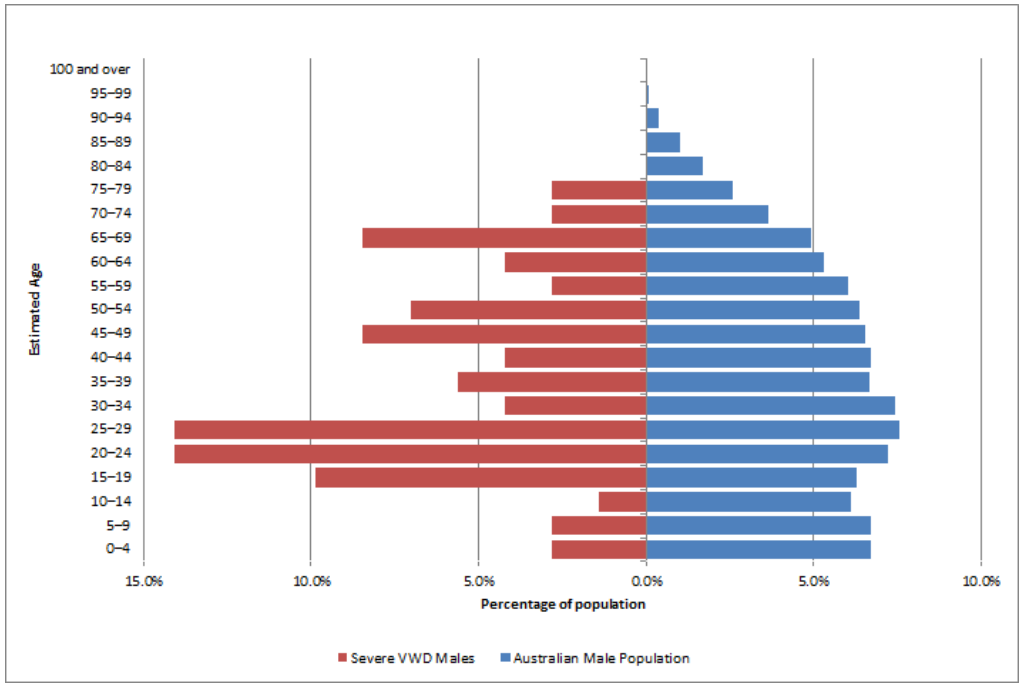

FIGURE 9.1 - DISTRIBUTION OF HEREDITARY MALE VWD SEVERE PATIENTS BY AGE IN 2016-17

TABLE (FIG 9.1) – DISTRIBUTION OF HEREDITARY MALE VWD SEVERE PATIENTS BY AGE IN 2016-17

Age group	2016 Australian Male Population	% 2016 Australian Male Population	VWD severe male patients	% VWD severe male patients
0–4	808,109	6.3%	<5	<5
5–9	804,159	6.3%	<5	<5
10–14	735,400	5.7%	<5	<5
15–19	755,917	5.9%	7	9.9%
20–24	866,128	6.8%	10	14.1%
25–29	909,656	7.5%	10	14.1%
30–34	892,953	7.4%	<5	<5
35–39	802,100	6.6%	<5	<5
40–44	808,149	6.7%	<5	<5
45–49	786,139	6.7%	6	8.5%
50–54	763,717	6.5%	5	7.0%
55–59	724,403	6.2%	<5	<5
60–64	638,275	5.5%	<5	<5
65–69	589,768	5.0%	6	8.5%
70+	1,126,973	9.4%	7	5.6%
All ages	**12,011,846**		**71**	

Table 11 sets out a breakdown by gender for the different types of VWD.

TABLE 11 – VWD PATIENTS BREAKDOWN BY TYPE AND GENDER

VWD Type	Female	Male	Total
Von Willebrand Disease - Uncharacterised	101	79	180
Von Willebrand Disease Type 1	917	470	1,387
Von Willebrand Disease Type 2 - Uncharacterised	61	48	109
Von Willebrand Disease Type 2A	70	61	131
Von Willebrand Disease Type 2B	33	31	64
Von Willebrand Disease Type 2M	109	81	190
Von Willebrand Disease Type 2N	27	12	39
Von Willebrand Disease Type 3	19	22	41
Total	**1,337**	**804**	**2,141**

INHIBITOR STATUS

Table 12 provides a description of the inhibitor status used in the ABDR. Table 13 shows the status of inhibitors for patients as at 30 June 2017. Inhibitors are immunoglobulins made by the body's immune system to react against replacement clotting factor proteins. This occurs when the immune system perceives the proteins as foreign or harmful to the body. When this happens, the inhibitors prevent the usual replacement factors (Factor VIII or IX) from working properly to stop bleeding.
Inhibitor detection is conducted using the Bethesda assay, with or without the Nijmegen modification (Verbruggen et al. 1995), and results are expressed in Bethesda units (BU)[5]. If the inhibitor titre is high (>5 BU/ml), factor replacement therapy is ineffective and bleeding persists. With low titre inhibitor (<5 BU/ml), haemostasis may be achieved with higher doses. Patients with severe Haemophilia A with high-titre inhibitors are most at risk for recurrent bleeds and chronic haemarthroses.

FEIBA and Recombinant Factor VIIa (brand name NovoSeven) are both used to treat patients that have developed inhibitors. In the setting of managing inhibitors for haemophilia, the drivers for clinical demand for FEIBA are similar to those for NovoSeven. Predicting or interpreting changing demand trends is not possible with any accuracy, as the product is only used in a small number of patients each year. Use patterns will vary from year to year and will not only depend on the number of patients treated, but their severity of disease, the potency of inhibitors, whether secondary prophylaxis is practiced, the number and severity of spontaneous bleeds, and the amount of elective surgery undertaken in this patient group.

[5] Bethesda units (BU) = a measure of inhibitor activity – the amount of inhibitor that inactivates 50% or 0.5 units of a coagulation factor during the incubation period

TABLE 12 - DESCRIPTION OF INHIBITOR STATUS USED IN ABDR

Inhibitor Event Type	Screening or Inhibitor Status
Initial Inhibitor Status	• *Inhibitor Testing Not Performed* - No inhibitor test has ever been performed for this patient • *Unknown* – Used if a patient has been tested but the results are unknown (i.e. transferred from overseas)
Screening Test Result	• *Negative* - Patient has a negative screening test result (then enter Inhibitor Status) • *Equivocal* - Not determined • *Present* - Patient has a positive screening test result
Screening Test (Result is Negative) or Inhibitor Test	• *Currently present – not on ITI* - Patient has an inhibitor but is not currently on ITI therapy • *Never Present* – No inhibitor detected for this test or previous tests performed • *Previously present – high responder (>5 BU/mL)* – Patient is negative this occasion but previously had a high inhibitor level to FVIII / FIX where the titre level is greater than 5 BU/mL • *Previously present – low responder (<5 BU/mL)* – Patient is negative this occasion but previously had a low inhibitor level to FVIII / FIX where the titre level less than 5 BU/mL • *On ITI* – Patient is on Immune Tolerance Induction (ITI) therapy or Tolerisation • *Unknown* – recorded as blank • *Present* – Patient has a positive inhibitor test result (Migrated data from previous version of ABDR and can no longer be used) • *Historic* - Patient does not currently have an inhibitor but has previously had one (Migrated data from previous version of ABDR and can no longer be used) • *Tolerised* - Patient has previously had an inhibitor in the past and been successfully tolerised (Migrated data from previous version of ABDR and can no longer be used) previous titre eg high or low responder – not known

TABLE 13 - PATIENT INHIBITOR STATUS NUMBERS

	30-Jun-16	30-Jun-17
HMA	**2,298**	**2,433**
Currently Present - Not on ITI	37	47
Equivocal	5	5
Historic	<5	<5
Inhibitor Testing Not Performed	846	848
Negative	6	9
Never Present	1,209	1,277
On ITI	17	24
Present	7	12
Previously Present - High Responder (>=5 BU/mL)	70	104
Previously Present - Low Responder (<5 BU/mL)	99	104
Tolerised	<5	<5
HMB	**547**	**565**
Currently Present - Not on ITI	<5	<5
Equivocal		<5
Inhibitor Testing Not Performed	278	268
Negative	<5	5
Never Present	259	283
On ITI	<5	<5
Previously Present - High Responder (>=5 BU/mL)	<5	<5
Previously Present - Low Responder (<5 BU/mL)	<5	<5
VWD	**2,081**	**2,166**
Currently Present - Not on ITI		<5
Inhibitor Testing Not Performed	2,035	2,094
Never Present	53	63
On ITI	<5	<5
Present	<5	<5
Previously Present - High Responder (>=5 BU/mL)	<5	<5
Previously Present - Low Responder (<5 BU/mL)		<5

* As noted in the section *Data quality issues* (p15) the data has been improved since previous ABDR Annual Reports. The figures presented here represent the most accurate data currently available. The census date for number of people in the registry is 30 June, the last day of the financial year.

INCIDENCE OF MAJOR DISORDERS

When we consider the incidence of bleeding disorders in global terms we see great variety in data and the reported prevalence. Table 14 details the incidence statistics from the World Federation of Hemophilia (WFH) global survey 2016 released in 2017.

TABLE 14 - INCIDENCE STATISTICS FROM WORLD FEDERATION OF HEMOPHILIA GLOBAL SURVEY 2016

Country	Population	HMA/HMB	VWD	OBD	HMA/HMB per 100,000	VWD per 100,000	OBD per 100,000	Factor VIII per capita	Factor IX per capita
Australia	24,127,159	2,576	2,092	722	10.68	8.67	2.99	6.69	1.09
New Zealand	4,692,700	447	230	68	9.53	4.90	1.45	5.41	0.80
UK	65,637,239	8,031	10,627	7,981	12.24	16.19	12.16	8.67	1.45
USA	323,127,513	16,949	11,118	5,147	5.25	3.44	1.59	9.53	1.66
Canada	36,286,425	3,893	4,437	1,932	10.73	12.23	5.32	8.04	1.51
France	66,896,109	7,205	2,055	864	10.77	3.07	1.29	7.31	1.15
Sweden *	9,798,871	1,068	1,512	513	10.90	15.43	5.24	8.97	1.79
Germany	82,667,685	4,358	3,930		5.27	4.75		7.08	0.84
South Africa	55,908,865	2,206	632	223	3.95	1.13	0.40	1.05	0.17
Japan	126,994,511	6,200	1,222	367	4.88	0.96	0.29	5.77	1.01

Abbreviations; OBD - other bleeding disorders; defined in the WFH Global Survey 2016 as "rare factor deficiencies, and inherited platelet disorders" (i.e. not HMA, HMB, VWD)
* Sweden's figures are from the 2015 Annual Survey updated for population, France's Factor VIII and Factor IX per capita figures are from the 2015 Annual Survey

In 2010, Stonebreaker *et al*[6] reported on HMA prevalence data for 106 countries from the WFH annual global surveys and the literature. They found that the reported HMA prevalence varied considerably among countries, even among the wealthiest of countries. Prevalence data reported from the WFH compared well with prevalence data from the literature, but patient registries (such as the ABDR) generally provided the highest quality prevalence data.

In 2011, the same group reported on the prevalence of Haemophilia B[7]. Data was reported for 105 countries from the WFH annual global surveys. They reported that the prevalence varied considerably among countries, even among the wealthiest of countries.

Prevalence data is extremely valuable information for the planning efforts of national healthcare agencies in setting priorities and allocating resources for the treatment of bleeding disorders.

[6] Stonebraker JS, Bolton-Maggs PHB, Soucie JM, Walker I, Brooker M. (2010). A study of variations in the reported hemophilia A prevalence around the world. Haemophilia 16(1): 20–32.
[7] Stonebraker JS, Bolton-Maggs PHB, Soucie JM, Walker I, Brooker M. (2011). A study of variations in the reported hemophilia B prevalence around the world. Haemophilia 18(3): 1-4.

Patient Treatment in 2016-17

The data in this section relates to patients who received treatment (products) during the 2016-17 financial year. Figure 10 and Figure 11 show data for the period 2012-13 to 2016-17, and chart the relative volume of therapeutic products issued according to patient severity. Patients with greater severity of bleeding disorders received more products.

PRODUCTS ISSUED TO PATIENTS

Figure 10 shows the proportion of hereditary HMA patients receiving treatment (1,009 patients in 2016-17) by severity. For the five financial years, around 60% (by volume) of all FVIII products issued were for patients with severe HMA.

Figure 11 shows the proportion of hereditary HMB patients receiving treatment (218 patients in 2016-17) by severity. For the five financial years, around 40% (by volume) of all FIX products issued were for patients with severe HMB. There are far fewer HMB patients in the registry than there are HMA patients.

Around 40% of the patients in the ABDR are diagnosed with HMA (see Table 3). In relative terms, HMA is the most important consideration for national supply planning, and the key factor is the issue of product to severe HMA patients.

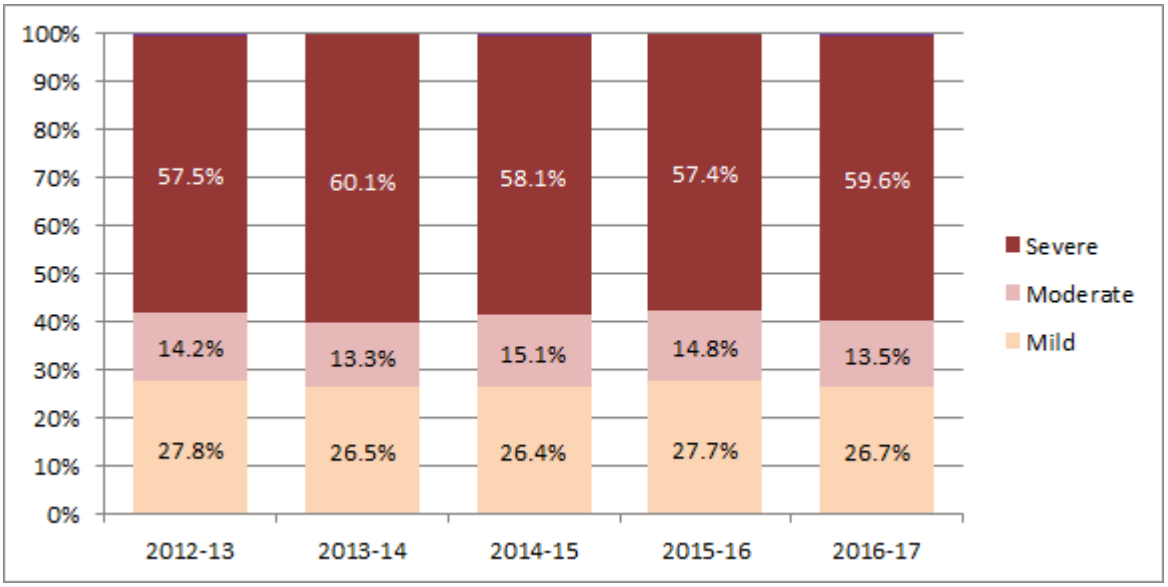

FIGURE 10 - PERCENTAGE OF PATIENTS RECEIVING PRODUCT BY SEVERITY FOR HMA - HEREDITARY BLEEDING DISORDERS
Note: A very small number of patients have a severity recorded as Not Applicable or Unknown. These are not shown in the above chart.

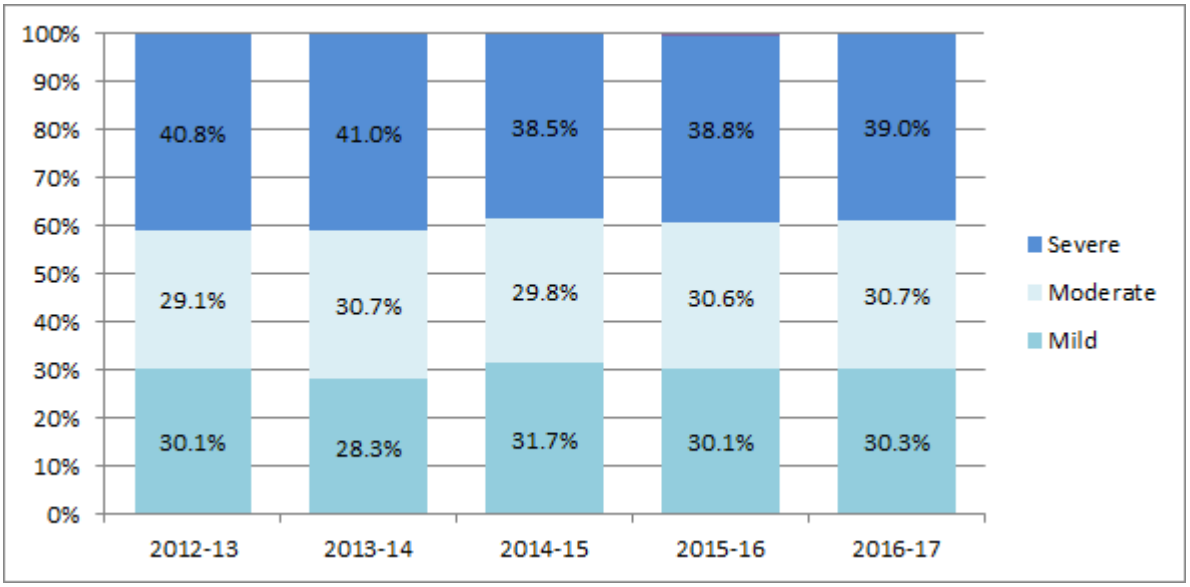

FIGURE 11 - PERCENTAGE OF PATIENTS RECEIVING PRODUCT BY SEVERITY FOR HMB - HEREDITARY BLEEDING DISORDERS
Note: Proportion of patients receiving product by severity for HmB – Acquired bleeding disorders are too small to present in graphical format. A very small number of patients have a severity recorded as Not Applicable or Unknown. These are not shown in the above chart.

Table 15, Table 16 and Table 17 detail the volume (IU) of product issued for HMA, HMB, VWD and other diagnosis patients in 2016-17. The volumes are subdivided by severity and treatment regimen as stated in the ABDR record. The largest and most important sectors are products for severe HMA patients for *on demand* and *prophylactic* treatment regimens. The volume issued for prophylactic treatment of severe HMA is the single greatest determining factor for supply planning.

TABLE 15 - IU OF PRODUCT ISSUED FOR HMA, HMB AND VWD PATIENTS, BY SEVERITY AND TREATMENT REGIMEN IN 2016-17 - HEREDITARY BLEEDING DISORDERS

	Mild	Moderate	Severe	Unknown**	Total**
HMA (IU FVIII Products)†	**5,359,250**	**15,435,750**	**135,886,760**	**20,000**	**156,701,760**
On Demand	4,446,500	5,487,000	14,344,500	20,000	24,298,000
Prophylaxis	807,000	9,877,000	115,528,002		126,212,002
Tolerisation			4,806,000		4,806,000
Unknown*	105,750	71,750	1,208,250		1,385,750
HMB (IU FIX Products)‡	**2,279,250**	**8,472,000**	**15,880,650**		**26,631,900**
On Demand	1,937,750	3,372,500	2,635,500		7,945,750
Prophylaxis	240,500	4,905,500	13,180,000		18,326,000
Tolerisation			54,000		54,000
Unknown*	101,000	194,000	11,150		306,150
VWD (IU FVIII Product) ++	**364,500**	**344,750**	**3,952,000**	**2,073,000**	**6,734,250**
On Demand	273,000	305,750	1,268,000	726,000	2,572,750
Prophylaxis	31,250		2,133,000	1,053,000	3,217,250
Tolerisation			543,000		543,000
Unknown*	60,250	39,000	8,000	294,000	401,250

† FVIII Products included are Advate, Biostate and Xyntha
‡ FIX Products included are BeneFIX, MonoFIX and Rixubis
++ FVIII Products include Advate and Biostate
* This represents a blank/not completed/empty field for the treatment regimen in the ABDR
** The total in this table combines the values for patients with mild, moderate and severe conditions. The severity of a patient's condition is not always known at initial presentation. This table includes product issues to patients with unknown severities.

TABLE 16 - IU OF PRODUCT ISSUED FOR HMA, HMB AND VWD PATIENTS, BY SEVERITY AND TREATMENT REGIMEN IN 2016-17 - ACQUIRED BLEEDING DISORDERS

	Mild	Moderate	Severe	Unknown**	Total**
HMA (IU FVIII Products)†			**10,000**	**45,000**	**55,000**
On Demand					
Unknown*			10,000	45,000	55,000
VWD (IU FVIII Product) ++			**9,000**	**333,000**	**342,000**
On Demand			9,000	187,000	196,000
Unknown*				146,000	146,000

† FVIII Products included are Advate, Benefix, Biostate and Xyntha
++ FVIII Products include Advate and Biostate
* This represents a blank/not completed/empty field for the treatment regimen in the ABDR
** The total in this table combines the values for patients with mild, moderate and severe conditions. The severity of a patient's condition is not always known at initial presentation. This table includes product issues to patients with unknown severities.

TABLE 17 - IU OF PRODUCTS ISSUED FOR OTHER PATIENTS, BY SEVERITY AND TREATMENT REGIMEN IN 2016-17 - OTHER DIAGNOSES

	Mild	Moderate	Severe	Unknown**	Total**
Other Factor Deficiency	**53,328**	**59,004**	**204,114**	**15,750**	**332,196**
On Demand	47,117	4,004	2,004	2,250	55,375
Prophylaxis	4,210	28,000	197,610	12,000	241,820
Unknown*	2,001	27,000	4,500	1,500	35,001
Other	**1,500**			**113,750**	**115,250**
On Demand	1,500				1,500
Prophylaxis				112,000	112,000
Unknown*				1,750	1,750

* This represents a blank/not completed/empty field for the treatment regimen in the ABDR
** The total in this table combines the values for patients with mild, moderate and severe conditions. The severity of a patient's condition is not always known at initial presentation. This table includes product issues to patients with unknown severities.

VOLUME (IU) OF PRODUCTS ISSUED FOR HMA AND HMB

Severe haemophilia requires lifelong treatment with expensive products. Clotting factor consumption is often expressed in IU/kg/year, and the ranges reported vary by population.[8,9] Figure 12 shows the clotting factor consumption of FVIII during 2016-17 for severe HMA patients on prophylaxis. There is a wide range of use across these age groups, which are not normally distributed. Median values for each age bracket are listed below. Note there are significant outliers which require further investigation.

Median IU/Kg/year	0-4 years	5-9 years	10-14 years	15-17 years	Adult
2016-17	5,253	4,411	4,175	2,649	3,274

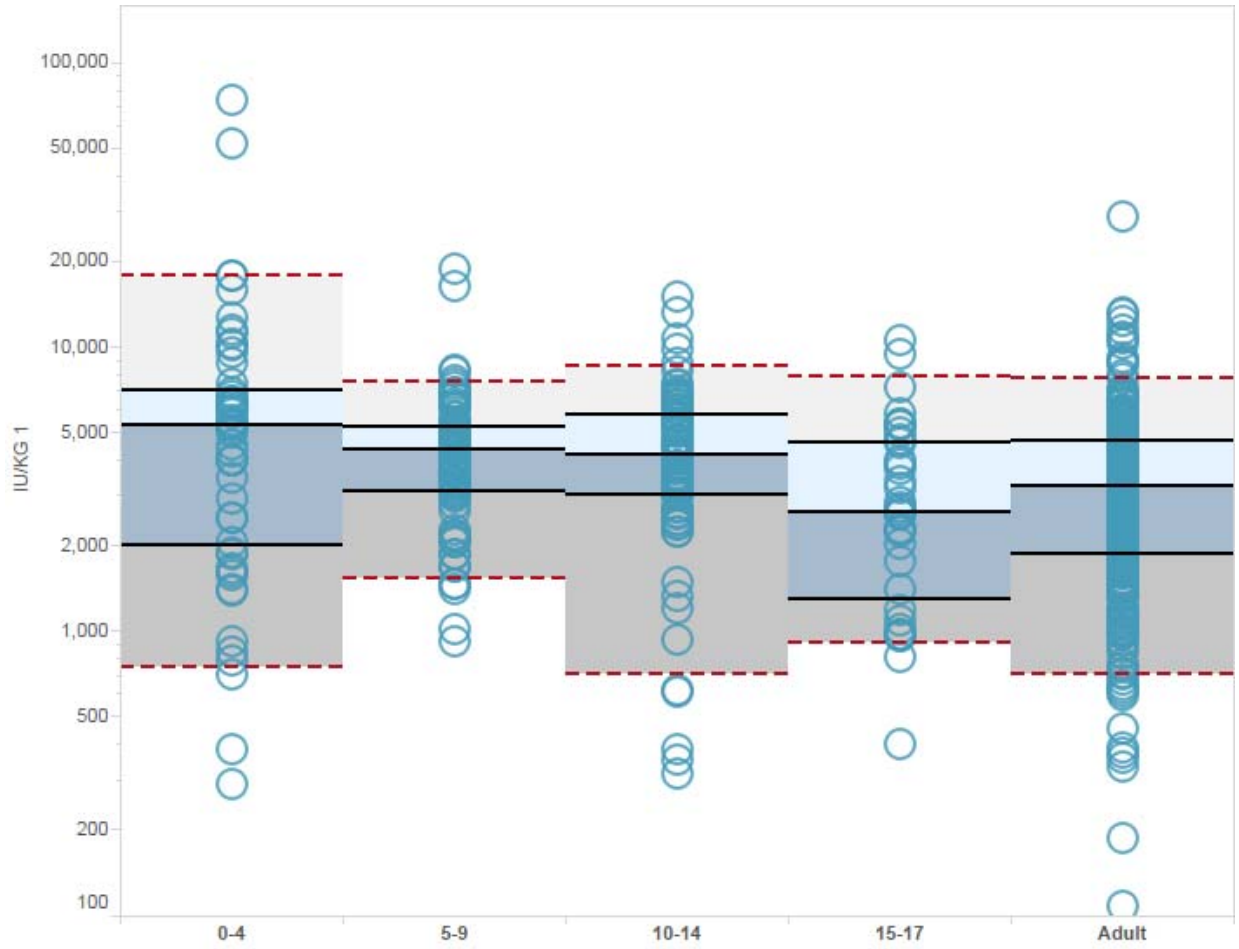

FIGURE 12 - FVIII PRODUCT USAGE (IU/KG/YEAR) IN SEVERE HMA PATIENTS ON PROPHYLAXIS

[8] Schramm W, Royal S, Kroner B, Berntorp E, Giangrande P, Ludlam CA, et al. (2002). Clinical outcomes and resource utilization associated with haemophilia care in Europe. Haemophilia 8(1): 33-43.

[9] Aledort LM, Haschmeyer RH, Pettersson H (1994) A longitudinal study of orthopaedic outcomes for severe factor-VIII-deficient haemophiliacs. The Orthopaedic Outcome Study Group. J Intern Med. 236(4): 391-399.

Figure 13 shows the clotting factor consumption of FVIII during 2016-17 for severe HMA patients on demand regimen. As in previous years there is a wide range of use across the paediatrics (includes adolescents) and adult age groups, which are not normally distributed.

Median IU/Kg/year	Paediatric	Adult
2016-17	477	1,165

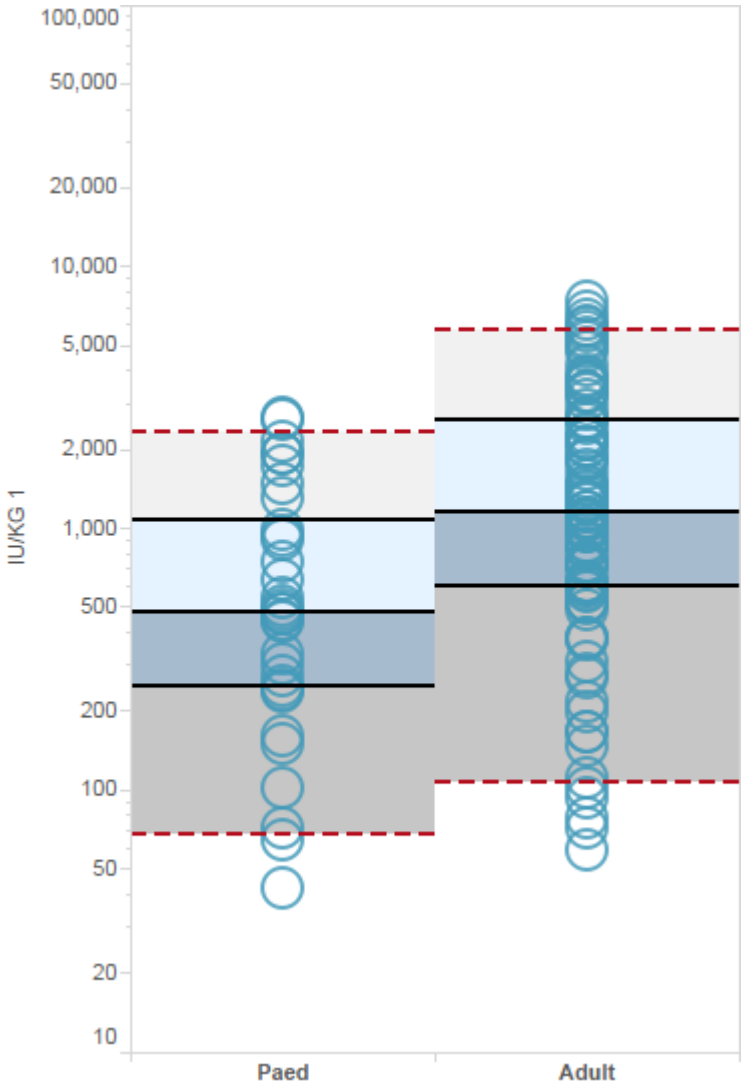

FIGURE 13 - FVIII PRODUCT USAGE (IU/KG/YEAR) IN SEVERE HMA PATIENTS ON DEMAND

Figure 14 shows the clotting factor consumption during 2016-17 for severe HMB patients on prophylaxis regimen.

Median IU/Kg/year	0-4 years	5-9 years	10-14 years	15-17 years	Adult
2016-17	3,885	4,397	2,905	2,358	3,255

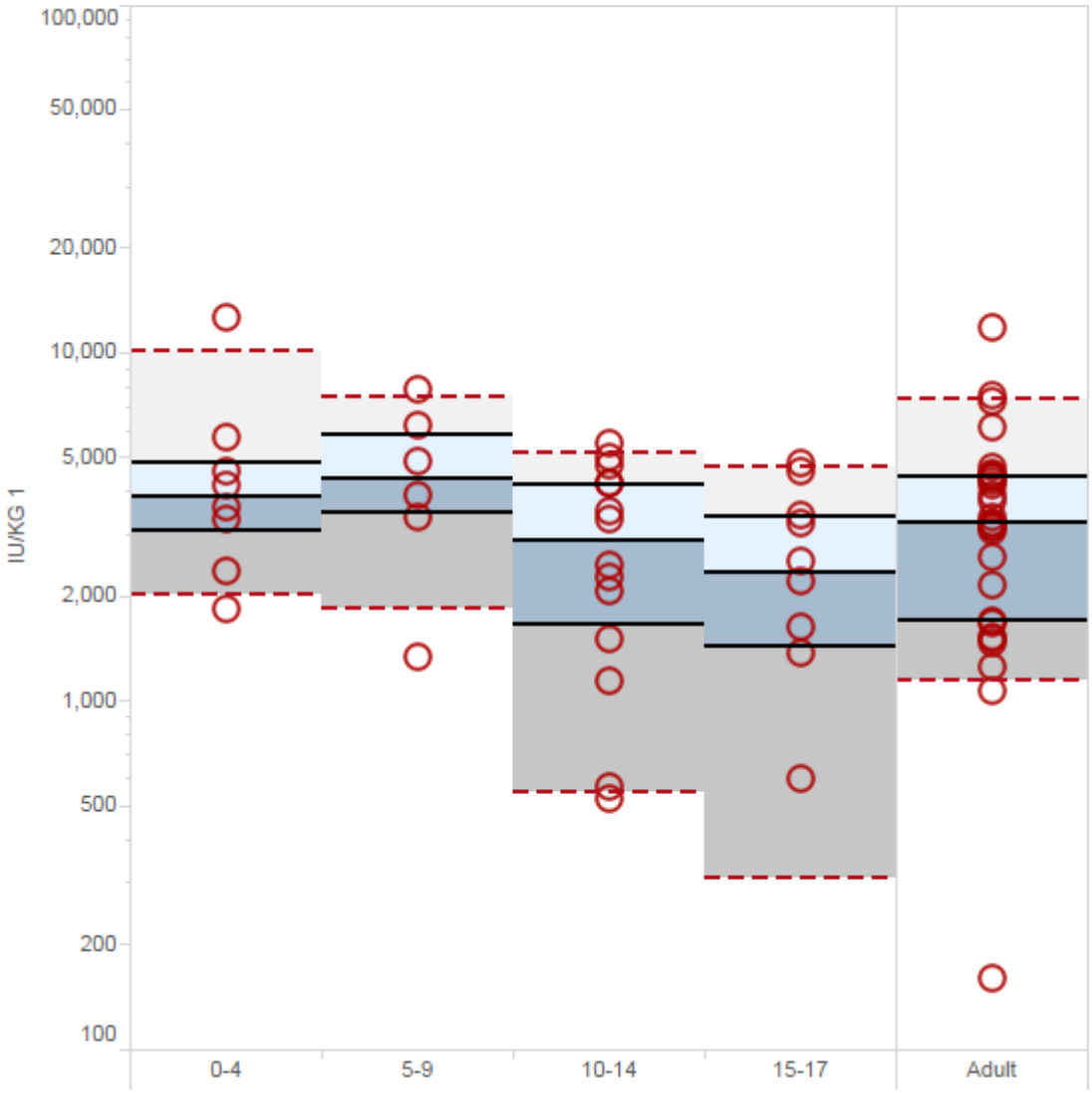

FIGURE 14 - FIX PRODUCT USAGE (IU/KG/YEAR) IN SEVERE HMB PATIENTS ON PROPHYLAXIS

Figure 15 shows the clotting factor consumption during 2016-17 for severe HMB patients on demand regimen.

Median IU/Kg/year	Paediatric	Adult
2016-17	333	826

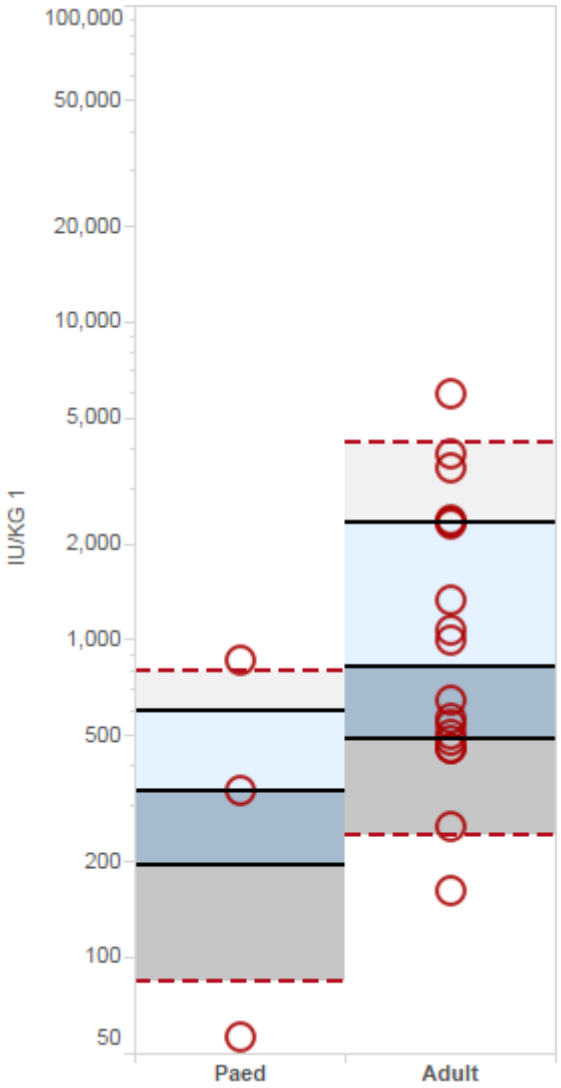

FIGURE 15 - FIX PRODUCT USAGE (IU/KG/YEAR) IN SEVERE HMB PATIENTS ON DEMAND

These figures are higher than some of those reported in the literature for adult patients, but reflect the shift in treatment practice towards regular prophylactic infusions to prevent bleeds, especially in children. Recent theoretical work allowed for the comparison of different treatment strategies, ranging from long-term on demand therapy to different prophylactic strategies.[10] In time the ABDR data should provide further insight into these issues.

[10] Fischer K, Pouw ME, Lewandowski D, Janssen MP, van den Berg HM, van Hout BA (2011). A modelling approach to evaluate long-term outcome of prophylactic and on demand treatment strategies for severe hemophilia A. Haematologica 96(5): 738-743.

VOLUME OF PRODUCTS ISSUED AND PATIENT COUNTS BY TREATMENT REGIMEN, SEVERITY, PRODUCT AND STATE

Table 18 and Table 19 show the volumes issued by product and treatment regimen, for hereditary HMA, HMB, VWD and other diagnoses. In both the adult and paediatric (includes adolescents) age groups the majority of product is issued for patients on prophylactic treatment regimens. The ABDR product issues data contains records where the treatment regimen is blank, unknown and not specified.

Table 20 and Table 21 show the number of patients and volumes issued by product and state. The totals are distinct counts of patients who received product. A patient may be counted more than once under each state as they may have received product from more than one state throughout the year. This applies to both hereditary and acquired HMA, HMB and VWD.

Table 22 shows the number of patients, volume issued and IU or mg/kg/year of products issued in 2016-17 by treatment regimen for acquired HMA, HMB and VWD.

Table 23 shows the number of patients and IUs issued by severity and regimen type for hereditary HMA and HMB. Values in this table exclude products issued to patients with unknown severity classification or treatment regimen, so they will vary from those figures shown in other parts of this report. Also, patients may receive more than one regimen type and may therefore be counted multiple times.

Table 24 shows the number of patients and volume of products issued by regimen type and product for hereditary HMA, HMB and VWD. Values in this table exclude products issued to patients with unknown treatment regimen, so they may vary from those figures shown in other parts of this report. Also, patients may receive more than one regimen type and may therefore be counted multiple times.

TABLE 18 - VOLUME OF PRODUCTS ISSUED IN 2016-17 BY TREATMENT REGIMEN - HEREDITARY BLEEDING DISORDERS

	Adult					Paediatric				
	On Demand	Prophylaxis	Tolerisation	Not specified	**Adult Total***	On Demand	Prophylaxis	Tolerisation	Not specified	**Paediatric Total***
HMA (IUs)	**23,536,510**	**82,579,994**	**195,000**	**1,015,250**	**107,326,754**	**1,387,000**	**46,545,002**	**4,969,508**	**370,500**	**53,272,010**
Advate	11,807,750	35,525,500	195,000	506,000	48,034,250	1,139,250	23,066,750	1,579,500	47,250	25,832,750
Biostate	1,106,500	3,264,500		12,500	4,383,500	31,250	4,778,500	2,558,008	37,500	7,405,258
FEIBA (Units)	624,500	220,000			844,500		1,045,500	358,500		1,404,000
**NovoSeven (mgs)	3,670	2,972			6,642	503	558	502		1,563
Prothrombinex (IUs)	0	729,500			729,500					
Trial Material	10	908,994			909,004	1,000	9,000			10,000
Xyntha	9,997,750	41,931,500		496,750	52,426,000	215,500	17,645,252	473,500	285,750	18,620,002
HMB (IUs)	**7,111,500**	**12,553,500**	**54,000**	**284,000**	**20,003,000**	**834,930**	**5,772,500**	**0**	**22,150**	**6,629,580**
BeneFIX	6,637,500	12,071,500		281,000	18,990,000	772,250	5,754,500		22,150	6,548,900
MonoFIX	30,000	38,000	54,000		122,000					
**NovoSeven (mgs)	234	121			355					
Rixubis	444,000	444,000		3,000	891,000	62,000	18,000			80,000
Trial Material						680				680
VWD (IUs)	**2,464,500**	**2,406,250**	**0**	**387,250**	**5,258,000**	**108,250**	**811,000**	**543,000**	**14,000**	**1,476,250**
Advate						2,000				2,000
Biostate	2,464,500	2,406,250		387,250	5,258,000	106,250	811,000	543,000	14,000	1,474,250
**NovoSeven (mgs)						26				26

* The total in this table combines the values for patients with mild, moderate and severe conditions. The severity of a patient's condition is not always known at initial presentation. This table includes product issues to patients with unknown/not specified treatment regimens. All products listed above are in IUs unless stated.
**IUs sums all the products except NovoSeven

TABLE 19 - VOLUME (IU) OF PRODUCTS ISSUED IN 2016-17 BY TREATMENT REGIMEN – OTHER DIAGNOSES

	Adult				Paediatric			
	On Demand	Prophylaxis	Not specified	Adult Total *	On Demand	Prophylaxis	Not specified	Paediatric Total *
Other Factor Deficiency	**50,775**	**165,650**	**3,501**	**219,926**	**4,600**	**76,170**	**31,500**	**112,270**
Factor X P Behring						2,420		2,420
Factor XI bpl	12,025	900	3,501	16,426	2,600			2,600
Fibrogammin	36,250	28,250		64,500	2,000	44,000	31,500	77,500
Fibrogammin P		12,500		12,500		9,750		9,750
**NovoSeven (mgs)	458	540	11	1,009	14	205		219
Prothrombinex - VF	2,500	124,000				20,000		20,000
Platelet Disorder	**32**			**32**	**30**		**1**	**31**
**NovoSeven (mgs)	32			32	30		1	31
Fibrinogen	**63**	**243**	**7**	**313**	**14**	**116**		**130**
Human Fibrinogen RiaSTAP (gms)	63	243	7	313	14	116		130
Other	**1,500**	**112,000**	**1,750**	**115,250**				
Biostate	1,500		1,750	3,250				
Ceprotin		112,000		112,000				

* The total in this table combines the values for patients with mild, moderate and severe conditions. The severity of a patient's condition is not always known at initial presentation. This table includes product issues to patients with unknown/not specified treatment regimens. All products listed above are in IUs unless stated.
**IUs sums all the products except NovoSeven

TABLE 20 - NUMBER OF PATIENTS FOR HEREDITARY HMA, HMB AND VWD BY STATE

	Number of Patients who received product during the year								
	ACT	NSW	NT	QLD	SA	TAS	VIC	WA	Total*
HMA									
Advate	10	188	5	147	88	11	100	43	**584**
Biostate		23		17	<5	<5	9	9	**62**
FEIBA		<5		<5		<5	5	<5	**16**
NovoSeven		5		7	5	<5	17	<5	**39**
Prothrombinex				<5					
Xyntha	<5	99	<5	47	23	12	111	62	**351**
HMB									
BeneFIX	<5	70	<5	59	16	<5	42	16	**202**
MonoFIX	<5	<5		<5				<5	
NovoSeven		<5					<5		
Rixubis		<5		<5	<5		<5	6	**13**
VWD									
Advate							<5		
Biostate	<5	52	<5	65	26	5	25	45	**221**
NovoSeven							<5		

* The Totals are distinct counts of Patients who received product and may be counted more than once under each state or across different states as they may have received more than one product or been treated in more than one state throughout the year.

TABLE 21 - VOLUME OF PRODUCT ISSUED FOR HEREDITARY HMA, HMB AND VWD BY STATE

	Volume of Product Issued through the year								
	ACT	**NSW**	**NT**	**QLD**	**SA**	**TAS**	**VIC**	**WA**	**Total***
HMA (IUs)	**1,185,750**	**53,653,758**	**692,500**	**38,982,000**	**15,719,500**	**4,543,250**	**28,196,252**	**16,849,750**	**159,822,760**
Advate	820,750	25,284,750	642,000	20,158,750	10,147,500	1,236,500	11,433,250	4,143,500	73,867,000
Biostate		5,015,758		5,984,250	7,000	89,500	476,250	261,000	11,833,758
FEIBA		495,500		929,000		196,000	652,000	64,000	2,336,500
**NovoSeven (mgs)		305		1,567	636	390	4,206	3,379	10,483
Prothrombinex				729,500					729,500
Xyntha	365,000	22,857,750	50,500	11,180,500	5,565,000	3,021,250	15,634,752	12,381,250	71,056,002
HMB (IUs)‡	**145,500**	**12,076,900**	**8,000**	**5,362,000**	**2,219,000**	**599,000**	**4,395,000**	**1,826,500**	**26,631,900**
BeneFIX	91,500	12,015,900	8,000	5,184,000	1,775,000	599,000	4,315,000	1,550,500	25,538,900
MonoFIX	54,000	58,000		4,000				6,000	122,000
**NovoSeven (mgs)		121					234		355
Rixubis		3,000		174,000	444,000		80,000	270,000	971,000
VWD (IUs)	**35,250**	**3,640,250**	**3,000**	**1,629,750**	**319,000**	**25,250**	**303,750**	**1,120,000**	**7,076,250**
Advate							2,000		2,000
Biostate	35,250	3,640,250	3,000	1,629,750	319,000	25,250	301,750	1,120,000	7,074,250
**NovoSeven (mgs)							26		26

* The total in this table combines the values for patients with mild, moderate and severe conditions. The severity of a patient's condition is not always known at initial presentation. This table includes product issues to patients with unknown/not specified treatment regimens. All products listed above are in IUs unless stated.
**IUs sums all the products except NovoSeven

TABLE 22 - VOLUME, PATIENT COUNTS AND IU OR MG/KG/YEAR OF PRODUCTS ISSUED IN 2016-17 BY TREATMENT REGIMEN - ACQUIRED

	Adult						
	On Demand	Prophylaxis	Tolerisation	Not specified	**Adult Total ***	**Patient Counts**	**IU or mg/kg/Year**
HMA (IUs)	**88,000**			**55,000**	**143,000**		**1,650**
Biostate				45,000	45,000	<5	503
FEIBA	88,000				88,000	<5	1,132
**NovoSeven (mgs)	441			1,837	2,278	8	15
Xyntha				10,000	10,000	<5	
VWD (IUs)	**196,000**			**146,000**	**342,000**		**2,736**
Biostate	196,000			146,000	342,000	10	2,736

* The total in this table combines the values for patients with mild, moderate and severe conditions. The severity of a patient's condition is not always known at initial presentation. This table includes product issues to patients with unknown/not specified treatment regimens. All products listed above are in IUs unless stated.

**IUs sums all the products except NovoSeven

TABLE 23 - IU VOLUME OF PRODUCT ISSUED AND PATIENT COUNTS FOR HEREDITARY HMA AND HMB BY SEVERITY AND REGIMEN TYPE

		Haemophilia A		Haemophilia B	
Severity*	**Regimen type****	**Total IUs**	**Number of patients**	**Total IUs**	**Number of patients**
Adult - Mild	On demand	4,191,750	192	1,578,500	49
	Prophylaxis	329,500	5	36,000	<5
Adult - Moderate	On demand	4,808,500	60	2,910,500	38
	Prophylaxis	6,756,000	27	3,972,000	13
Adult - Severe	On demand	13,891,760	95	2,622,500	18
	Prophylaxis	75,274,494	259	8,545,500	29
	Tolerisation	195,000	<5	54,000	<5
Adult - Total		**105,447,004**		**19,719,000**	
Paediatric - Mild	On demand	254,750	41	359,250	11
	Prophylaxis	477,500	6	204,500	<5
Paediatric - Moderate	On demand	678,500	28	462,000	11
	Prophylaxis	3,369,000	20	933,500	6
Paediatric - Severe	On demand	453,750	32	13,680	<5
	Prophylaxis	41,653,002	229	4,634,500	33
	Tolerisation	4,611,008	18		
Paediatric - Total		**51,497,510**		**6,607,430**	

* Values in this table exclude products issued to patients with unknown severity classification or treatment regimen, so they will vary from those figures shown previously.
**Patients may receive more than one regimen type and may therefore be counted multiple times.

TABLE 24 - VOLUME OF PRODUCT ISSUED AND PATIENT COUNTS FOR HEREDITARY HMA, HMB AND VWD BY REGIMEN TYPE AND PRODUCT

			Advate		BeneFIX		Biostate		FEIBA		MonoFIX - VF	
Bleeding Disorder	**Paediatric / Adult**	**Regimen type***	**Total IUs**	**Number of patients ******	**Total IUs**	**Number of patients ******	**Total IUs**	**Number of patients ******	**Total Units**	**Number of patients ******	**Total IUs**	**Number of patients ******
Haemophilia A	Adult	On demand	11,807,750	240			1,106,500	27	624,500	7		
		Prophylaxis	35,525,500	129			3,264,500	7	220,000	<5		
		Tolerisation	195,000	<5								
	Paediatric	On demand	1,139,250	83			31,250	5				
		Prophylaxis	23,066,750	146			4,778,500	17	1,045,500	6		
		Tolerisation	1,579,500	9			2,558,008	9	358,500	<5		
	Total		**73,313,250**				**11,738,758**		**2,248,500**			
Haemophilia B	Adult	On demand			6,637,500	97					30,000	<5
		Prophylaxis			12,071,500	41					38,000	<5
		Tolerisation									54,000	<5
	Paediatric	On demand			772,250	24						
		Prophylaxis			5,754,500	41						
	Total				**25,235,750**						**122,000**	
Von Willebrand Disease	Adult	On demand					2,464,500	125				
		Prophylaxis					2,406,250	14				
	Paediatric	On demand	2,000	<5			106,250	29				
		Prophylaxis					811,000	6				
		Tolerisation					543,000	<5				
	Total		**2,000**				**6,331,000**					

*Values in this table exclude products issued to patients with unknown treatment regimen, so they will vary from those figures shown previously.
**Patients may receive more than one regimen type and may therefore be counted multiple times.

TABLE 24 CONTINUED - VOLUME OF PRODUCT ISSUED AND PATIENT COUNTS FOR HEREDITARY HMA, HMB AND VWD BY REGIMEN TYPE AND PRODUCT

			NovoSeven		Prothrombinex - VF		Rixubis		Trial Material		Xyntha	
Bleeding Disorder	**Paediatric / Adult**	**Regimen type***	**Total mgs**	**Number of patients ******	**Total IUs**	**Number of patients ******	**Total IUs**	**Number of patients ******	**Total IUs**	**Number of patients ******	**Total IUs**	**Number of patients ******
Haemophilia A	Adult	On demand	3,670	14					10	<5	9,997,750	89
		Prophylaxis	2,972	<5	729,500	<5			908,994	7	41,931,500	154
		Tolerisation										
	Paediatric	On demand	503	7					1,000	<5	215,500	15
		Prophylaxis	558	8					9,000	<5	17,645,252	96
		Tolerisation	502	6							473,500	<5
	Total		**8,205**		**729,500**				**919,004**		**70,263,502**	
Haemophilia B	Adult	On demand	234	<5			444,000	8				
		Prophylaxis	121	<5			444,000	<5				
		Tolerisation										
	Paediatric	On demand					62,000	<5	680	<5		
		Prophylaxis					18,000	<5				
	Total		**355**				**968,000**		**680**			
Von Willebrand Disease	Adult	On demand										
		Prophylaxis										
	Paediatric	On demand	26	<5								
		Prophylaxis										
		Tolerisation										
	Total		**26**	**5**								

*Values in this table exclude products issued to patients with unknown treatment regimen, so they will vary from those figures shown previously.
**Patients may receive more than one regimen type and may therefore be counted multiple times. Patient totals are the total number of distinct patients, excluding patients which are counted multiple times, so may not match the individual values.

Appendix A Characteristics of Rare Clotting Factor Deficiencies

TABLE 25 - CHARACTERISTICS OF RARE CLOTTING FACTOR DEFICIENCIES

Missing Factor	Incidence*	Inheritance	Severity of Bleeding	Treatment
Factor I Afibrinogenemia Hypofibrinogenemia Dysfibrinogenemia	5 in 10 million not available 1 in 1 million	Autosomal recessive Recessive or dominant Recessive or dominant	Usually mild, except in afibrinogenemia	•Fibrinogen conc. (Not funded in Australia) •Cryoprecipitate •Fresh frozen plasma
Factor II	1 in 2 million	Autosomal recessive	Moderate to severe when factor levels are low; usually mild	•Prothrombin complex conc. •Fresh frozen plasma
Factor V	1 in 1 million	Autosomal recessive	Moderate to severe when factor levels are low; usually mild	•Fresh frozen plasma
Combined Factor V and Factor VIII	1 in 1 million†	Autosomal recessive‡	Usually mild	•Fresh frozen plasma •Factor VIII conc. •Desmopressin
Factor VII	1 in 500,000	Autosomal recessive	Severe when factor levels are low	•Recombinant Factor VIIa conc. •Factor VII conc. •Fresh frozen plasma
Factor X	1 in 1 million	Autosomal recessive	Moderate to severe when factor levels are low	•Prothrombin complex conc. •Fresh frozen plasma
Combined deficiency of vitamin K-dependent clotting factors	not available	Autosomal recessive	Usually mild, but a few families have reported very low levels and more severe symptoms	•Vitamin K •Prothrombin complex conc. •Fresh frozen plasma
Factor XI	1 in 100,000	Recessive or dominant	Mild to moderate when factor levels are low	•Factor XI concentrate •Antifibrinolytic drugs •Fibrin glue •Fresh frozen plasma
Factor XIII	1 in 3 million	Autosomal recessive	Moderate to severe when factor levels are low	•Factor XIII conc. •Cryoprecipitate •Fresh frozen plasma

Note: Australian Prothrombin Complex Concentrate is not used for FVII deficiency

* Estimates only

† 1 in 100,000 in some populations, including Israel, Iran, and Italy

‡ Very rarely, Factor VIII deficiency can be inherited separately from only one parent

Appendix B Haemophilia Treatment Centres

THE OBJECTIVES OF HTCS

Haemophilia Treatment Centres provide comprehensive care for people with haemophilia. Their roles include:

- Compilation and distribution of guidelines for best practice directed toward optimal care of patients with disorders of haemostasis
- Providing protocols for the accurate diagnosis of patients with bleeding disorders
- Providing protocols for the regular review of infectious disease markers in patients and their families
- The allocation and distribution of therapeutic blood and recombinant products together with advice regarding the use of blood and recombinant products, at a state and national level
- The establishment of review programs to assess outcomes of therapies
- Provision of regularly updated data to the national Haemophilia Registry (ABDR)
- Participation in basic and clinical research

OPERATING CONCEPT

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. One collaborative centre for each state and territory may suffice but this must include adult and paediatric type centres.

Haemophilia Centres provide:

- a single point accountability for the care of patients with bleeding disorders with responsibility for the coordination, allocation and distribution of therapeutic resources for the treatment of patients, i.e. coagulation products derived either from blood donors or recombinant technologies
- a clinical service by experienced staff for patients with bleeding disorders and their families at short notice at any time of the day or night
- organisation of home therapy programs by the centre or in collaboration with other haemophilia treatment facilities
- a counselling and advisory service for people with haemophilia and their families including genetic counselling and family planning
- specialist medical expertise, principally haematology, surgery (the surgeons would have to be accredited to the Haemophilia Centre) rheumatology, infectious diseases and dental services
- specialist allied health services to include physiotherapy, social work and podiatry
- a laboratory service able to carry out all investigations required for the accurate diagnosis of haemophilia and other inherited disorders of haemostasis and to have access, in association with other centres, to specialised testing facilities, for example gene typing
- a system of record for all investigations, treatments, allocation of therapeutic products and adverse reactions
- a capability to participate in research including clinical trials
- educational programs for medical staff, other personnel, patients and their families which promote care of patients with disorders of haemostasis

- an outreach service to isolated patients and treating medical services. The outreach service may include:-
    - A haemophilia treatment facility located in a hospital that does not provide all the specialist services
    - Designated supervising medical practitioner
- data management to facilitate the use of an information system database, such as the Australian Bleeding Disorders Registry, used in the clinical environment to aid in the capturing of data critical to HTC staff for the day to day management of people with bleeding disorders and for supply management and policy purposes.

All isolated patients (where care is managed in an outreach program) should be registered at, and be reviewed regularly by, a Haemophilia Treatment Centre which would arrange delivery of and monitor the supply of therapeutic coagulation products.

The HTC must maintain on-going dialogue with the client group in each state and territory. The role of State and Territory Governments is to designate 'Haemophilia Treatment Centres' and negotiate the funding of the HTC including the purchase of therapeutic blood and recombinant products for distribution within states (or regions) and territories. In some states committees have been established to consider and schedule elective surgery.

DATA QUALITY OF HTC DATA COLLECTIONS

The following organisations are represented at various HTCs nationally:

- Australian Haemophilia Nurses Group (AHNG)
- Australia/New Zealand Haemophilia Social Workers' and Counsellors' Group (ANZHSWCG)
- Australia/New Zealand Physiotherapist Group (ANZHPG)
- Haemophilia Foundation of Australia (HFA).

These member representatives have provided input into the initial design of the ABDR and continue to provide input from their respective areas of specialty.

The Data Managers at each HTC are members of the Data Managers' Group (DMG). DMG Co-Chairs are elected and coordinate teleconferences, between all Data Managers, on a regular basis. The DMG Co-Chairs also have the functionality of raising issues, to the NBA, on behalf of their group. AHCDO has a major role in providing support to ABDR Data Managers through the funded model for Data Managers.

The advantages of this model of Haemophilia Data Co-ordination are:

- Accurate and complete data entry
- Dedicated and focused data management
- Regular reporting and analysis of collated information
- New product initiation of unresolved haemophilia care related questions
- Clinical audit of current policies and monitoring of agreed national standards.

A number of ongoing data quality initiatives were first implemented in 2010-11, including:

- Regular teleconferences for ABDR DMG
- 'Advanced Search' functionality of the ABDR whereby Data Managers are able to extract information from the ABDR on an ad hoc basis
- Reviews of data definitions undertaken by DMG Co Chairs
- NBA financial support, through AHCDO funding, for HTC Data Managers
- The ABDR Update is a functional tool in the form of a Newsletter. This provides an update on issues such as changes to the ABDR and functionality enhancements. This update is a means of keeping all ABDR stakeholders informed.

Comprehensive automated and manual data cleansing and validation processes that occurred as part of the 4th Generation ABDR Redevelopment project released in August 2012 enhanced the ABDR data accuracy and consistency presented in this report. The 4th Generation ABDR was successfully implemented on 13 August 2012.

However, there are still some data quality issues that impact the data presented in this report. Some post migration tasks for Data Managers to clean the data include:

- Verify patients with more than one diagnosis
- Duplicate diagnoses to be deleted and Inhibitor Tests to be combined under the persisting diagnosis
- Verify severity ratings and treatment regiments for some patient records
- There are also a number of low level data verification activities.

LIST OF HTCS

TABLE 26 - HAEMOPHILIA TREATMENT CENTRES

Hospital	Haemophilia Treatment Centre	State
The Canberra Hospital	Haemophilia Clinic	ACT
Calvary Mater Newcastle	Haemophilia Treatment Centre	NSW
Royal Prince Alfred Hospital	Haemophilia Treatment Centre	NSW
Sydney Children's Hospital	Centre for Children's Cancer and Blood Disorders	NSW
The Children's Hospital at Westmead	Haemophilia Treatment Centre	NSW
Prince of Wales Hospital	Bleeding Disorders Clinic	NSW
Westmead Hospital	Bleeding Disorders Clinic	NSW
Royal Darwin Hospital	Haemophilia Treatment Centre	NT
Royal Brisbane and Women's Hospital	Queensland Haemophilia Centre	QLD
Lady Cilento Children's Hospital	Queensland Haemophilia Centre Child and Adolescent Service	QLD
Royal Adelaide Hospital	South Australia Haemophilia Treatment Centre	SA
Women's and Children's Hospital	South Australia Haemophilia Treatment Centre	SA
Royal Hobart Hospital	Tasmanian Haemophilia Treatment Centre	TAS
The Alfred Hospital	Ronald Sawyers Haemophilia Centre	VIC
Royal Children's Hospital	Henry Ekert Haemophilia Treatment Centre	VIC
Princess Margaret Hospital	Paediatric Haemophilia Centre	WA
Hollywood Private Hospital	Hollywood Hospital Haemophilia Treatment Centre	WA
Fiona Stanley Hospital	Adult Haemophilia Centre	WA

Appendix C National Supply of Products

It is the responsibility of the NBA to manage the national blood supply to ensure that healthcare providers have sustainable, reliable and efficient access to blood and blood products needed for patient care. The NBA ensures blood supply security by working with states and territories to determine and manage an annual supply plan and budget and negotiating and managing blood supply contracts and arrangements with local and overseas suppliers.

NATIONAL SUPPLY PLAN AND BUDGET

A key element of the NBA's role in ensuring security of supply is to develop, coordinate and monitor the annual national supply plan and budget, including obtaining annual approval from health ministers.

This is achieved by:

- developing a national estimate of product demand
- liaising with jurisdictions and stakeholders to refine the estimated demand for products
- collecting and distributing data on product issued and reporting variations to jurisdictions on the approved supply plan
- intensively managing products if they are in short supply.

Figure 16 illustrates the national supply by product category for 2016-17, and shows issues of clotting factor products was 14.4% ($156.3 million).

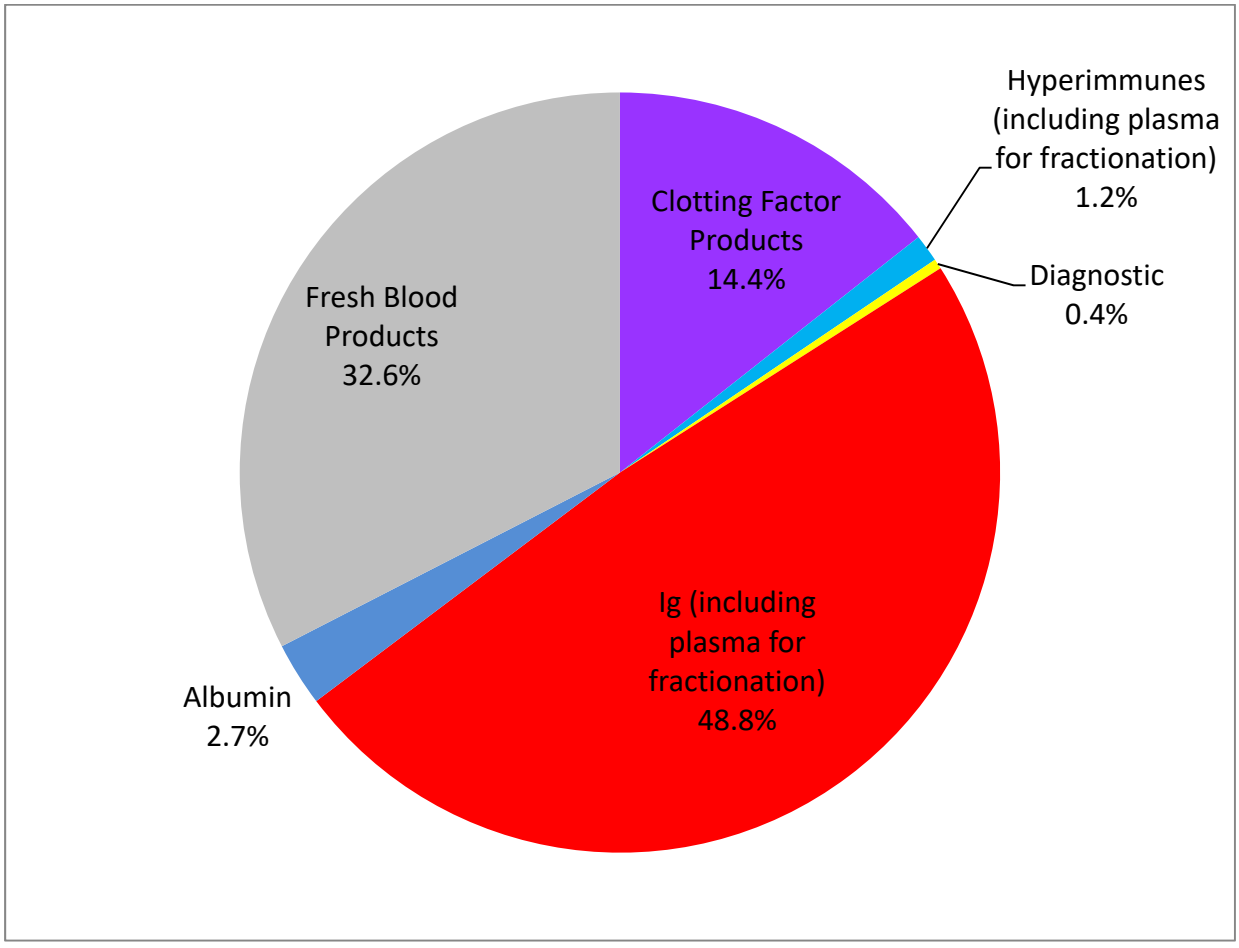

FIGURE 16 - NATIONAL ISSUES BY PRODUCT CATEGORY 2016-17

Note: Plasma for Fractionation costs paid to the Blood Service for collection has been attributed to IVIg and Hyperimmunes

Throughout 2016–17, products were supplied to meet clinical demand and supply risks were effectively managed. The approved budget for 2016–17 covering the supply and management of blood and blood products and services under contract was $1,153.17 million, comprising $614.63 million for fresh blood products and plasma collection and $519.04 million for plasma and recombinant products The remaining $19.49 million included items such as support for the publication of PBM Guidelines, maintenance of the Australian Haemophilia Centre Directors' Organisation (AHCDO) and administration of the Australian Bleeding Disorders Registry (ABDR).

ISSUES OF CLOTTING FACTORS

Issues of clotting factor products represent those deliveries from suppliers to all Australian Health Providers, including hospitals and Haemophilia Treatment Centres.

Figure 17 indicates that the demand for Factor VIII products in 2016-17 increased by 1.5 per cent when compared to 2015-16. The demand for recombinant Factor VIII decreased by 0.5 per cent over 2015-16. Plasma derived Factor VIII demand increased by 18.9 per cent. Patient participation in company clinical trials for recombinant Factor VIII products continues to contribute to the variability of year-to-year product growth.

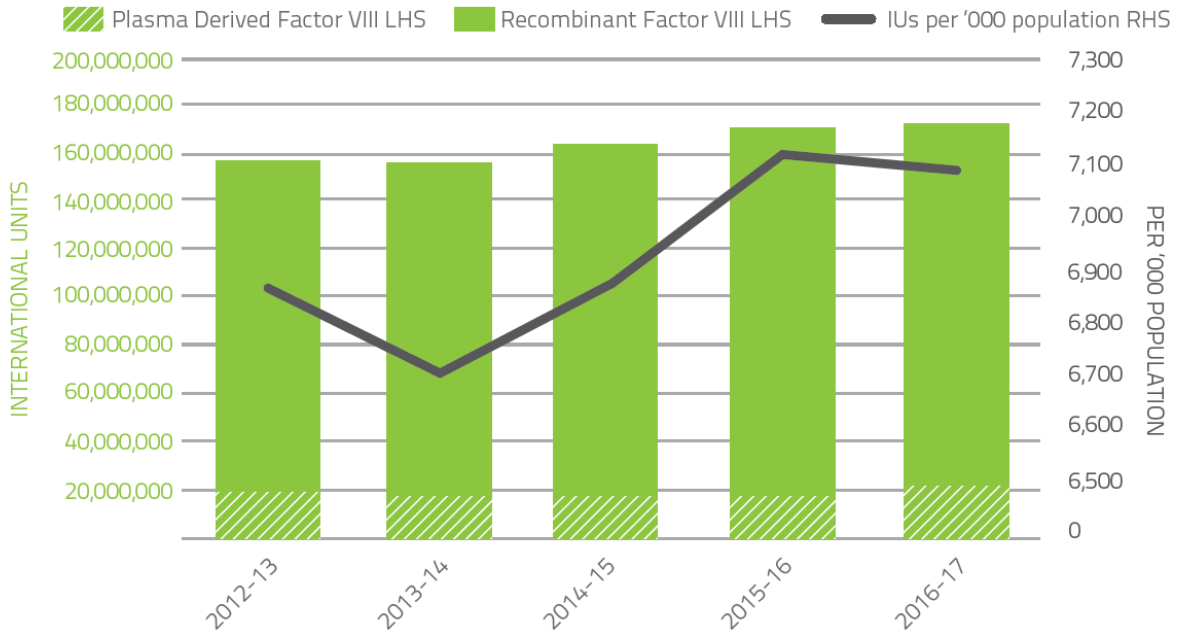

FIGURE 17 - ISSUES OF FACTOR VIII PRODUCTS, 2012-13 TO 2016-17 PER '000 POPULATION

Figure 18 indicates that demand for Factor IX products in 2016-17 increased by 1.6 per cent compared to 2015-16. Plasma derived Factor IX demand decreased by 15.6 per cent in 2016-17 due to a reduction in specific patient requirements. Demand for Recombinant Factor IX increased by 1.6 per cent in 2016-17. Patient participation in company clinical trials for recombinant Factor IX products continues to contribute to the variability of year-to-year product growth.

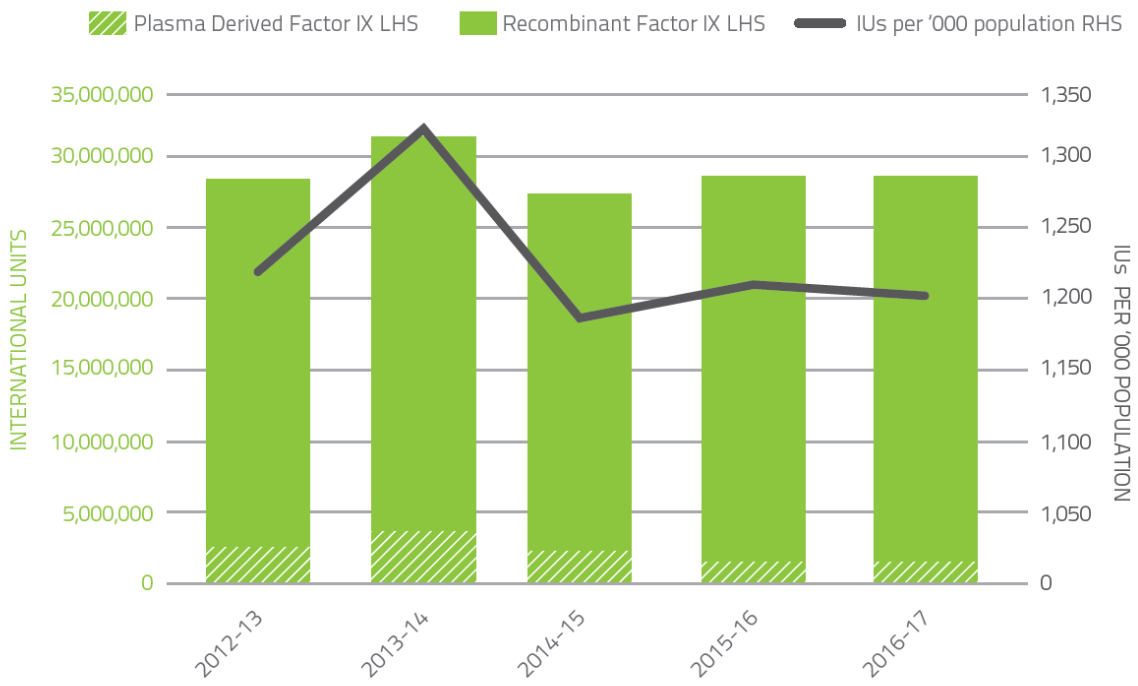

FIGURE 18 - ISSUES OF FACTOR IX PRODUCTS, 2012-13 TO 2016-17 PER '000 POPULATION

Figure 19 and Figure 20 show demand for Recombinant Factor VIIa decreased by 34.4 per cent and 45.2 per cent for FEIBA compared to 2015-16. Demand for Recombinant Factor VIIa and FEIBA can change significantly from year to year as a result of the variable needs of a small number of patients.

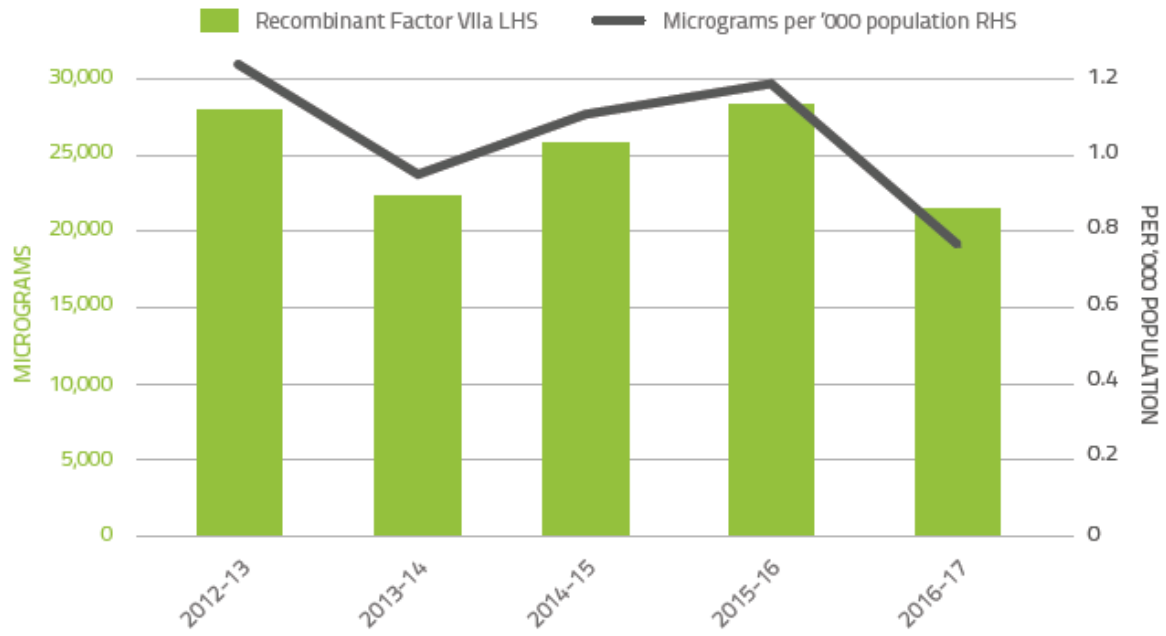

FIGURE 19 - ISSUES OF RECOMBINANT FACTOR VIIA PRODUCTS, 2012-13 TO 2016-17 PER '000 POPULATION

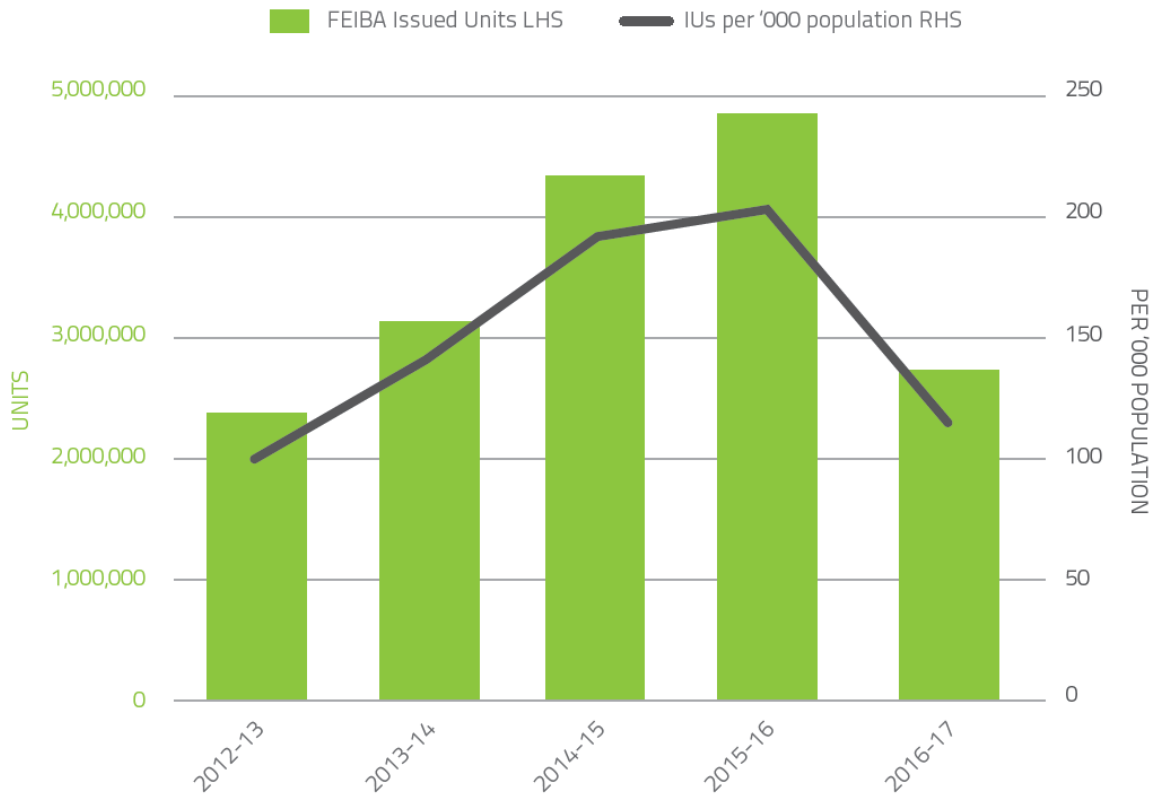

FIGURE 20 - ISSUES OF FEIBA, 2012-13 TO 2016-17 PER '000 POPULATION

CHRONOLOGY OF PRODUCTS SUPPLIED

Various products have been supplied through national arrangements. Since 2009-10 the following arrangements for the supply of products have occurred.

2011-12	Commenced supply of Kogenate
2012-13	Ceased supply of Recombinate and Advate
2014-15	Commenced supply of Advate and Rixubus
2015-16	Ceased supply of Factor VII Concentrate Commenced supply of RiaSTAP
2016-17	Ceased supply of Kogenate FS

Appendix D History of the ABDR

The ABDR was first established in 1988 using a 'Paradox' database at each Haemophilia Treatment Centre in Australia. The aims of the ABDR were to provide a clinical tool for improved management and national demographics of patients with haemophilia and other inherited bleeding disorders.

The first demographic Haemophilia registry was established by the Haemophilia Foundation of Australia (HFA), under auspices of the Medical Advisory Panel (MAP), in 1991 with an initial survey of Haemophilia Treatment Centres (HTC) established in Australia. Following on this initial survey the MAP took on responsibility for developing an ongoing registry and database associated with a University. The registry was based on a Paradox database with a comprehensive data collection including demographics, factor usage and bleed data. It was intended that software would be updated regularly by circulation of floppy disc updates and annual reports produced. Issues identified included no dedicated data entry staff, variability of IT support in institutions, unstable database requiring significant maintenance, time for data entry, and complexity. Unfortunately the registry did not progress.

In view of issues identified, in 2000 a new database using Access was developed with a single initial page collecting demographic and basic clinical data – 'medical registry'. Financial support was provided for data entry. Identification was by a code including multiple initials of name and date of birth as used by National HIV registries in Australia. Duplicate entries were identified and individual HTCs were asked to resolve differences based on activity of PWH and HTC. Initial demographics and diagnoses were provided for an annual report – initially to Department of Health and Aging, subsequently to National Blood Authority and presented at various forums. Data was vital for identifying product needs of the PWH community at a time of introduction of recombinant products. The ABDR achieved Quality Assurance status with the Commonwealth to assist with concerns about privacy. Ongoing issues identified were related to privacy, data collection (with one state not being involved) and coverage of the database, and it appeared total product usage was not complete.

The National Blood Authority (NBA) was established in 2003 and in 2007 it was proposed to develop the ABDR further with a web based clinical registry. Funding from the NBA allowed updating of the database. Widespread consultation was undertaken with HTCs to draw up specifications for a clinical database. The project was tendered to a commercial provider to enable 'third party custody' of data. The ABDR was to be capable of ordering products in 'real time' at HTCs. Governance of the development and operation was by a steering committee consisting of Australian Haemophilia Centre Directors Organisation (AHCDO), HFA, NBA and jurisdictional representatives.

An internet-based, standardised data entry database involving all states was introduced in December 2008. But the database highlighted significant resource and IT issues in HTCs and hospitals with slow response and significant variation of practice within HTCs. This hampered complete data collection with lack of feedback to HTCs, inability to provide ad hoc reporting for HTCs and nationally available reports. Annual reports only provided broad information with NBA providing figures for factor usage. The commercial provider was unable to address these issues.

Issues with existing software and support by the commercial provider necessitated a different approach. Further funding from the NBA enabled redevelopment of the ABDR using industry standard software in a 'Like for like' development. Data is now being held within NBA – requiring strict security protocols and separation of staff analysing data from those managing the system. Deficiencies of previous software were addressed with development of online reports to assist HTC management. Further expansion to include data from physiotherapy and social work, counselling pages and adverse events were developed. The 4th generation ABDR was released on August 13, 2012.

The ABDR has evolved with improvements in technology and feedback from stakeholders. In 2014 the ABDR entered a new phase with MyABDR – a smartphone application to enable patient input of bleed data and factor usage directly to the ABDR. The ABDR project has improved communication between HTCs for transfers and knowledge of 'travellers'.

The NBA delivered a number of updates and improvements to the Registry in 2014-15 to enhance the functionality and the user experience with MyABDR. The innovation delivered by the patient portal to ABDR, MyABDR, was recognised by the ICT industry through the receipt of two national iAwards merits in the Health and Government categories in August 2014 and through ITnews naming the NBA's Chief Information Officer as 'Healthcare CIO of the Year' in February 2015.

There has been further identification of PWH and opportunity for standardisation of terminology. There is wide involvement of other professionals – nursing, physiotherapy, social workers/counselling. Adverse event reporting has commenced. Benchmarking between HTCs is possible with improvement in data recoding enabling opportunities for improvement.

BENEFITS OF THE 4TH GENERATION ABDR

The NBA redeveloped the ABDR and deployed the 4th generation ABDR on August 13, 2012. It provides the following benefits:

- Single point of access for clinicians for treatment of patients
- Patient information relating to all clinical information associated with the treatment of haemophilia
- Information exchange between states and Haemophilia Treatment Centres
- National demographic information (age, gender etc.) of persons with bleeding disorders
- National data on inhibitor incidence and outcomes of treatment
- Allied health (physiotherapy and social work) monitoring and outcomes
- Recording of personal usage of factor replacement for clinical monitoring
- Data for forward planning and funding of factor concentrates on a national basis
- MyABDR is a secure app for smartphones and web site for people with bleeding disorders or parents/caregivers to record home treatments and bleeds. As an alternative, there is also a MyABDR paper-based treatment diary.

CURRENT POSITION OF THE DEVELOPMENT OF THE ABDR

Today the Australian Bleeding Disorders Registry and MYABDR are fully operational. The ABDR Steering committee continues to oversee the project.

The National Blood Authority's role continues around provision of resources to maintain ABDR operations and to ensure timely and accurate reporting from the ABDR through provision of support to Data Managers. Data Managers, funded and supported by AHCDO, are located at HTCs across Australia.

Appendix E Patient Registration Form

PATIENT REGISTRATION FORM

Clinician/Nurse to complete. **Fields marked with an *asterisk are mandatory**, optional fields are shaded grey.

☐ New patient ☐ Change of name ☐ Change of address

Patient

ABDR ID (Existing patients only) | Title | Australian Resident Status (Please tick) ☐ Australian Citizen/Permanent Resident ☐ Overseas Visitor ☐ Temporary Visa

*First name | Second name / Initial | *Family name

Known as / Alias | *Gender ☐ Male ☐ Female | *Date of birth / / | Previous family name/s

*Address
1
2
3
*Suburb
*State
*Postcode
Country

☐ Home phone ☐ Work phone ☐ Mobile

*Tick preferred contact method; at least one contact must be supplied.

☐ Home email ☐ Work email

Patient contact (mandatory if patient is under 18)

☐ Mother ☐ Father ☐ Spouse ☐ Grandparent ☐ Emergency ☐ Other Please specify: _____

Title | First name | Second name / Initial | Last name

Address
1
2
3
Suburb
State
Postcode
Country

☐ Home phone ☐ Work phone ☐ Mobile ☐ Home email ☐ Work email Tick best contact method

Best contact number or email address

Diagnosis See overleaf for # options

* Date diagnosed / /

*Bleeding disorder #

*Severity (Mild / Moderate / Severe / Unknown / Not applicable)

Baseline factor date / / (Where applicable)

Baseline factor level % (Where applicable)

*Weight in kilograms

Treatment See overleaf for + ^ options

*Regimen +

*Product name ^

*Total dose

*Frequency

Comments

Attending Physician and Clinic / Hospital Address Missing data will be requested by an ABDR Data Manager.

*Title | *First name | *Last name

*Name of Clinic / Hospital

*Best contact number or email address

*Address
1
2
3
*Suburb
*State
*Postcode

DECLARATION:

These details are true and correct at the time of completing this form. I have read the *ABDR User Conditions* and the *Clinicians FAQ on the ABDR* and I understand my role and obligations in populating the ABDR. The patient is also aware of the purpose for capturing their details in the ABDR and is aware of privacy and confidentiality protection arrangements as described overleaf. The ABDR Pamphlet has been given to patient.

Name _____ **Signature** _____ **Date** / /

When complete fax to your nearest Treatment Centre or Clinic – see www.ahodo.org.au for details.

Effective November 2016.

ABDR
Australian Bleeding Disorders Registry

ATTENTION: ABDR DATA MANAGER

#Bleeding Disorder

Factor II deficiency (Prothrombin)
Factor V deficiency
Factor VII deficiency
Factor VIII deficiency (Haemophilia A)
Factor IX deficiency (Haemophilia B)
Factor X deficiency
Factor XI deficiency
Factor XII deficiency
Factor XIII deficiency
Symptomatic Carrier Factor VIII deficiency (Haemophilia A)
Symptomatic Carrier Factor IX deficiency (Haemophilia B)
Asymptomatic Carrier Factor VIII deficiency (Haemophilia A)
Asymptomatic Carrier Factor IX deficiency (Haemophilia B)
von Willebrand Disease Type 1
von Willebrand Disease Type 2 – Uncharacterised
von Willebrand Disease Type 2A
von Willebrand Disease Type 2B
von Willebrand Disease Type 2M
von Willebrand Disease Type 2N
von Willebrand Disease Type 3
von Willebrand Disease – Uncharacterised
Fibrinogen – Afibrinogenemia
Fibrinogen – Hypofibrinogenemia
Fibrinogen – Dysfibrinogenemia
Fibrinogen dysfunction – Uncharacterised
Platelet – Glanzmann's thrombasthenia
Platelet – Bernard-Soulier
Platelet – May Hegglin
Platelet – Macrothrombocytopenias
Platelet – Storage pool (dense granule) deficiency
Platelet – Primary secretion defect
Platelet – Uncharacterised
Acquired factor VIII inhibitor (Acquired Haemophilia A)
Acquired von Willebrand's Disease
Vascular disorders – Ehlers Danlos Syndrome
Vascular disorders – Uncharacterised
Other, please specify

+Treatment Regimen

On demand
Prophylaxis
Tolerisation
Secondary Prophylaxis

^Product Name (Type)

Advate® (rFVIII)
BeneFIX® (rFIX)
Biostate® (pdFVIII)
Ceprotin® (Protein C)
Cryoprecipitate
DDAVP (Synthetic hormone)
Factor Eight Inhibitor Bypass Agent (FEIBA®) (Bypassing Agent)
Factor VII Concentrate® (pdFVII)
Factor XI bpl® (pdFXI)
Factor XI LFB Hemoleven® (pdFXI)
Fibrogammin P® (pdFXIII)
Fresh Frozen Plasma (FFP)
Haemocomplettan P 1g (pdFXIII)
Intravenous Immunoglobulin (IVIg)
Kogenate (rFVIII)
Kogenate FS – Blood Service (rFVIII)
MonoFIX® - VF (pdFIX)
NovoSeven® (rFVIIa)
NovoSeven RT® (rFVIIa)
Platelets
Prothrombinex™ - VF (pdPCC)
Recombinate® (rFVIII)
ReFacto® (rFVIII)
Xyntha (rFVIII)
Xyntha Dual Chamber (rFVIII)

ABDR
Australian Bleeding Disorders Registry

ATTENTION: ABDR DATA MANAGER

ABDR Patient Pamphlet

What is the ABDR? The Australian Bleeding Disorders Registry (**ABDR**) is a database that collects all clinical information related to the treatment of people with bleeding disorders, like an electronic medical file. This includes information about patient diagnosis, treatment details, hospital admissions and administrative information as well as details on ordering, supply and use of clotting factor products. Information is entered into the ABDR by staff at haemophilia treatment centres. The ABDR is managed by the National Blood Authority. The ABDR was first established in 1988 and has been upgraded many times with the latest significant upgrade in 2012.

Why do you need it? The ABDR provides your health care team and support staff with a record enabling them to monitor and manage your treatment over time to improve your quality of life. Depersonalised information available from the ABDR may be used by authorised organisations to understand and improve treatment for bleeding disorders. The ABDR also provides governments with information on total clotting factor product requirements to make sure there is enough available to meet the needs of all Australians with bleeding disorders.

What about privacy? Only the health care team and support staff involved in providing medical services to you have access to your personal information. Other authorised users only have access to limited, depersonalised and/or summary information where all identifying information is removed to protect your privacy.

Does information about me have to be included? A minimum amount of information about you is required to ensure the continuous supply of clotting factor product is available to meet your treatment needs.

Where can I get more information? Further information about the ABDR can be obtained from the Australian Haemophilia Centre Directors' Organisation (AHCDO) on (03) 9885 1777, email info@ahcdo.org.au or visit www.ahcdo.org.au

Endorsement from Haemophilia Foundation Australia

Haemophilia Foundation Australia supports the ABDR. It helps doctors and other treating health professionals to understand more about the care and treatment needs of people affected by bleeding disorders. The ABDR will assist and guide planning to ensure treatment product is available when it is needed. We are confident that the steps in place will mean accurate, reliable and confidential data is available and that no patient details can be identified outside haemophilia centres.

www.haemophilia.org.au

Endorsement from Australian Haemophilia Centre Directors' Organisation

The ABDR is a valuable tool that provides an overview of those affected with haemophilia and other bleeding disorders in Australia. Data from the ABDR is the best information available for clinicians to advise governments making policy decisions regarding treatment needs and product availability.

National statistics available through the ABDR will give AHCDO an overview of practise and allow opportunities for improvement. This data can be pooled to compare Australian treatment standards with international benchmarks. The ABDR will continue to provide the ability to assess quality of life and other important clinical questions arising across Australia.

AHCDO's partnership on this initiative with the National Blood Authority, Haemophilia Foundation Australia and other specialist health professional groups is vital to the pursuit of excellence in clinical treatment practices.

www.ahcdo.org.au

Copies of this pamphlet can be obtained by contacting the National Blood Authority at support@blood.gov.au or 13 000 BLOOD (13 000 25663)

Acronyms and glossary of terms

ACRONYMS

ABDR	Australian Bleeding Disorders Registry
AHCDO	Australian Haemophilia Centre Directors' Organisation
BU (BU/ml)	Bethesda unit (expressed as Bethesda units per millilitre)
DDAVP	Desmopressin (1-desamino-8-D-arginine vasopressin) a derivative of the antidiuretic hormone, used to treat patients with von Willebrand disease. It does not come under the national blood agreement funding arrangements and its use is often not recorded in the NBA's issues database.
FEIBA	Factor VIII Inhibitor Bypassing Activity
FVIIa / rFVIIa	Factor VIIa (seven 'a') / Recombinant Factor VIIa
FVIII / rFVIII	Factor VIII (eight) / Recombinant Factor VIII
HFA	Haemophilia Foundation Australia
HMA	Haemophilia A (Factor VIII deficiency)
HMB	Haemophilia B (Factor IX deficiency)
HTC	Haemophilia Treatment Centre – A specialist centre at certain hospitals where comprehensive care is undertaken for people with haemophilia. Non HTCs are other hospitals who are encouraged to work with HTCs in their region.
IDMS	The NBA's Integrated Data Management System
IU	International Units
MyABDR	A secure app for smartphones (Android and iOS) and a web site for people with bleeding disorders or parents/caregivers to record home treatments and bleeds.
NBA	National Blood Authority
OBD	Other bleeding disorders
PWH	People with Haemophilia
VWD	von Willebrand disease
WFH	World Federation of Hemophilia

GLOSSARY OF TERMS

bleeding disorders	Diseases that cause abnormal or exaggerated bleeding and poor blood clotting
blood products	Products manufactured from donated blood
fractionation	Blood plasma fractionation refers to the general processes of separating the various components of blood plasma

National Blood Authority
Australia