NATIONAL BLOOD AUTHORITY
AUSTRALIA

AUSTRALIAN BLEEDING DISORDERS REGISTRY

Annual Report 2013-14

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Australian Bleeding Disorders Registry (ABDR) Annual Report 2013-14 published by the National Blood Authority.

ISSN 1839-0811 (online version)

This report is available online at http://www.blood.gov.au/data-analysis-reporting

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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 Centre's (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 5,385 patients in the Australian Bleeding Disorders Registry (ABDR) in 2013-14
    - 2,181 patients with Haemophilia A (647 patients with severe Haemophilia A)
    - 530 patients with Haemophilia B (96 patients with severe Haemophilia B)
    - 1,912 patients with von Willebrand Disease
- 1,487 patients received product in 2013-14, 964 Haemophilia A patients, 204 Haemophilia B Patients, 242 von Willebrand Disease Patients and 77 other factor deficiency patients
- A total of 143,921,250 IU of recombinant Factor VIII products were used by Haemophilia A patients in 2013-14
    - Prophylactic use by severe Haemophilia A patients accounted for 93,406,250 IU, which was 64.9 per cent of the volume issued.
- A total of 28,055,000 IU of recombinant Factor IX products were used by Haemophilia B patients in 2013-14
    - Prophylactic use by severe Haemophilia B patients accounted for 11,666,500 IU, which was 41.6 per cent of the volume issued
- Demand for Factor VIII products decreased by 0.8 per cent when compared to 2012-13 (NBA Annual Report)
    - Recombinant FVIII decreased by 1.3 per cent (NBA Annual Report)
    - Plasma derived FVIII increased by 3.5 per cent due to additional requirements for immune tolerisation therapy (NBA Annual Report)
- Demand for Factor IX increased by 8.6 per cent compared to 2012-13 (NBA Annual Report)
    - Plasma derived FIX increased by 48.5 per cent due to specific patient requirements
    - Recombinant FIX increased 4.6 per cent largely as a result of newly diagnosed patients
    - Patients commencing or ceasing participation in company clinical trials also contributed to the variability of year-to-year growth rates for both FVIII and FIX products. (NBA Annual Report)
- A total of $201.8 million was expended on issued clotting factor products in 2013-14

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.

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 2,711 people with haemophilia A and B, 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 a protein in their blood called von Willebrand factor (VWF) that helps 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 1,947 people with VWD in the ABDR which will not reflect the numbers with symptomatic 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. Less is known about these disorders because they are diagnosed so rarely.

The World Federation of Hemophilia produced a summary Table 17 (Appendix A, p38) 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 anemia (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 fetus). 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

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).

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). In some patients, therapy is complicated when their body develops inhibitors that destroy the replacement clotting factors and other treatment is necessary.

[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 haemophilia, Haemophilia 19(1):e1-47.

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 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 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. A description of the aims and governance of HTCs is provided at Appendix B.

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.

MyABDR is 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 2013-14 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
- Ms Kim Stewart, NSW Health – Jurisdictional Blood Committee nominee
- Mr Michael Stone – National Blood Authority

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. Future development of the system will provide 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 a data analyst to use a Business Intelligence tool to store and access the de-identified data.

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 a data dictionary for users. Application of this data dictionary 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 are still some data quality issues that impact the data presented in this report and review of these issues continues to be addressed.

NEW ABDR SYSTEM

The 4th Generation ABDR was successfully implemented on 13 August 2012. Training for all Haemophilia Training Centres was provided in the week of the release. Feedback to date is that the next generation is already showing better 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. Continued work on the data integrity of the registry has been undertaken in 2013-14 and it is expected that further refinement will be provided in 2014-15.

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.

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.

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 2009-10 to 2013-14.

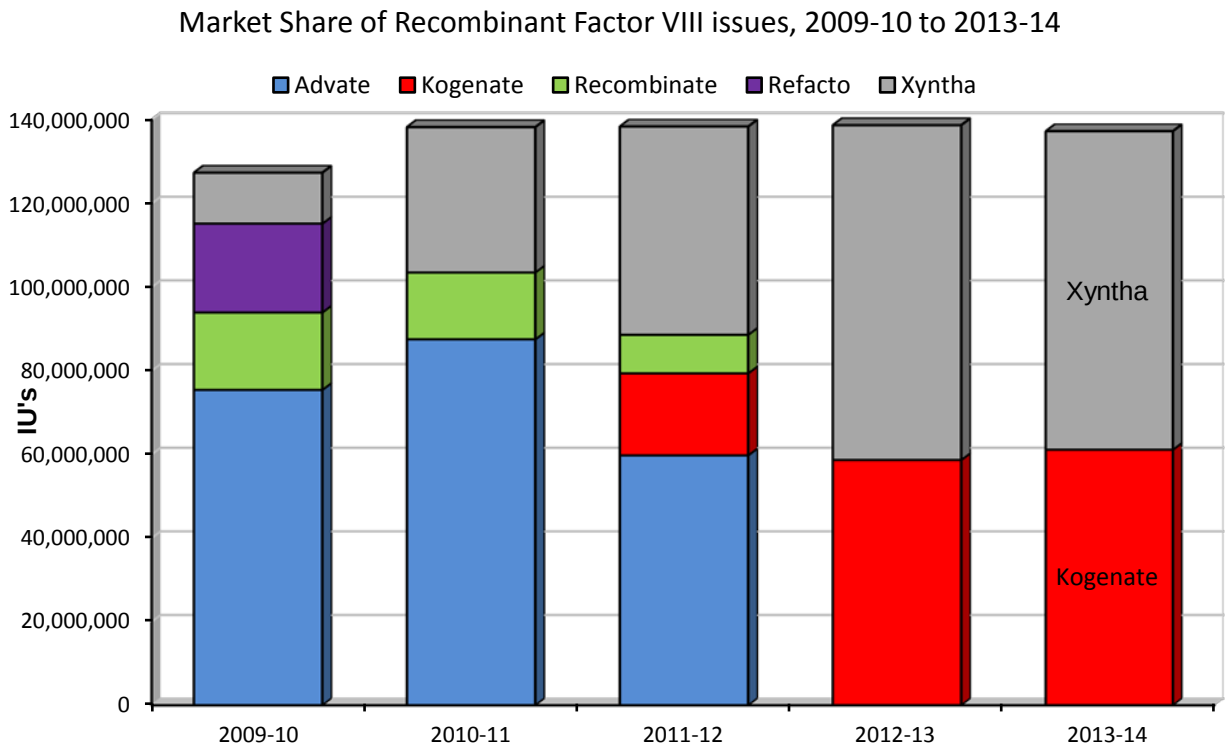

FIGURE 2 MARKET SHARE OF RECOMBINANT FVIII ISSUES 2009-10 TO 2013-14

Figure 2 illustrates the changes that occurred during 2011 to 2013, brought about by new national supply arrangements, with a transition away from Advate and Recombinate, an increase in the issue of Xyntha and the introduction of Kogenate. The new supply arrangements have provided high level national efficiencies without detriment to the patient population. The 2013-14 market share ratio of Xyntha to Kogenate is similar to 2012-13.

The most challenging aspect of HMA management is the development of FVIII inhibitors; previously untreated patients are at the highest risk for inhibitor formation. Currently, first, second and third generation rFVIII products are commercially available. Whereas first generation rFVIII concentrates (Kogenate and Recombinate) are stabilised with human albumin, second generation rFVIII products (ReFacto and Kogenate FS) contain sucrose instead of albumin in the final formulation. Finally, third generation rFVIII products (Advate and Xyntha) are manufactured without additional human or animal plasma proteins.

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 2009-10 to 2013-14. As noted in the section on *Data quality issues* (page 14) 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 2013-14 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 lists the number of people in the registry and the number treated by latest broad diagnosis for the years 2009-10 to 2013-14. An individual patient may have more than one diagnosis/disorder; in these cases they will be counted for each diagnosis for years, 2009-10 to 2011-12. Table 5 and Table 6 expand the data in Table 3 to show the number of people in the registry and the number treated by detailed diagnosis for the years 2009-10 to 2013-14.

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				
	2009-10	2010-11	2011-12	2012-13	2013-14	2009-10	2010-11	2011-12	2012-13	2013-14
HMA†	2,116	2,217	2,316	2,391	2,181	833	880	895	983	964
HMB†	501	527	544	564	530	183	191	189	205	204
Other‡	156	165	214	144	151	<5	<5	7	<5	10
Other Factor Deficiency	277	306	326	306	318	<5	26	35	35	43
Platelet Disorder	179	204	224	222	233	<5	9	<5	14	15
Vascular	8	9	9	7	9	-	-	-	-	
Fibrinogen				36	40	-	-	-	8	6
VWD	1,815	1,940	2,068	2,127	1,912	190	161	169	215	242
Unclassified				10	11	-	-	-	5	<5

* As noted in the section *Data quality issues* (p14) 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.
† Includes some female carriers who are symptomatic.
‡The ABDR allows for a diagnosis of 'Other' to be recorded for patients with rare and less prevalent disorders.

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 2013-14. 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 2013-14 there were 102 patients with two diagnoses and less than 5 patients with three diagnoses. Patients with two diagnoses reported in 2012-13 were 139. Of the 102 patients with two diagnoses, 6 received product during 2013-14.

TABLE 4 NUMBER OF PEOPLE IN THE REGISTRY AND TREATED BY BROAD DIAGNOSIS

Diagnosis	Patients Numbers in ABDR Registry*			Number who Received Product during the year
	Bleeding Disorder 1	Bleeding Disorder 2	Bleeding Disorder 3	
HMA†	2,181	38	<5	10
HMB†	530	4		<5
Other‡	151	<5		-
Other Factor Deficiency	318	18		<5
Platelet Disorder	231	8		
Vascular	9	-		
Fibrinogen	40	<5		
VWD	1,912	31	<5	<5
Unclassified	11			
Total	**5,385**	**102**	**<5**	**14**

* As noted in the section *Data quality issues* (p14) 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.
† Includes some female carriers who are symptomatic.
‡The ABDR allows for a diagnosis of 'Other' to be recorded for patients with rare and less prevalent disorders.

TABLE 5 NUMBER OF PEOPLE IN THE REGISTRY AND TREATED BY DETAILED DIAGNOSIS FOR HMA, HMB AND VWD

	Number in ABDR Registry*					Number who Received Product during the year				
	2009-10	2010-11	2011-12	2012-13	2013-14	2009-10	2010-11	2011-12	2012-13	2013-14
HMA										
Factor VIII Deficiency (HmA)	1,793	1,852	1,918	1,954	1,736	818	856	873	952	937
Asymptomatic Carrier Factor VIII Deficiency (HmA)	210	233	253	259	271	5	6	6	8	6
Symptomatic Carrier Factor VIII Deficiency (HmA)	82	95	103	117	132	8	13	11	14	15
Acquired Factor VIII Inhibitor (Acquired HmA)	33	40	47	61	42	<5	5	5	9	6
HMB										
Factor IX Deficiency (HmB)	422	435	449	460	423	171	175	176	197	198
Asymptomatic Carrier Factor IX Deficiency (HmB)	50	60	63	65	66	6	<5	<5	<5	<5
Symptomatic Carrier Factor IX Deficiency (HmB)	29	32	32	39	41	6	9	6	5	5
VWD†										
Acquired von Willebrand Factor Disease	11	12	15	16	16	<5	-	-	5	5
von Willebrand Disease – Uncharacterised	424	442	462	433	230	13	10	12	11	16
von Willebrand Disease Type 1	1,038	1,122	1,200	1,258	1,224	78	59	64	110	126
von Willebrand Disease Type 2 - Uncharacterised	93	99	110	110	95	9	16	10	11	10
von Willebrand Disease Type 2A	70	75	84	100	95	14	13	14	22	20
von Willebrand Disease Type 2B	48	48	53	53	54	12	9	7	10	7
von Willebrand Disease Type 2M	73	81	85	93	136	9	10	15	15	23
von Willebrand Disease Type 2N	17	20	21	20	22	<5	<5	<5	<5	5
von Willebrand Disease Type 3	45	45	47	44	40	29	31	27	28	30
Other					162					13

* As noted in the section *Data quality issues* (p14) 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.

TABLE 6 NUMBER OF PEOPLE IN THE REGISTRY AND TREATED BY DETAILED DIAGNOSIS FOR 'OTHER DISORDERS'

	Number in ABDR Registry*					Number who Received Product during the year				
	2009-10	2010-11	2011-12	2012-13	2013-14	2009-10	2010-11	2011-12	2012-13	2013-14
Other Factor Deficiency										
Factor V Deficiency	14	15	15	14	10	<5	<5	<5	<5	<5
Factor VII Deficiency	52	53	53	54	56	5	5	9	8	8
Factor X Deficiency	14	14	18	17	18	<5	<5	<5	<5	<5
Factor XI Deficiency	142	162	170	181	199	<5	5	7	11	20
Factor XII Deficiency†	22	24	25	23	16	-	-	-	<5	<5
Factor XIII Deficiency	17	18	18	17	19	7	8	9	9	9
Platelet Disorder										
Platelet - Bernard-Soulier	<5	<5	<5	<5	<5	-	-	-	<5	
Platelet - Glanzmann's Thrombasthenia	8	12	14	14	15	<5	<5	<5	<5	<5
Platelet - Macrothrombocytopenias	8	9	9	10	10	-	-	-	<5	
Platelet - May Hegglin	<5	<5	<5	<5	<5	-	<5	-	-	
Platelet - Primary Secretion Defect	<5	<5	<5	<5	5	-	-	-	-	<5
Platelet - Storage Pool (Dense Granule) Deficiency	17	23	29	27	34	-	-	<5	<5	<5
Platelet - Uncharacterised	139	153	164	161	162	<5	5	-	8	9
Vascular										
Vascular Disorders - Ehlers Danlos Syndrome	8	9	9	7	9	-	-	-	-	-
Fibrinogen										
Fibrinogen - Afibrinogenemia	<5	6	6	6	5	-	<5	<5	<5	<5
Fibrinogen - Dysfibrinogenemia	12	12	18	22	23	<5	<5	<5	<5	<5
Fibrinogen - Hypofibrinogenemia	<5	<5	5	6	11	-	-	-	-	-
Fibrinogen Dysfunction - Uncharacterised	<5	<5	<5	<5	<5	-	-	-	-	-

* As noted in the section *Data quality issues* (p14) 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) patients[2]. Table 7 and Table 8 detail the numbers of patients in the registry who received product (therapeutic treatment) during the period 2009-10 to 2013-14; by broad diagnosis and by severity.

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

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.

[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 the present report to better reflect the manner in which patients are treated in HTCs.

TABLE 7 NUMBER OF ADULTS IN THE REGISTRY AND TREATED BY BROAD DIAGNOSIS AND SEVERITY FOR HMA, HMB AND VWD

	Number in ABDR Registry*					Number who Received Product during the year				
Adult (aged 18 years and over)	**2009-10**	**2010-11**	**2011-12**	**2012-13**	**2013-14**	**2009-10**	**2010-11**	**2011-12**	**2012-13**	**2013-14**
HMA										
Mild	903	963	1,010	1,064	989	113	160	188	219	203
Moderate	186	191	199	190	153	70	86	82	89	81
Severe	428	444	466	504	391	253	272	280	328	336
HMB										
Mild	232	250	258	271	248	38	52	50	54	44
Moderate	82	88	91	94	88	29	31	40	45	48
Severe	56	58	61	69	56	37	40	39	47	48
VWD										
Mild	945	1,014	1,087	1,143	979	26	50	41	77	85
Moderate	187	205	227	229	234	22	34	32	43	51
Severe	106	113	120	128	121	25	38	32	46	48

* As noted in the section *Data quality issues* (p14) 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 8 NUMBER OF PAEDIATRIC AND ADOLESCENT IN THE REGISTRY AND TREATED BY BROAD DIAGNOSIS AND SEVERITY FOR HMA, HMB AND VWD

	Number in ABDR Registry*					Number who Received Product*				
Paediatric and Adolescent (aged less than 18 years)	**2009-10**	**2010-11**	**2011-12**	**2012-13**	**2013-14**	**2009-10**	**2010-11**	**2011-12**	**2012-13**	**2013-14**
HMA										
Mild	179	175	178	163	164	50	45	46	52	45
Moderate	68	68	65	64	68	43	50	50	49	49
Severe	246	258	258	249	256	238	241	258	236	245
HMB										
Mild	43	39	44	44	49	8	5	8	8	15
Moderate	25	24	22	21	21	14	18	16	13	13
Severe	42	43	41	37	40	40	37	39	37	36
VWD										
Mild	227	241	236	230	229	15	8	11	9	17
Moderate	41	45	46	46	47	5	6	5	6	5
Severe	32	30	30	29	30	13	15	12	10	13

* As noted in the section *Data quality issues* (p14) 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. Excludes those severities recorded as *Unknown, Not Applicable and Blank*.

BY AGE GROUP AND DETAILED DIAGNOSIS

In the next two tables, data is presented for Adult (aged 18 years and over) and Paediatric and Adolescent (aged under 18 years) patients[3]. Table 9 and Table 10 detail the numbers of patients in the registry who received product (therapeutic treatment) during the period 2009-10 to 2013-14; the numbers are subdivided by detailed diagnosis.

The data shows slight growth in the number of patients in the four year period to 2012-13 for HMA and HMB. In 2013-14 the results show variations, both increases and decreases. The most notable being the decrease in adult HMA and HMB patient. This pattern was evident for patients receiving product in 2013-14 due to implemented strategies to improve the 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, treatment plans, ages and dates of death. Continued work on the data integrity of the registry has been undertaken in 2013-14 and it is expected that further refinement will be provided in 2014-15.

[3] 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 the present report to better reflect the manner in which patients are treated in HTCs.

TABLE 9 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				
	2009-10	2010-11	2011-12	2012-13	2013-14	2009-10	2010-11	2011-12	2012-13	2013-14
HMA – Adult (aged 18 years and over)										
Factor VIII Deficiency (HmA)	1,313	1,365	1,430	1,489	1,264	504	532	538	614	600
Asymptomatic Carrier Factor VIII Deficiency (HmA)	206	229	249	253	261	5	6	6	8	6
Symptomatic Carrier Factor VIII Deficiency (HmA)	67	78	84	100	113	8	9	8	12	13
Acquired Factor VIII Inhibitor (Acquired HmA)	33	40	47	61	42	<5	5	6	9	6
HMA – Paediatric (aged less than 18 years)										
Factor VIII Deficiency (HmA)	480	487	488	465	472	333	339	357	338	337
Asymptomatic Carrier Factor VIII Deficiency (HmA)	<5	<5	<5	6	10	-	-	-	-	-
Symptomatic Carrier Factor VIII Deficiency (HmA)	15	17	19	17	19	-	<5	<5	<5	<5
Acquired Factor VIII Inhibitor (Acquired HmA)	-	-	-	-	-	-	-	-	-	-
HMB – Adult (aged 18 years and over)										
Factor IX Deficiency (HmB)	317	333	346	363	322	112	119	113	140	134
Asymptomatic Carrier Factor IX Deficiency (HmB)	47	56	59	61	60	5	<5	<5	<5	<5
Symptomatic Carrier Factor IX Deficiency (HmB)	25	29	29	34	35	6	9	6	<5	5
HMB – Paediatric (aged less than 18 years)										
Factor IX Deficiency (HmB)	105	102	103	97	101	62	59	63	57	64
Asymptomatic Carrier Factor IX Deficiency (HmB)	<5	<5	<5	<5	6	<5	-	-	-	-
Symptomatic Carrier Factor IX Deficiency (HmB)	<5	<5	<5	5	6	-	-	-	<5	-

* As noted in the section *Data quality issues* (p14) 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.

TABLE 10 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				
	2009-10	2010-11	2011-12	2012-13	2013-14	2009-10	2010-11	2011-12	2012-13	2013-14
VWD – Adult (aged 18 years and over)										
Acquired von Willebrand Factor Disease	11	12	15	16	16	<5	-	-	5	5
von Willebrand Disease - Uncharacterised	347	365	386	369	170	8	10	12	8	12
von Willebrand Disease Type 1	833	897	977	1,050	1,016	66	48	51	96	109
von Willebrand Disease Type 2 - Uncharacterised	62	67	75	78	65	6	10	<5	8	9
von Willebrand Disease Type 2A	57	61	69	79	72	14	11	14	20	16
von Willebrand Disease Type 2B	40	43	45	44	45	11	8	7	8	6
von Willebrand Disease Type 2M	52	59	64	68	107	6	9	13	14	20
von Willebrand Disease Type 2N	17	19	20	19	20	<5	<5	<5	<5	5
von Willebrand Disease Type 3	31	33	35	35	32	20	21	19	22	23
VWD – Paediatric (aged less than 18 years)										
von Willebrand Disease - Uncharacterised	77	77	76	64	60	5	<5	<5	<5	<5
von Willebrand Disease Type 1	205	225	223	208	208	13	11	14	14	17
von Willebrand Disease Type 2 - Uncharacterised	31	32	35	32	30	<5	6	6	<5	<5
von Willebrand Disease Type 2A	13	14	15	21	23	-	<5	<5	<5	<5
von Willebrand Disease Type 2B	8	5	8	9	9	<5	<5	-	<5	<5
von Willebrand Disease Type 2M	21	22	21	25	29	<5	<5	<5	<5	<5
von Willebrand Disease Type 2N	-	<5	<5	<5	<5	-	-	-	-	-
von Willebrand Disease Type 3	14	12	12	9	8	9	11	8	6	7

* As noted in the section *Data quality issues* (p14) 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 all 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 40 patients that have unknown or other locations (down from 117 in 2012-13)

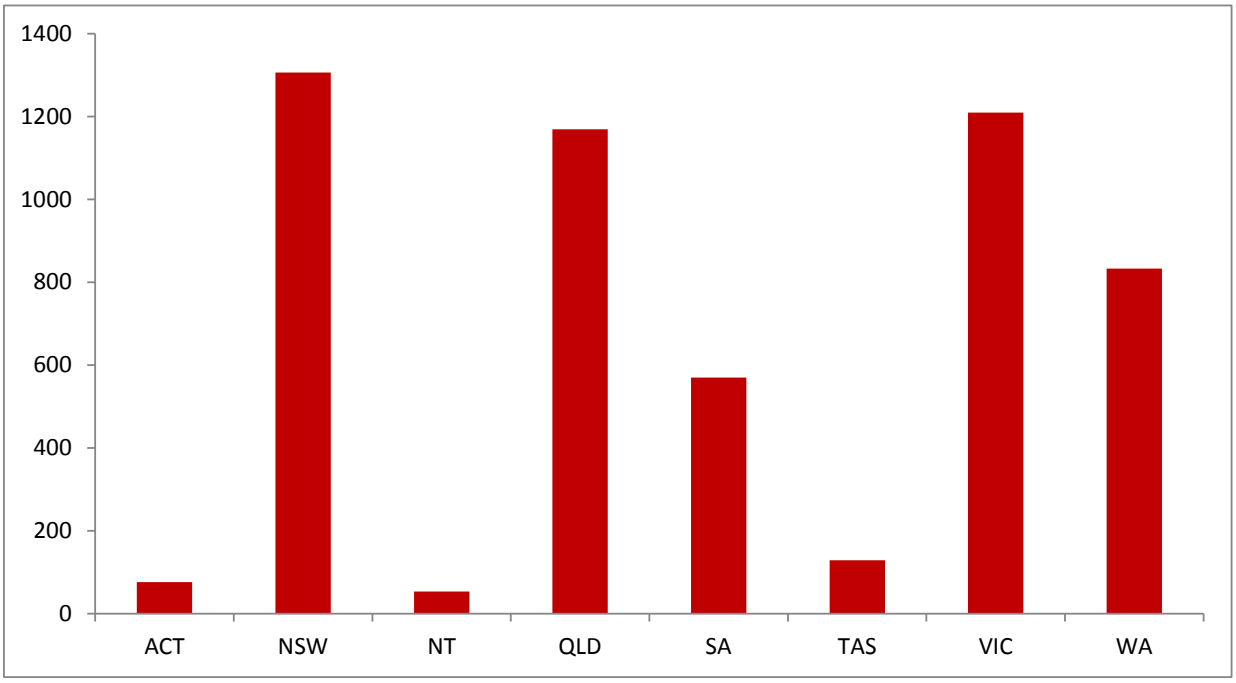

FIGURE 3 NUMBERS OF ACTIVE PEOPLE IN THE REGISTRY AS AT 30 JUNE 2014

Table 11 lists the numbers of patients with severe HMA and HMB by state and territory. Excluded from Table 11 are 7 patients that have unknown or other locations.

TABLE 11 NUMBERS OF PATIENTS WITH SEVERE HMA AND HMB BY LOCATION

State/Territory	HMA	HMB
ACT	14	<5
NSW	183	30
NT	6	-
QLD	153	18
SA	56	<5
TAS	15	<5
VIC	142	31
WA	71	10
Grand Total	**647**	**96**

BY SEX AND AGE DISTRIBUTION

The figures in this section present the sex and age distribution of patients in the ABDR in 2013-14, compared to the general Australian population[4]. The general population are represented by vertical bars and the ABDR patients are represented by line plots.

Figure 4 charts the distribution of male severe HMA patients against the male population. The disorder is genetically linked to a patient's sex, and usually affects males. There is a relatively lower number of older patients (from the age grouping of 45-49 years onwards). The life expectancy of HMA patients has improved dramatically[5] 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.

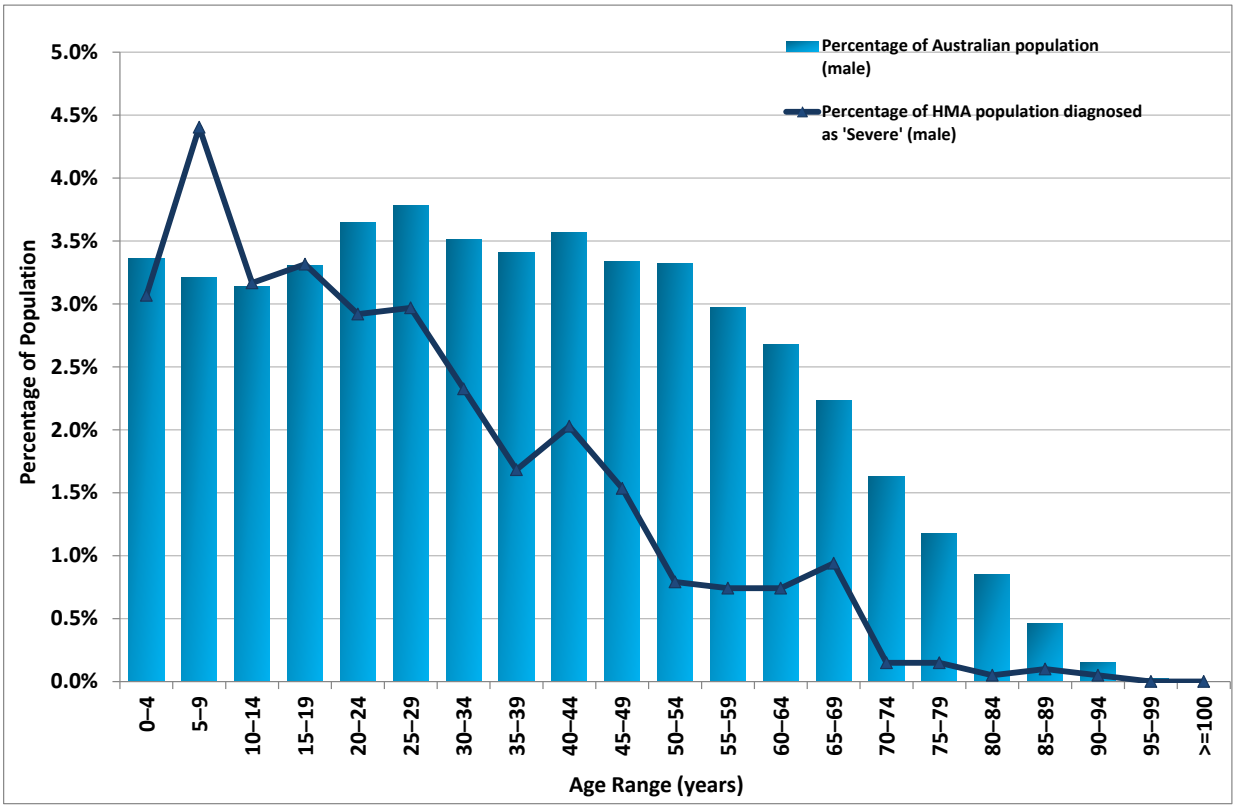

FIGURE 4 DISTRIBUTION OF MALE HMA SEVERE PATIENTS BY AGE IN 2013-14

[4] Australian Demographic Statistics, March 2014. Australian Bureau of Statistics, Cat. No. 31010. Released 25 September 2014 (Table 7)

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

Figure 5 charts the distribution of male severe HMB patients against the male population. As with HMA, HMB is also genetically linked to a patient's sex, 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 a low patient numbers (n=100) in this group and no conclusions should be drawn.

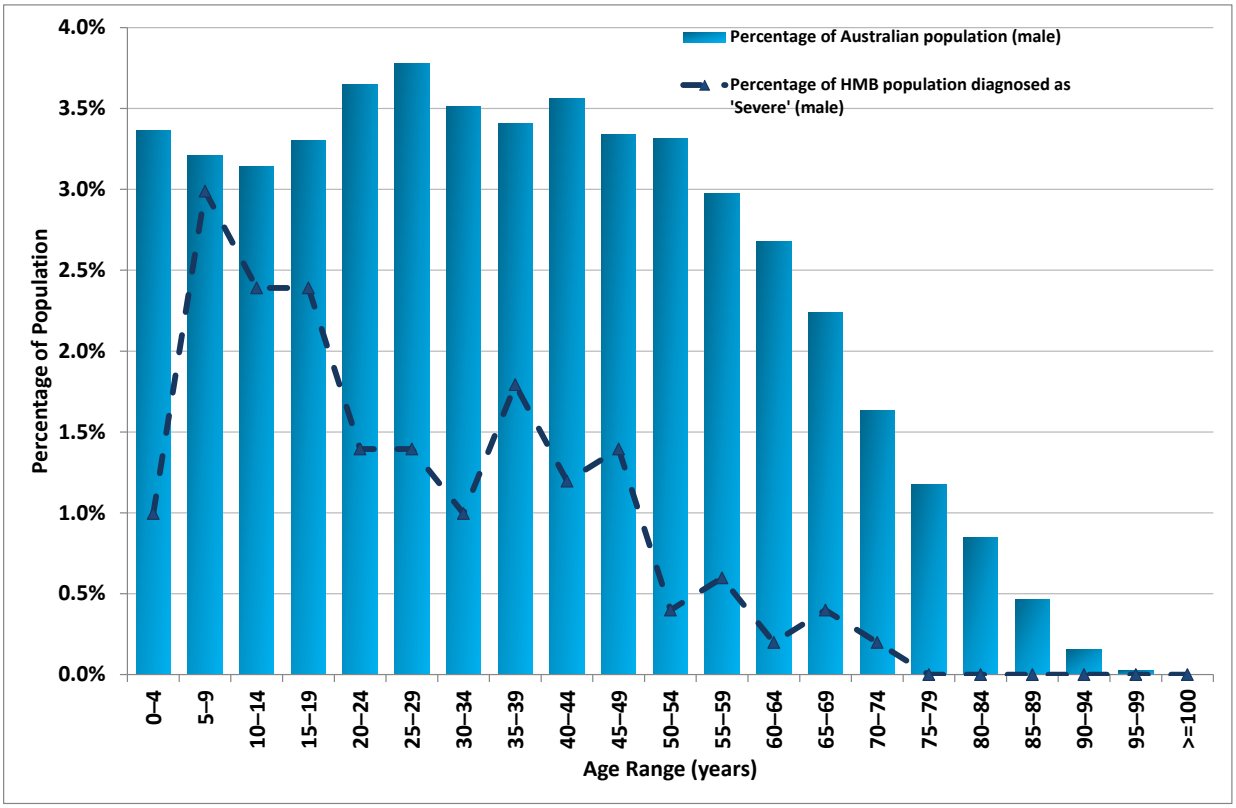

FIGURE 5 DISTRIBUTION OF MALE HMB SEVERE PATIENTS BY AGE IN 2013-14

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 2014. 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)[6]. 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.

TABLE 12 DESCRIPTION OF INHIBITOR STATUS USED IN ABDR

Inhibitor Event Type	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 or Inhibitor Test	• *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 –P*atient 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)

[6] 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

Inhibitor Event Type	Inhibitor Status
	• *Currently present – not on ITI* - Patient has an inhibitor but is not currently on ITI therapy • *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) • *Transient* - Patient developed an inhibitor and lasted for a short time (eg 1 week to many weeks) (Migrated data from previous version of ABDR and can no longer be used)

TABLE 13 PATIENT INHIBITOR STATUS NUMBERS

	30 June 2014
HMA	**2,181**
Historic	8
Inhibitor Testing Not Performed	868
Never Present	1,072
On ITI	26
Present	7
Previously Present - High Responder (>=5 BU/mL)	72
Previously Present - Low Responder (<5 BU/mL)	81
Tolerised	<5
Currently Present - Not on ITI	43
HMB	**530**
Inhibitor Testing Not Performed	310
Never Present	212
On ITI	<5
Previously Present - High Responder (>=5 BU/mL)	<5
Previously Present - Low Responder (<5 BU/mL)	<5
Currently Present - Not on ITI	<5
VWD	**1,912**
Inhibitor Testing Not Performed	1,869
Never Present	37
On ITI	<5
Previously Present - High Responder (>=5 BU/mL)	<5
Previously Present - Low Responder (<5 BU/mL)	<5
Currently Present – Not on ITI	<5

* As noted in the section *Data quality issues* (p14) 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 2012 released in December 2013.

TABLE 14 INCIDENCE STATISTICS FROM WORLD FEDERATION OF HAEMOPHILIA GLOBAL SURVEY 2012

Country	Population	HMA/HMB	VWD	OBD	HMA/HMB per100,000	VWD per 100,000	OBD per 100,000
Australia	**22,015,576**	**2,860**	**2,068**	**773**	**12.99**	**9.39**	**3.51**
New Zealand	4,327,944	421	195	31	9.73	4.51	0.72
UK	63,047,162	6,742	9,697	8,355	10.69	15.38	13.25
USA	313,847,465	18,628	8,035	1,796	5.94	2.56	0.57
Canada	34,300,083	3,657	3,963	1,693	10.66	11.55	4.94
France	65,630,692	6,035	1,496	413	9.20	2.28	0.63
Sweden	9,103,788	1,014	1,474	332	11.14	16.19	3.65
Germany	81,305,856	4,660	4,450	-	5.73	5.47	-
Spain	47,042,984	1,953	710	211	4.15	1.51	0.45
Netherlands	16,730,632	1,210	2,500	46	7.23	14.94	0.27

Abbreviations; OBD - other bleeding disorders; defined in the WFH Global Survey 2012 as "rare factor deficiencies, and inherited platelet disorders" (i.e. not HMA, HMB, VWD)

In 2010, Stonebreaker *et al*[7] reported on 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[8]. 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.

Table 15 details the incidence in 2013-14 of HMA, HMB and VWD per 100,000 people in Australia by broad diagnosis and severity.

[7] 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.
[8] 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.

TABLE 15 INCIDENCE OF HMA, HMB AND VWD PER 100,000 IN AUSTRALIA BY BROAD DIAGNOSIS AND SEVERITY

	Male					Female					Persons				
	2009-10	2010-11	2011-12	2012-13	2013-14	2009-10	2010-11	2011-12	2012-13	2013-14	2009-10	2010-11	2011-12	2012-13	2013-14
HMA	**16.5**	**16.4**	**16.2**	**17.2**	**15.4**	**2.7**	**2.7**	**2.7**	**3.5**	**3.8**	**9.6**	**9.5**	**9.4**	**10.3**	**9.6**
Mild	7.7	7.6	7.5	8.5	7.9	1.7	1.7	1.7	2.1	2.3	4.7	4.6	4.6	5.3	5.1
Moderate	2.4	2.5	2.4	2.2	1.9	0.0	0.0	0.0	0.1	0.1	1.2	1.2	1.2	1.1	1.0
Severe	6.1	6.0	5.9	6.3	5.6	0.1	0.1	0.1	0.2	0.2	3.1	3.1	3.0	3.3	2.8
HMB	**3.8**	**3.7**	**3.7**	**3.9**	**3.7**	**0.8**	**0.8**	**0.7**	**1.0**	**1.0**	**2.2**	**2.2**	**2.2**	**2.4**	**2.3**
Mild	1.9	1.8	1.8	2.0	1.9	0.5	0.5	0.5	0.7	0.7	1.2	1.2	1.2	1.4	1.3
Moderate	0.9	0.9	0.9	1.0	0.9	0.0	0.0	0.0	0.0	0.0	0.5	0.5	0.5	0.5	0.5
Severe	0.9	0.9	0.9	0.9	0.8	0.0	0.0	0.0	0.0	0.0	0.4	0.4	0.4	0.5	0.4
VWD	**7.3**	**7.3**	**7.2**	**7.6**	**6.7**	**9.4**	**9.4**	**9.3**	**10.8**	**10.1**	**8.4**	**8.3**	**8.2**	**9.2**	**8.4**
Mild	4.5	4.5	4.4	4.5	3.8	6.5	6.5	6.3	7.3	6.8	5.5	5.5	5.4	5.9	5.3
Moderate	1.1	1.1	1.1	1.1	1.1	1.0	1.0	1.0	1.3	1.4	1.1	1.1	1.1	1.2	1.2
Severe	0.7	0.7	0.7	0.8	0.7	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.7	0.7

Patient Treatment in 2013-14

The data in this section relates to patients who received treatment (products) during the 2013-14 financial year. Figure 6 and Figure 7 show data for the period 2009-10 to 2013-14, 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

Figure 6 shows the proportion of HMA patients receiving treatment (964 patients) by severity. For the five financial years, around 60% (by volume) of all FVIII products issued were for patients with severe HMA.

Figure 7 shows the proportion of HMB patients receiving treatment (204 patients) 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.

About half 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.

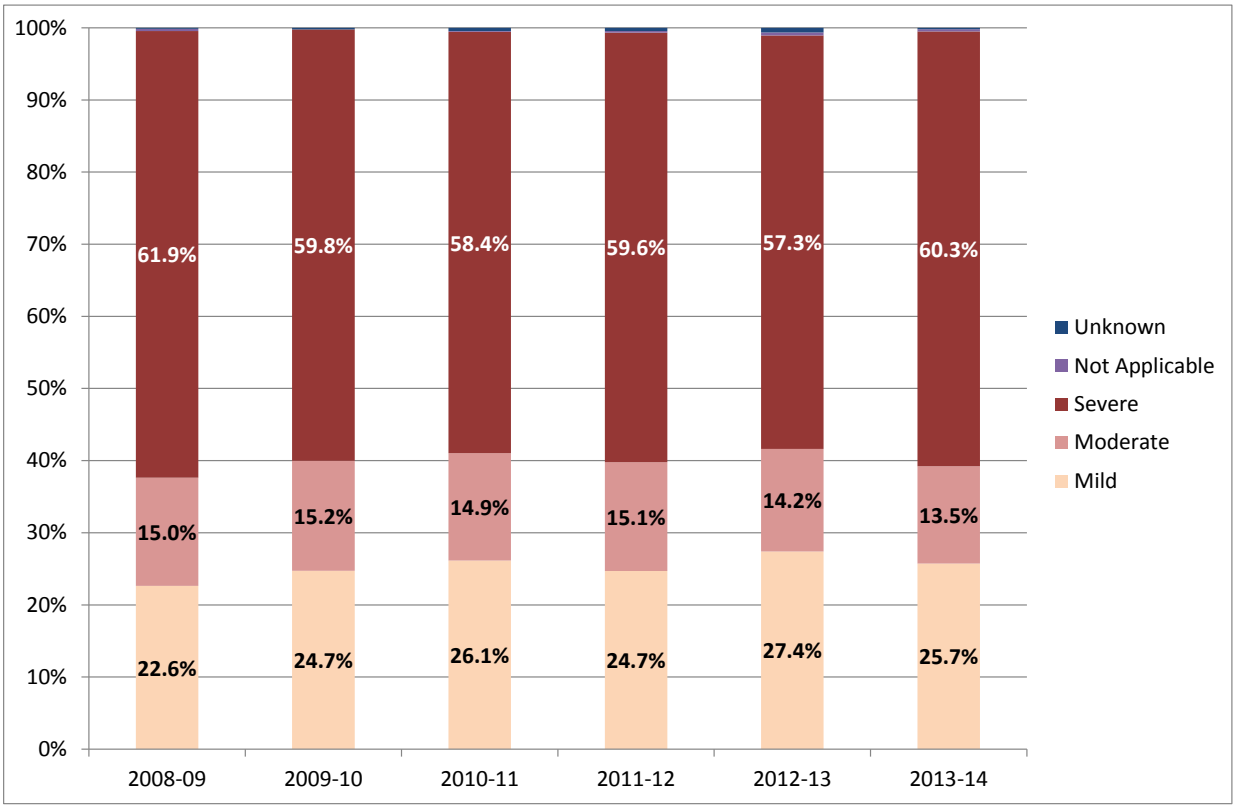

FIGURE 6 PROPORTION OF PATIENTS RECEIVING PRODUCT BY SEVERITY FOR HMA

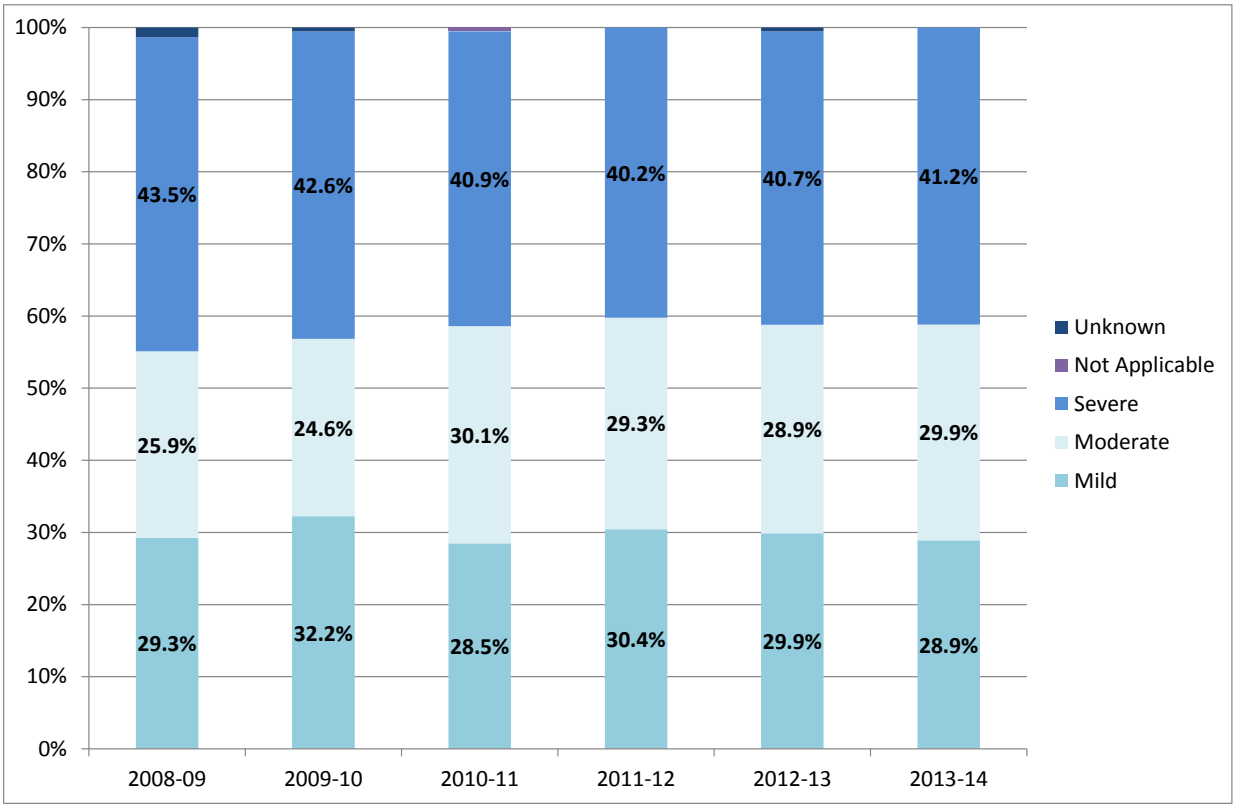

FIGURE 7 PROPORTION OF PATIENTS RECEIVING PRODUCT BY SEVERITY FOR HMB

Table 16 details the volume (IU) of product issued for HMA, HMB and VWD patients in 2013-14. The volumes are subdivided by severity and treatment regimen. 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 16 IU OF PRODUCT ISSUED FOR HMA, HMB AND VWD PATIENTS, BY SEVERITY AND TREATMENT REGIMEN IN 2013-14

	Mild	Moderate	Severe	Unknown*	Total**
HMA (IU FVIII Products)†	**5,300,750**	**16,102,250**	**125,521,950**	**10,000**	**146,934,950**
On Demand	3,741,750	6,091,750	21,586,500	1,500	31,421,500
Prophylaxis	707,250	9,752,000	94,752,950		105,212,200
ITT - Tolerisation	76,000		7,915,250		7,991,250
Unknown*	775,750	258,500	1,267,250	8,500	2,310,000
HMB (IU FIX Products)‡	**2,972,000**	**7,573,750**	**19,434,500**	**0**	**29,980,250**
On Demand	2,351,000	3,096,750	4,031,000		9,478,750
Prophylaxis	471,000	4,178,000	12,403,500		17,052,500
Tolerisation			2,978,000		2,978,000

	Mild	Moderate	Severe	Unknown*	Total**
Unknown*	150,000	299,000	22,000		471,000
VWD (IU FVIII Product) ++	**644,250**	**541,000**	**4,377,750**	**451,503**	**6,014,503**
On Demand	367,750	483,000	1,653,000	379,003	2,882,753
Prophylaxis	128,000	10,000	2,623,750	35,500	2,797,250
Unknown*	148,500	48,000	101,000	37,000	334,500

† FVIII Products included are Advate, Benefix, Biostate, Kogenate, Recombinate and Xyntha
‡ FIX Products included are BeneFIX, Kogenate and MonoFIX
++ FVIII Products include 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.

VOLUME (IU) OF PRODUCTS ISSUED FOR HMA AND HMB

Table 17 lists the volumes (IU) issued by age group and treatment regimen. In both the adult and paediatric (includes adolescents) age groups the majority of product is issued for patients on prophylactic treatment regimens, followed by on demand regimens. The ABDR product issues data contains a large amount of records where the treatment regimen is blank, unknown and not specified.

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.[9,10] Figure 8 shows the clotting factor consumption during 2013-14 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 the age groups were 4,163 IU/kg/year (0-4 years), 4,578 IU/kg/year (5-9 years), 4,329 IU/kg/year (10-14 years) and 3,118 IU/kg/year (15-17 years). The adult population, (18 years and over) had a median value of 3,094 IU/kg/year.

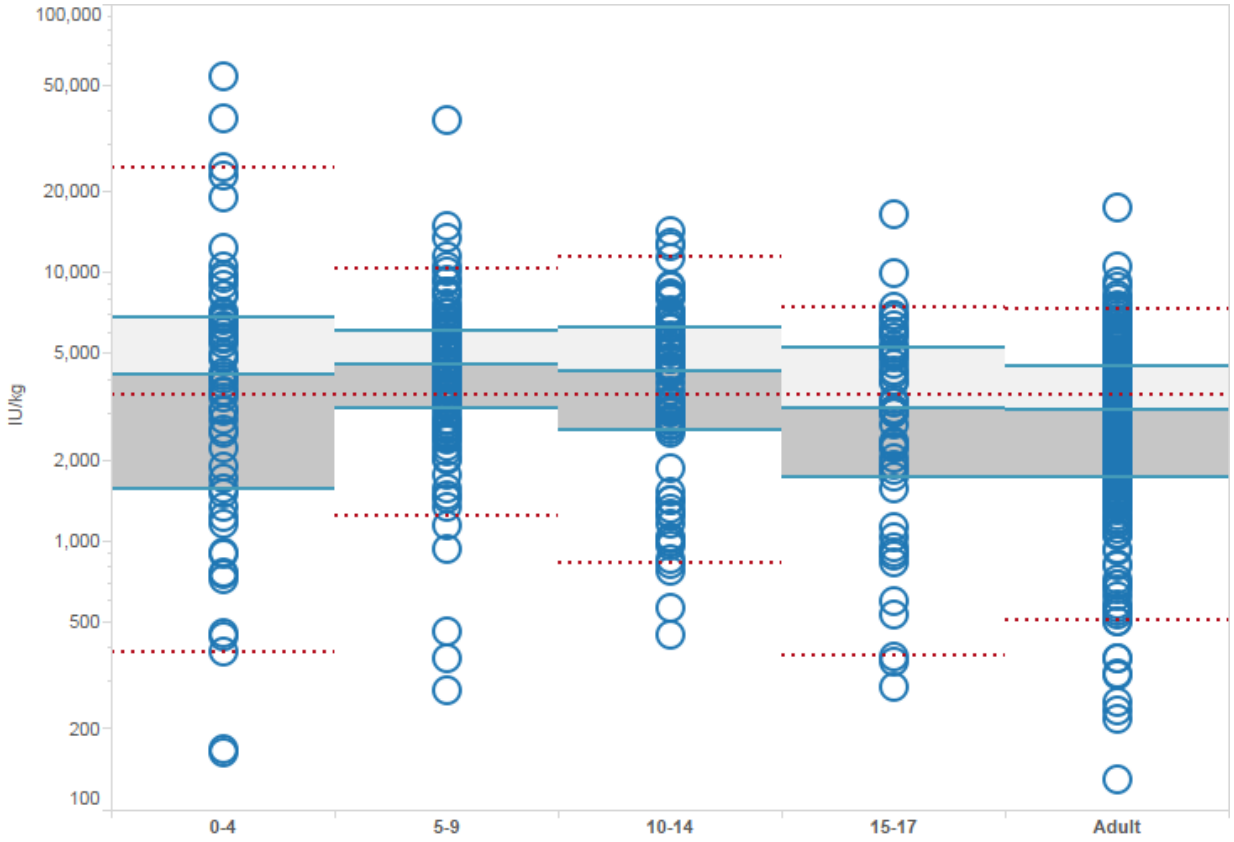

Figure 8 Product usage (IU/kg/year) in severe HMA patients on prophylaxis

[9] 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.
[10] 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 9 shows the clotting factor consumption during 2013-14 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 values for the paediatric age group was 483 IU/kg/year (0 to 17 years) and the adult population, (18 years and over) had a median value of 1,410 IU/kg/year.

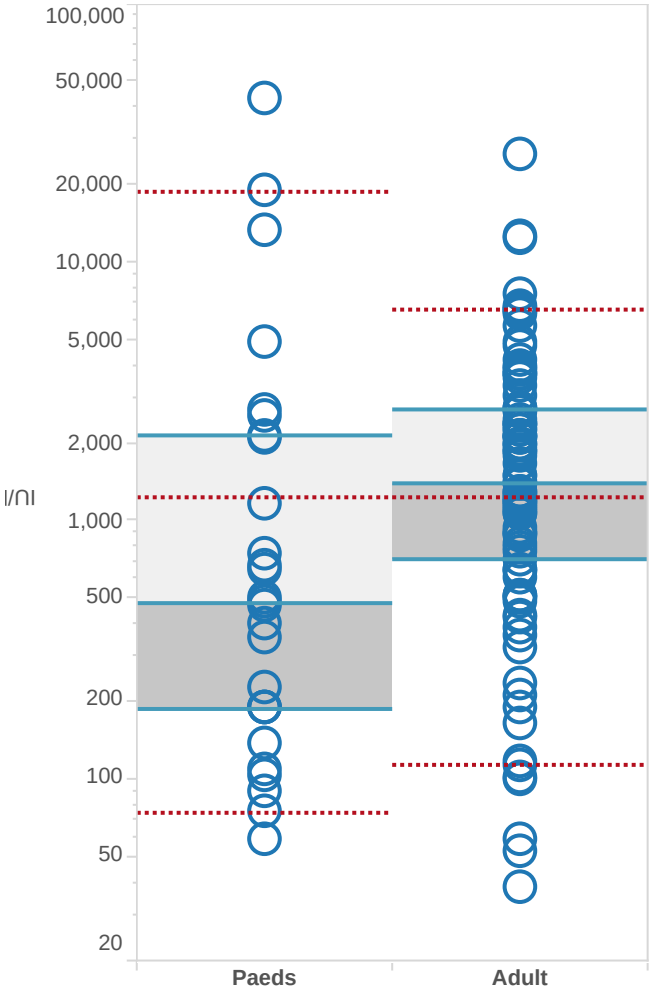

FIGURE 9 PRODUCT USAGE (IU/KG/YEAR) IN SEVERE HMA PATIENTS ON DEMAND

Figure 10 shows the clotting factor consumption during 2013-14 for severe HMB patients on prophylaxis regimen. Median values for the age groups were 9,426 (2,283 IU/kg/year for 2012-13) IU/kg/year (0-4 years), 3,795 IU/kg/year (5-9 years), 2,874 IU/kg/year (10-14 years) and 2,744 IU/kg/year (15-17 years). The adult population, (18 years and over) had a median value of 3,538 IU/kg/year.

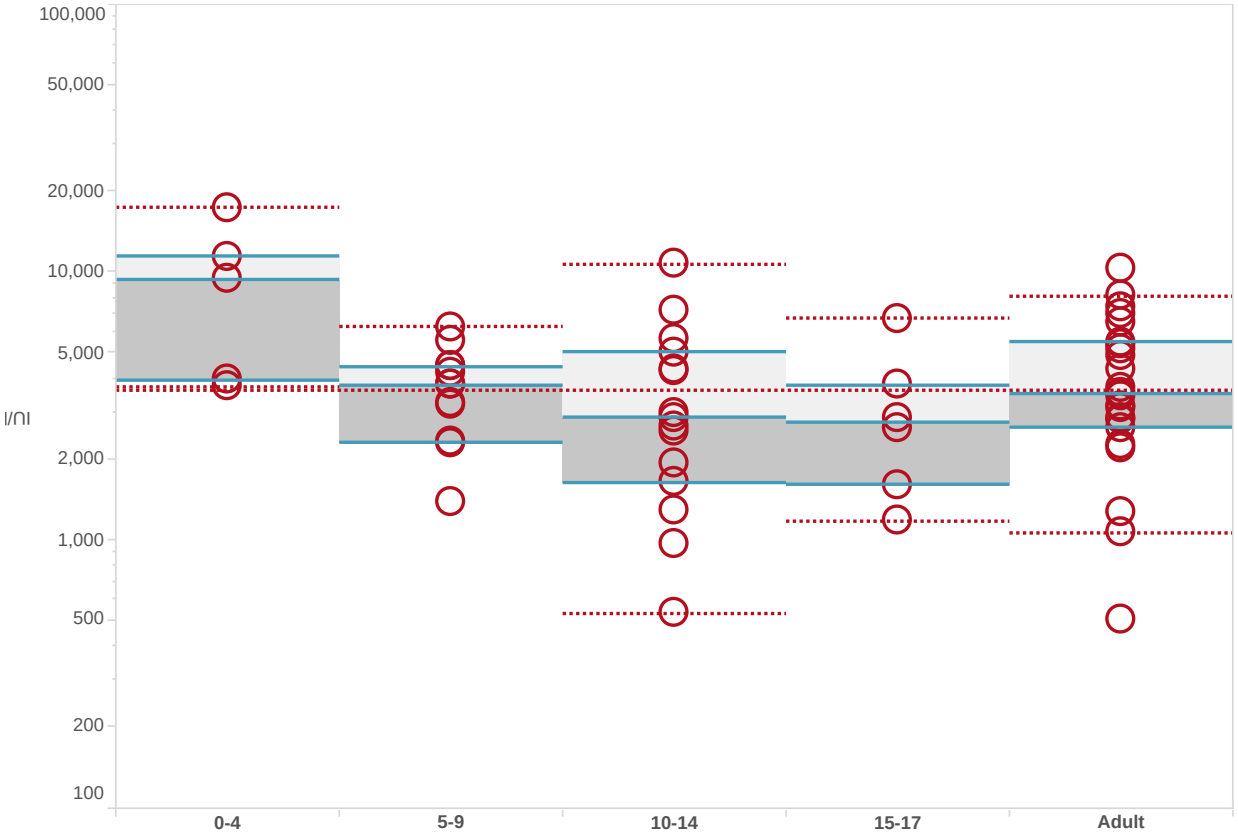

FIGURE 10 PRODUCT USAGE (IU/KG/YEAR) IN SEVERE HMB PATIENTS ON PROPHYLAXIS

Figure 11 shows the clotting factor consumption during 2013-14 for severe HMB patients on demand regimen. Median values for the paediatric (includes adolescents) age group was 1,059 IU/kg/year (0 to 17 years) and the adult population, (18 years and over) had a median value of 1,212 IU/kg/year.

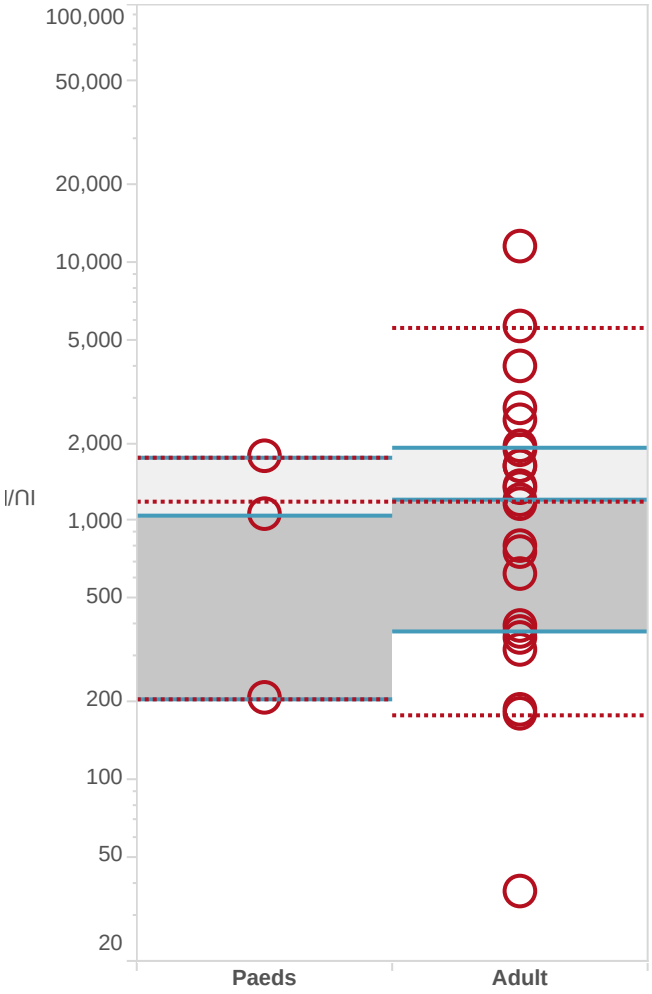

FIGURE 11 PRODUCT USAGE (IU/KG/YEAR) IN SEVERE HMB PATIENTS ON DEMAND

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.[11] In time, the ABDR data should provide further insight into these issues.

[11] 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.

TABLE 17 VOLUME (IU) OF PRODUCTS ISSUED IN 2013-14 TO ADULT AND PAEDIATRIC PATIENTS BY TREATMENT REGIMEN

	Adult					Paediatric				
	On Demand	Prophylaxis	Tolerisation	Not specified	**Adult Total ***	On Demand	Prophylaxis	Tolerisation	Not specified	**Paediatric Total ***
HMA (IU FVIII Products)†	**29,658,500**	**63,762,000**	**5,239,500**	**2,108,750**	**100,768,750**	**1,763,000**	**41,450,200**	**2,751,750**	**201,250**	**46,166,200**
Advate	2,000	158,000	0	0	160,000	0	200	0	0	200
BeneFIX	30,000	0	0	0	30,000	0	0	0	0	0
Biostate	3,152,500	1,828,500	1,898,000	124,000	7,003,000	10,250	1,728,500	1,505,750	94,500	3,339,000
Kogenate FS	10,043,500	24,947,750	1,372,000	893,750	37,257,000	1476250	19753750	853250	89500	22,172,750
Recombinate	0	0	0	0	0	500	0	0	0	500
Xyntha	16,430,500	36,827,750	1,969,500	1,091,000	56,318,750	276,000	19,967,750	392,750	17,250	20,653,750
*NovoSeven (mgs)	7,577	750	643	1,358	10,328	119	1,099	473		1,691
*FIEBA (Units)	1,079,000	97,000	261,000	36,000	1,473,000	6,000	872,000	72,500	7,500	958,000
HMB (IU FIX Products)‡	**8,920,393**	**11,847,105**	**2,978,000**	**442,500**	**24,187,998**	**559,250**	**5,206,500**	**0**	**28,500**	**5,794,250**
BeneFIX	8,269,500	11,846,000	0	442,500	20,558,000	555,250	5,186,500	0	28,500	5,770,250
Kogenate	0	0	0	0	0	4,000	20,000	0	0	24,000
MonoFIX	650,000	0	2,978,000	0	3,628,000	0	0	0	0	0
*NovoSeven (mgs)	893	1105			1,998					0
VWD (IU Biostate)	**2,755,753**	**1,953,500**	**0**	**315,000**	**5,024,253**	**127,000**	**843,750**	**0**	**19,500**	**990,250**

† FVIII Products included are Advate, Biostate, Kogenate, Recombinate and Xyntha
‡ FIX Products included are BeneFIX, and MonoFIX
* 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.

Appendix A Characteristics of Rare Clotting Factor Deficiencies

TABLE 18 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 Disorder 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

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
Royal Darwin Hospital	Haemophilia Treatment Centre	NT
Royal Brisbane and Women's Hospital	Queensland Haemophilia Centre	QLD
Royal 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
The Haemophilia Centre of WA	Incorporating:	
	· Fremantle Hospital	WA
	· Princess Margaret Hospital	WA
	· Royal Perth Hospital	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. 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 12 illustrates the national supply by product category for 2013-14, and shows the cost of clotting factor products was 19.3% ($201.8 million).

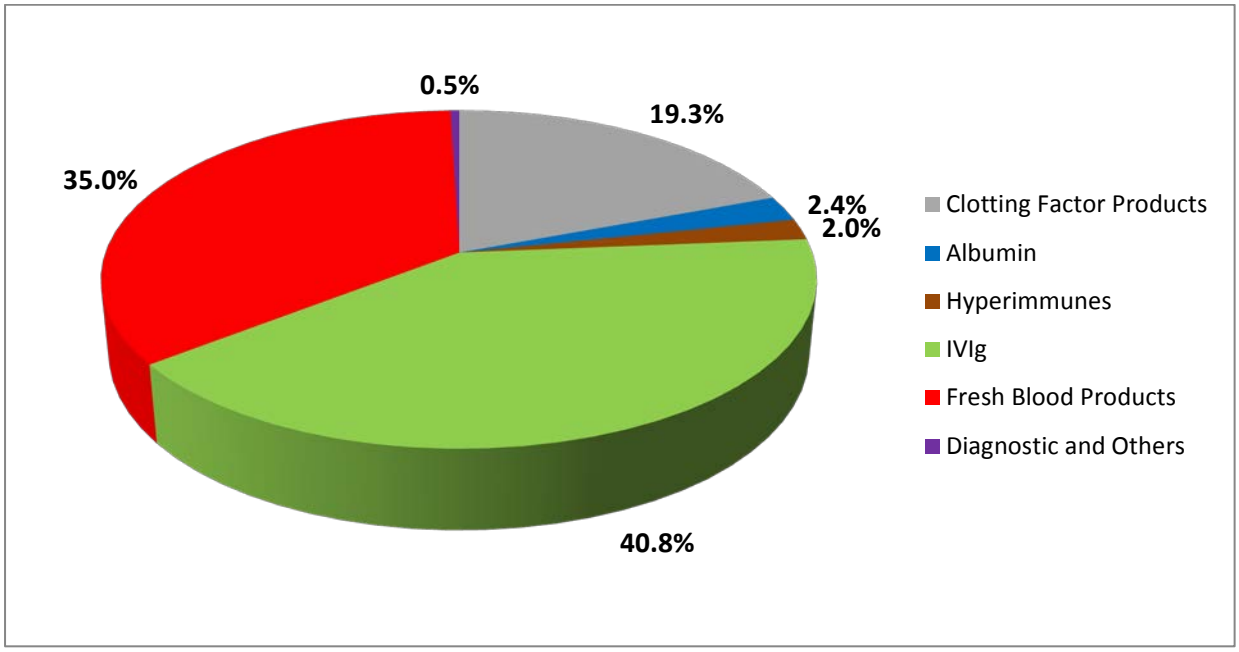

FIGURE 12 NATIONAL EXPENDITURE BY PRODUCT CATEGORY 2013-14

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

Throughout 2013-14, products were supplied to meet clinical demand and supply risks were effectively managed. The costs for 2013-14 covering the supply and management of blood and blood products under contract was $1,046.3 million, comprising $366.6 million for fresh blood products excluding plasma collection and $679.7 million for plasma and recombinant products including plasma collection.

ISSUES OF CLOTTING FACTORS

Figure 13 indicates that the demand for factor VIII products decreased by 0.8% when compared to 2012–13. The demand for recombinant FVIII decreased by 1.3% compared to the demand for 2012-13. Conversely plasma derived FVIII demand increased 3.5% due to additional requirements for immune tolerisation therapy.

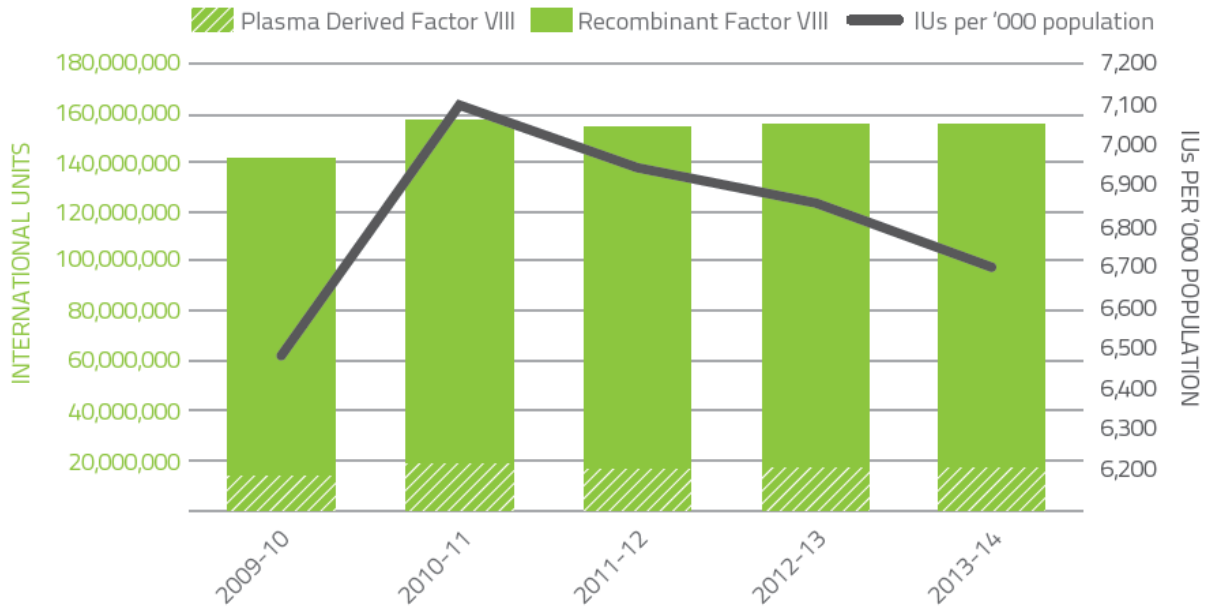

FIGURE 13 ISSUES OF FACTOR VIII PRODUCTS, 2009-10 TO 2013-14

Figure 14 shows demand for factor IX (FIX) products in 2013–14 increased by 8.6% compared to 2012-13. Plasma derived FIX increased by 48.5% due to specific patient requirements. Recombinant FIX increased 4.6% largely as a result of newly diagnosed patients.
Patients commencing or ceasing participation in company clinical trials also contributed to the variability of year-to-year growth rates for both FVIII and FIX products.

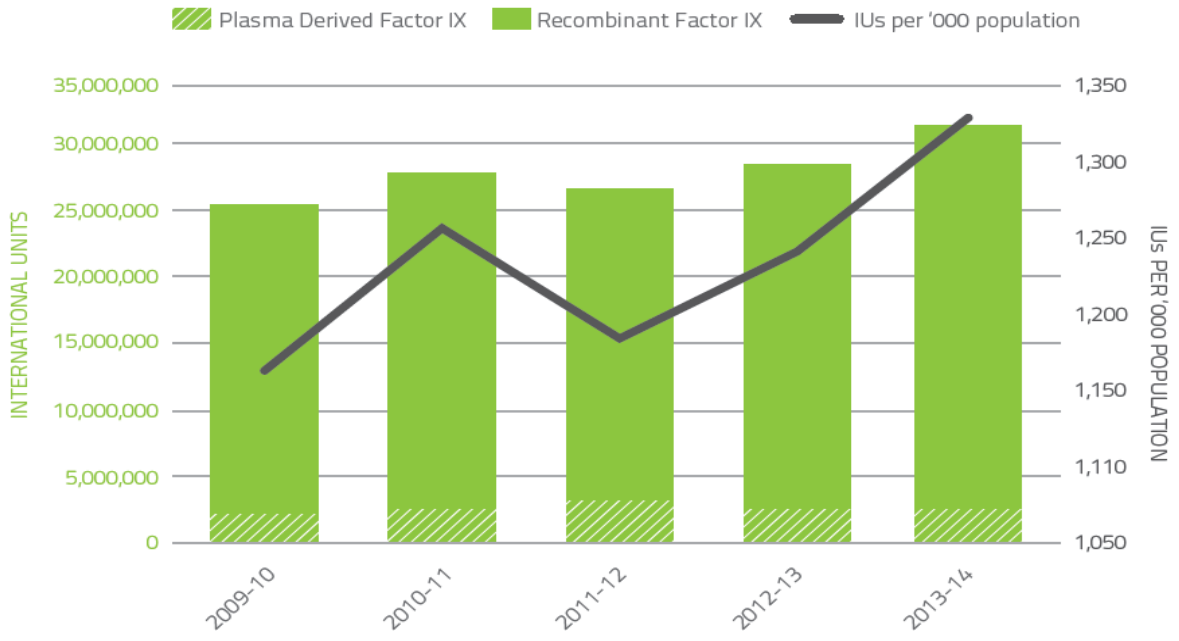

FIGURE 14 ISSUES OF FACTOR IX PRODUCTS, 2009-10 TO 2013-14

Figure 15 and Figure 16 shows the demand for rFV11a and factor eight inhibitor bypass agent (FEIBA). The demand for these products may vary significantly from year to year as a result of the impact of a small number of patients experiencing very high needs from time to time. The 2013-14 level of demand for rFVIIa returned to the level of previous years and was 21% lower than the unexpected demand in 2012-13. A major influence of the unusual 2012-13 demand was a higher than usual number of acquired haemophilia A patients requiring treatment. FEIBA demand increased with demand in 2013-14 exhibiting a 33.6% increase compared to 2012-13.

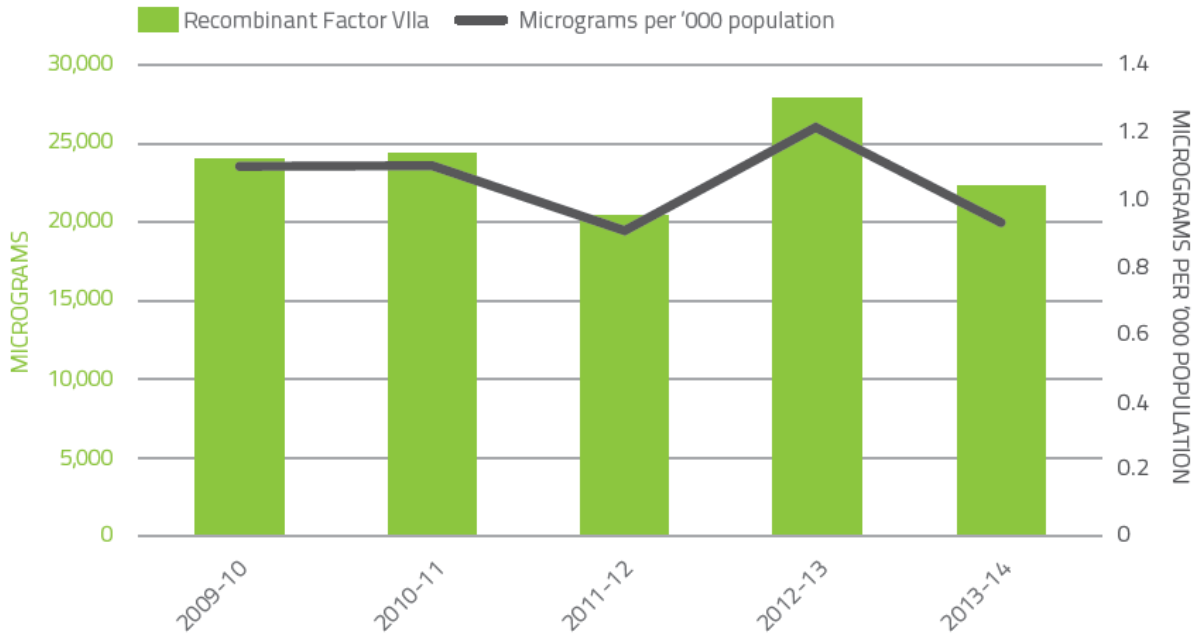

FIGURE 15 ISSUES OF RECOMBINANT FACTOR VIIA PRODUCTS, 2009-10 TO 2013-14

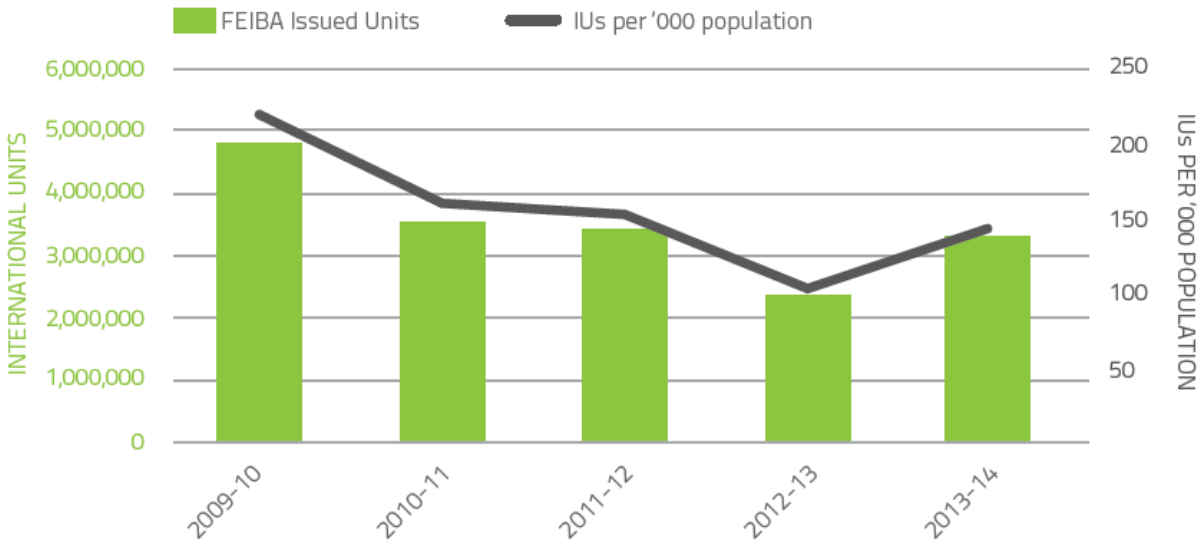

FIGURE 16 ISSUES OF FEIBA, 2009-10 TO 2013-14

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 Commonwealth to assist with concerns about privacy. Ongoing issues identified were related to privacy and data collection with one state not being involved and coverage of the database, as 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 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 August 13, 2012.

The ABDR has evolved and improved with improvements in technology and feedback from stakeholders. The ABDR enters 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'.

There has been further identification of PWHs and opportunity for standardisation of terminology. The ABDR is clinical tool to enable management external to the HTC eg outreach clinics. 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, sex 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

ABDR
Australian Bleeding Disorders Registry

ATTENTION: ABDR DATA MANAGER

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 ☐ Australian Citizen/Permanent Resident ☐ Overseas Visitor ☐ Temporary Visa

*First name | Second name / initial | *Family name

Known as / alias | *Gender ☐ Male ☐ Female | *Date of Birth DD / MM / YYYY | Previous family name/s

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

☐ Home phone ☐ Work phone ☐ Mobile

☐ Home email ☐ Work email

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

Patient contact (if necessary):

☐ Mother ☐ Father ☐ Carer ☐ Grand Parent ☐ Emergency ☐ Other Please specify

Title | First name | Second name / initial | Family name

Address
1
2
3
Suburb | State | Postcode

☐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 presented DD / MM / YYYY | *Bleeding disorder #

*Severity (Mild / Moderate / Severe / unknown / not applicable) | Date diagnosed DD / MM / YYYY | 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 | *Family 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. The patient is aware of the purpose for capturing their details in the ABDR and is aware of privacy and confidentiality protection arrangements as described overleaf. ABDR Pamphlet has been given to patient.

Name _____ Signature _____ Date DD/MM/YYYY

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

Effective April 2009

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)
Fresh Frozen Plasma (FFP)
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)
MonoFIX® - VF (pdFIX)
NovoSeven® (rFVIIa)
NovoSeven RT® (rFVIIa)
Platelets
Prothrombinex™ - VF (pdPCC)
Recombinate® (rFVIII)
ReFacto® (rFVIII)

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 a service provider engaged by the National Blood Authority. The ABDR was first established in 1988 and has been upgraded many times with the latest significant upgrade in 2008.

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 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 ABDR Secretariat at abdr@nba.gov.au or 02 6211 8311.

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

Effective April 2009

Acronyms and glossary of terms

ACRONYMS

ABDR	Australian Bleeding Disorders Registry
AHCDO	Australian Haemophilia Centres Directors' Organisation
BU (BU/ml)	Bethesda unit (expressed as Bethesda units per millilitre)
DDAVP	Desmopressin (1-desamino-8-D-arginine vasopressin; DDAVP) 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
IDMS	Integrated data management system – The NBA's integrated data management system.
IU	International Units
MyABDR	MyABDR is 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
PWBD	People with a bleeding disorder
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