UDC
The Universal Data Collection Program
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Report on the Universal Data Collection Program

Includes data collected from May 1998 through December 2004

CDC
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The *Report on the Universal Data Collection Program* is accessible via internet at http://www.cdc.gov/ncbddd/hbd/surveillance.htm Confidential information, referrals, and educational material on hemophilia and other bleeding disorders are also available by calling the National Hemophilia Foundation's information line, HANDI, at 800-42-HANDI.

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Commentary

The two most common congenital bleeding disorders are von Willebrand disease (VWD) and hemophilia. VWD is caused by the defective synthesis or function of a protein, von Willebrand factor that is necessary for normal blood clotting. VWD occurs with equal frequency in men and women. Although the prevalence of this disease is not precisely known, it is estimated that between one and two percent of the population are affected. There are different types and severity of VWD. Symptoms include heavy or prolonged menstrual bleeding, easy bruising, frequent or prolonged nosebleeds, and prolonged bleeding following surgery, dental work, childbirth, or injury.

Hemophilia is caused by a defect in the gene located on the X chromosome that contains the genetic code for one of the clotting factor proteins necessary for normal blood clotting. A deficiency of factor VIII is referred to as hemophilia A or "classic" hemophilia. In contrast, a deficiency of factor IX characterizes hemophilia B, also known as Christmas disease. The defect usually occurs on one of the two female X chromosomes and results in a carrier state. When males have the defect on their only X chromosome, they have the disease. Thus, almost all of the approximately 17,000 people with hemophilia in the United States are male.

People with severe hemophilia can experience serious bleeding into tissues, muscles, joints, and internal organs, often without any obvious trauma. Repeated bleeding into joints without adequate treatment results in crippling chronic joint disease, one of the severe complications of bleeding disorders. In the mid-1970s, treatment for hemophilia was improved through the use of clotting factor concentrates, products made from the plasma of donated blood. However, because blood donations from thousands of donors are pooled together to make these products, many people with bleeding disorders were infected with hepatitis B and C viruses and with human immunodeficiency virus (HIV), the virus that causes AIDS, before the risk of disease transmission in blood products was recognized and prevention measures taken.

In 1975, Congress initiated federal funding to specialized hemophilia treatment centers (HTCs) to provide comprehensive care to people with bleeding disorders. Since 1986, the Centers for Disease Control and Prevention (CDC) has been involved with the hemophilia community through the HTC system, primarily through risk-reduction efforts aimed at preventing secondary infection of family members with HIV.

In 1991, CDC received a request from the National Hemophilia Foundation to expand their collaborative activities within the bleeding disorders community. Meetings with patients and hemophilia care providers were held during 1992 to determine the areas of highest priority. Based on recommendations from these constituents, a congressional mandate was issued to CDC, with the goal of reducing the human suffering and financial burden of bleeding disorders by focusing national emphasis on prevention and early intervention. The issues of greatest concern identified by the bleeding disorders community were: (1) the safety of the blood supply from infectious diseases and (2) the prevention of joint disease.

In response, CDC developed the Universal Data Collection Program (UDC). The purpose of UDC is two-fold: (1) to establish a sensitive blood safety monitoring system

among people with bleeding disorders and (2) to collect a uniform set of clinical outcomes information that can be used to monitor the occurrence of and potential risk factors for infectious diseases and joint complications.

People with bleeding disorders are enrolled in UDC by care providers in each of the nation's 140 federally funded HTCs. As part of the project, a uniform set of clinical data and plasma specimens is collected by HTC staff each year during each participant's annual comprehensive clinic visit. A portion of the plasma specimen is used to perform free screening tests for hepatitis A, B, and C viruses and for HIV. The remainder of the specimen is stored for use as needed in future blood safety investigations.

Enrollment in UDC began in May 1998. Information about eligibility requirements, enrollment procedures, and data collection can be found in the *Technical Notes* of this report. Participating HTCs are listed by region in the *Acknowledgements*. A regional map is included at the end of this report.

The purpose of this surveillance report is to disseminate the information being collected by UDC to public health workers, health educators and planners, other care providers, and patients in the bleeding disorders community. The report contains information about the demographic characteristics of the participants, their blood and factor product use, and the occurrence and treatment of joint and infectious diseases.

We hope that this information will prove useful to those involved in efforts to reduce or prevent the complications of these conditions.

The proper interpretation and appropriate use of surveillance data require an understanding of how the data are collected, reported, and analyzed. Therefore, readers of this report are encouraged to review the *Technical Notes*, beginning on page 18.

Highlights

This issue of the UDC Surveillance Report focuses on data collected from people who have been enrolled through December 2004. For the first time we have included data on children under 2 years of age enrolled in the UDC. Tables and figures that include only people 2 years of age or older are noted.

Since May, 1998, 15,682 people with bleeding disorders have been enrolled, and there have been 38,385 UDC visits. The overall national refusal rate is 7.6 %.

Figures 1 and 2 show new enrollment in UDC. The decline of new enrollees who have either hemophilia or VWD represents the success of UDC in capturing more and more of the population over time.

Figures 3 and 4 show UDC visits over time and by region. The number of UDC visits held per year appears to have plateaued in 2002 and have remained constant through the end of 2004.

Figures 5 and 6 show the refusal rates in UDC from May 1998 through December 2004 by year and region. Refusal rates have generally declined over time but appear to have increased slightly among people with hemophilia and VWD in 2004. The overall refusal rate is 7.3% for people with hemophilia and 8.6% for people with VWD. Refusal rates through December 2004 in regions I through IX remained below 15%, with a low of 3.6 % in Region IV-N among people with hemophilia to a high of 14.3% among people with VWD in Region V-E.

Refusal rates in Region X are unusually high due to low numbers of people enrolled in UDC.

Figure 7 shows the follow-up time for people enrolled in UDC. Nearly two-thirds of people enrolled in UDC have had more than one annual visit.

Figure 8 shows the number of people with a UDC visit in each year through December 2004 according to visit type. The number of people with a first time UDC visit has gone down as a proportion of total visits while those with follow-up visits have increased over time.

The distribution of demographic characteristics (Table 1) and sources of healthcare reimbursement (Table 2) have remained consistent over the course of the study. A little over 50% of people with hemophilia are ≤ 20 years of age and nearly all are males as expected. Over 60% of people with VWD are ≤20 years old and patients are more evenly divided among men and women. In both groups, persons under 2 years of age comprise less than 1% of the population. The population distribution by race and ethnicity is similar to that of the general population. With regard to healthcare reimbursement, about 60% of participants have some form of commercial insurance, about 30-35% have government sponsored coverage, and the remainder have other types of insurance. Only about 3-4% of patients are uninsured.

As shown in Table 3, one quarter of people in UDC with hemophilia have mild disease, 23.0% have moderate disease, and 51.5% have severe disease. 71.8% of people in UDC with VWD are classified as having Type 1, 10.6% as having Type 2, 6.8% as having Type 3, and 10.8% are classified as having other or unknown type of VWD.

Table 4 shows the average number of bleeds by disease severity and prophylaxis use among people with hemophilia and VWD. For people with moderate hemophilia, the reported bleeding frequency was similar for those who were using prophylaxis compared with those who received episodic care. On the other hand, people with severe disease on prophylaxis reported far fewer bleeds than those on episodic care. Among people with VWD, as expected, those with Type 3 VWD had the most bleeds. Bleeding was far more common in sites other than joints and muscles among people with VWD compared to those with hemophilia.

In Table 5, most people had no risk factors or symptoms associated with liver disease. 271 (31.3%) of the 873 people with hemophilia receiving any therapy for viral hepatitis had successful treatment of the disease. 1293 (11.0%) people with hemophilia had an intravenous access device (IVAD) in the year previous to their most recent visit. Of these, 147 (11.4%) had an IVAD associated infection.

Table 6 shows that the most common type of treatment used for all severity levels of hemophilia was episodic care. 10.8% of people with moderate disease used continuous prophylaxis and 7.9% of those with severe disease used intermittent prophylaxis. As expected, patients with severe disease were the most likely to be on continuous prophylaxis.

Prevalence of inhibitors (Table 7) is highest among people with severe hemophilia A. Inhibitors are much less common among people with hemophilia B.

The proportion of overall factor product use (Table 8) has remained consistent throughout the surveillance period. The majority of people with hemophilia use recombinant products. Twelve percent of patients with hemophilia A, 24% of those with hemophilia B and 40% of patients with VWD used no product during the year prior to their UDC visit.

The prevalence of multiple product use (Figure 9 and Tables 9-11) has increased when compared to previous UDC reports. In order to more accurately reflect multiple product use, the method used to calculate these data has changed. People who use no products have been excluded from the denominator, and multiple product use is now defined as using more than one product regardless of product type (e.g. a person using Bioclate and Helixate is denoted as using multiple products even though both products are Factor VIII recombinant products).

In Figure 9, multiple factor product use in people with hemophilia using any product is between approximately 20% and 30% for all age groups except those aged 6-10, where multiple product use is 31.6%. Overall multiple product use is 24.1%. For those under age 2 and from 2-5 years, multiple product use is similar.

Table 9 shows multiple product use is similar, between 22-25%, among people with hemophilia for all treatment types.

People with mild hemophilia have a slightly increased use of multiple factor products (29.3%) than people with moderate (23.9%) or severe (22.4%) disease. The overall prevalence of multiple factor product use among those using at least one factor product is 24.1% (Table 10).

Table 11 shows that among people with Hemophilia A and B, those with a high titer inhibitor are much more likely to use multiple factor products (43.0% and 35.5 % respectively) than those with low or negative inhibitor titers. This finding reflects the fact that people with inhibitors use other products to control bleeding episodes when their current product fails to do so.

Figure 10 illustrates that people with hemophilia A who have mild disease have a lower prevalence of intra-cranial hemorrhage (ICH) over time than those with moderate or severe disease. With the exception of people with severe disease in 1998, the prevalence of ICH among people with all severity levels of disease and over all years was under 1% and relatively stable over the time period. In people with hemophilia B (Figure 11), there was more variability in the prevalence of ICH across severity levels and over time. This is probably a reflection of the smaller number of people with Hemophilia B enrolled in UDC.

In Table 12, nearly one-half of people with severe hemophilia and nearly one-third of people with severe VWD report some restriction of activity. Data in Table 13 demonstrates that the average joint limitation value for people with Type 3 VWD (70.5) falls between the value for people with mild (55.1) and moderate (87.1) hemophilia.

Figure 12 shows the prevalence of natural or acquired immunity to hepatitis A by age group and year in people with hemophilia. In every year, the prevalence is higher in the group 21 years of age and older. This figure also

suggests that the immunity levels are decreasing over time.

Figure 13 shows the prevalence of natural or acquired immunity to hepatitis A by region in people with hemophilia. Overall immunity rates are approximately 60% but the rates vary from about 50% in Region VII to nearly 70% in Region IX.

Figure 14 shows the prevalence of natural or acquired immunity to hepatitis A by age group and year among people with VWD. The prevalence of immunity appears to be increasing among those under 21 and decreasing among those ages 21 and older.

Figure 15 shows the prevalence of natural or acquired immunity to hepatitis B by age group and year in people with hemophilia. The prevalence appears to be decreasing in both age groups over time despite the availability and widespread usage of hepatitis B vaccine in childhood.

Figure 16 shows the prevalence of natural or acquired immunity to hepatitis B by region in people with hemophilia. Overall immunity rates are approximately 80% and vary remarkably little between regions.

Figure 17 shows the prevalence of natural or acquired immunity to hepatitis B among people with VWD by age and time. Compared to people with hemophilia, the rates are lower in both age groups but the difference is more pronounced in the older age group. People with VWD are more likely than hemophilia patients to receive blood products that are not virally inactivated such as fresh frozen plasma. Therefore, hepatitis B vaccination may be especially important for this population.

Prevalence of hepatitis C infection for people with hemophilia and VWD is shown in Figure 18. Higher infection rates in adults reflect exposure to the disease prior to viral inactivation of factor products. Figure 19 shows that immunity to hepatitis A among people with hemophilia who are also infected with hepatitis C varies between 55-75% across regions.

Prevalence of HIV among people with hemophilia and VWD is shown in Figure 20. HIV infection rates are extremely low in all people with VWD; however, approximately one-third of people with hemophilia between the ages of 21 and 60 years are HIV-infected.

Tables 14 and 15 illustrate the number of people with hemophilia who use continuous prophylaxis by age group and severity. Continuous prophylaxis use drops off markedly in people who are $\geq$21 years old. Interestingly, those less than 2 years of age with severe disease are twice as likely to be on continuous prophylaxis as those with mild or moderate disease in their age category. Furthermore, those with severe disease in this age group, have a similar or higher prevalence of continuous prophylaxis when compared with those in older age groups (or all ages in the case of hemophilia B) with moderate and mild disease. Prophylaxis is used most often by people with severe disease regardless of hemophilia type, less so by people with moderate disease, and rarely by people with mild disease. Among people with both moderate and severe disease, continuous prophylaxis use increases through the mid-teens and begins to decrease in the late teens, the decline in use occurring slightly earlier among people with severe type B hemophilia. Continuous prophylaxis use by people with moderate disease increases more slowly than in those with

severe disease. One reason for this pattern of use could be that it may take longer for these people to experience enough bleeding episodes to merit the initiation of continuous prophylaxis.

Table 16 shows the prevalence of overweight and obesity among people enrolled in UDC. People with hemophilia and VWD aged 13 to 19 years are almost twice as likely to be overweight as children of the same age group in the U.S. population. Obesity, which could only be compared for those 20 or older, is at a similar rate as in the U.S. population for people with hemophilia but appears higher for people with VWD than in the general population.

Figure 21 shows no significant difference between people with hemophilia and those with VWD in the proportion who are overweight. However, the proportion of people with VWD who are obese is significantly higher than that among those with hemophilia ($p=0.05$).

In Table 17, among people with hemophilia, there is an inverse relationship between disease severity and being overweight or obese. Compared to people with hemophilia, there appears to be less of a correspondence between overweight and obesity prevalence and severity among people with VWD.

Figure 22 shows the regional distribution of overweight or obese persons with hemophilia and VWD. The prevalence of overweight and obesity among people with hemophilia across regions is between 40% and 60%, while the prevalence varies between 40% and just over 70% among people with VWD.

Figure 1. New enrollment in UDC, May 1998 – December 2004

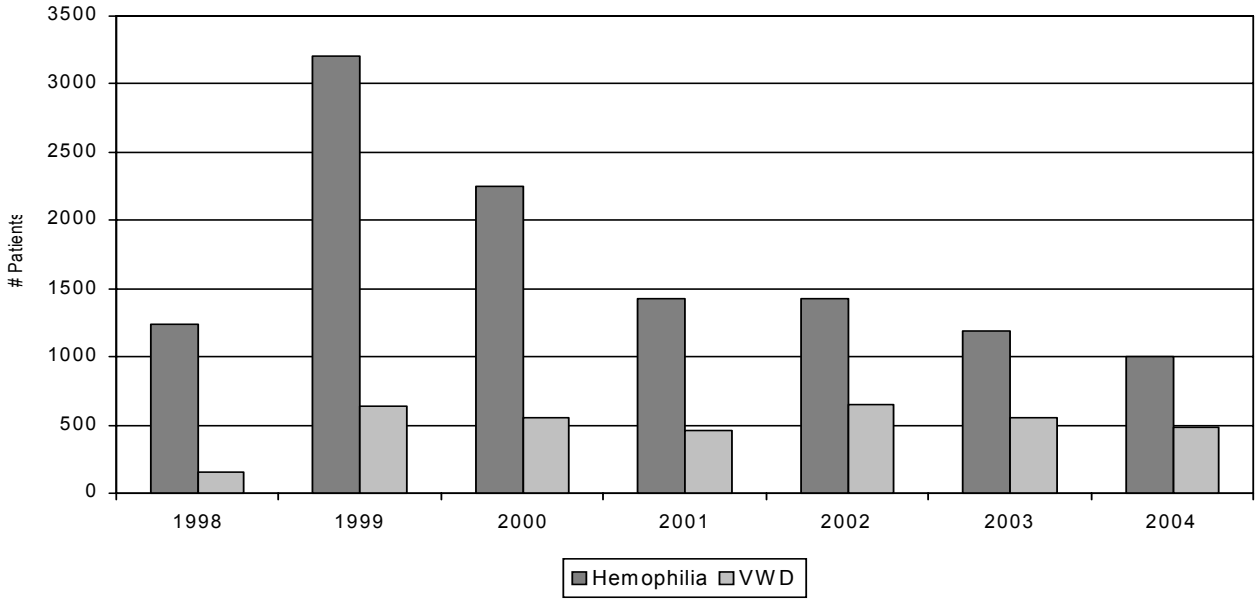
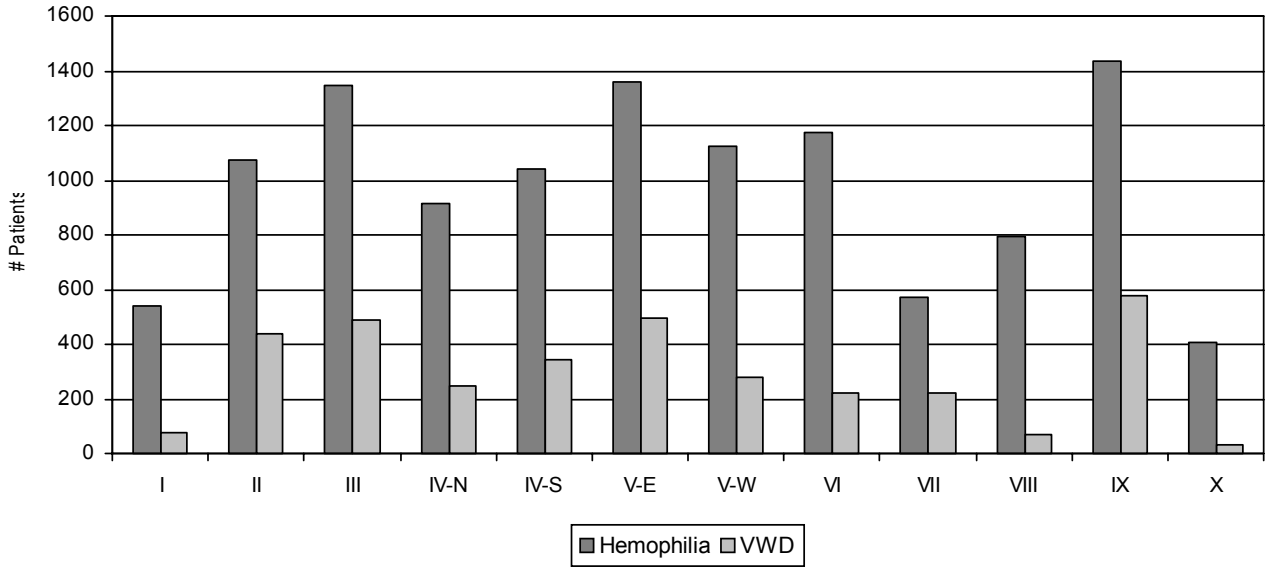


Figure 2. Total patients enrolled in UDC by region* through December 2004



*See map (page39) for regional designations.

Figure 3. UDC visits by year, May 1998- December 2004

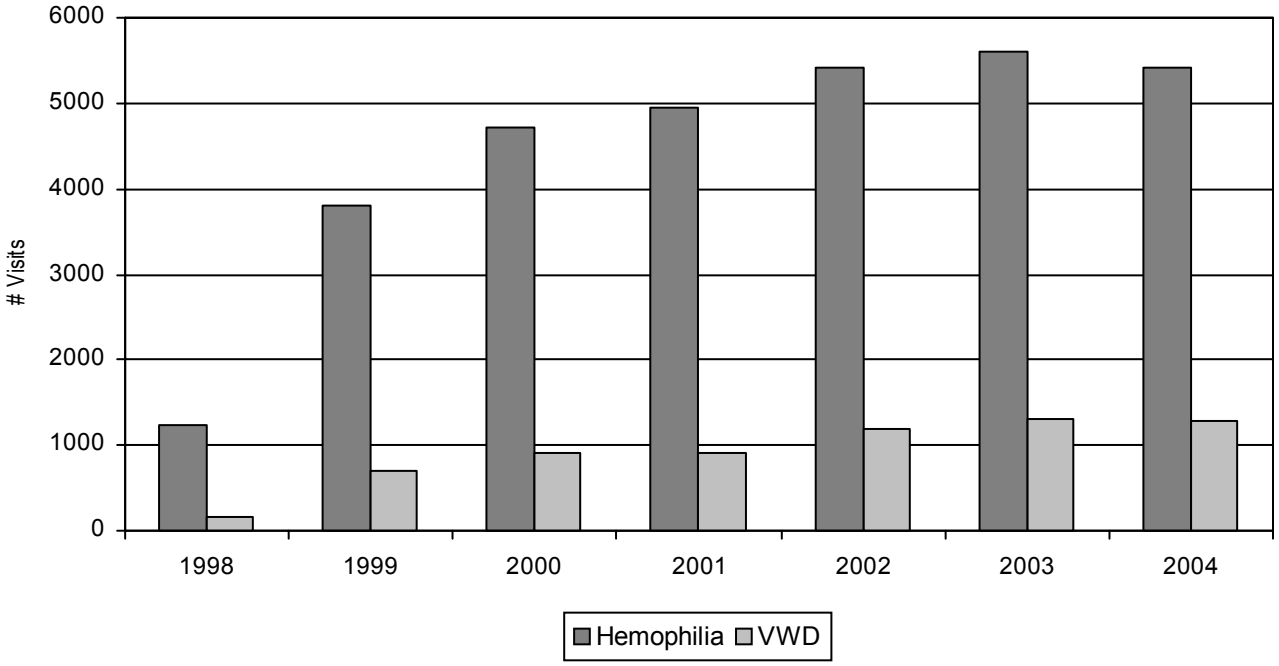
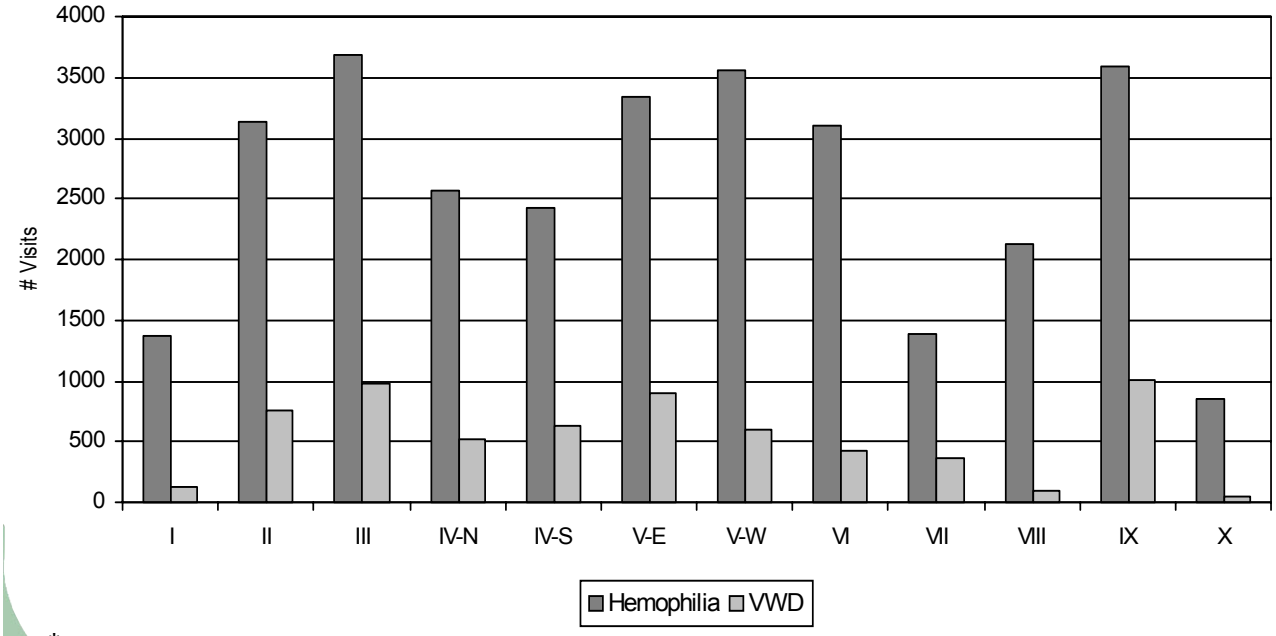


Figure 4. Total UDC visits by region* through December 2004



*See map (page39) for regional designations.

Figure 5. Refusal rates in UDC by year, May 1998 – December 2004

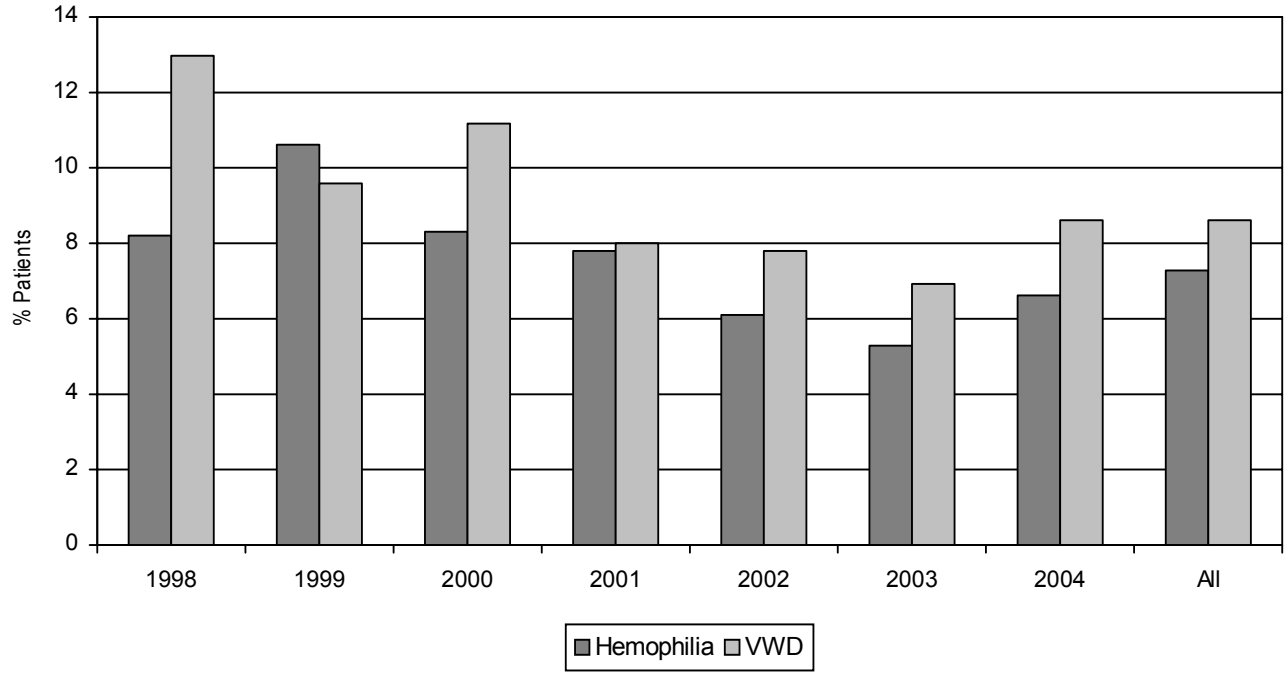
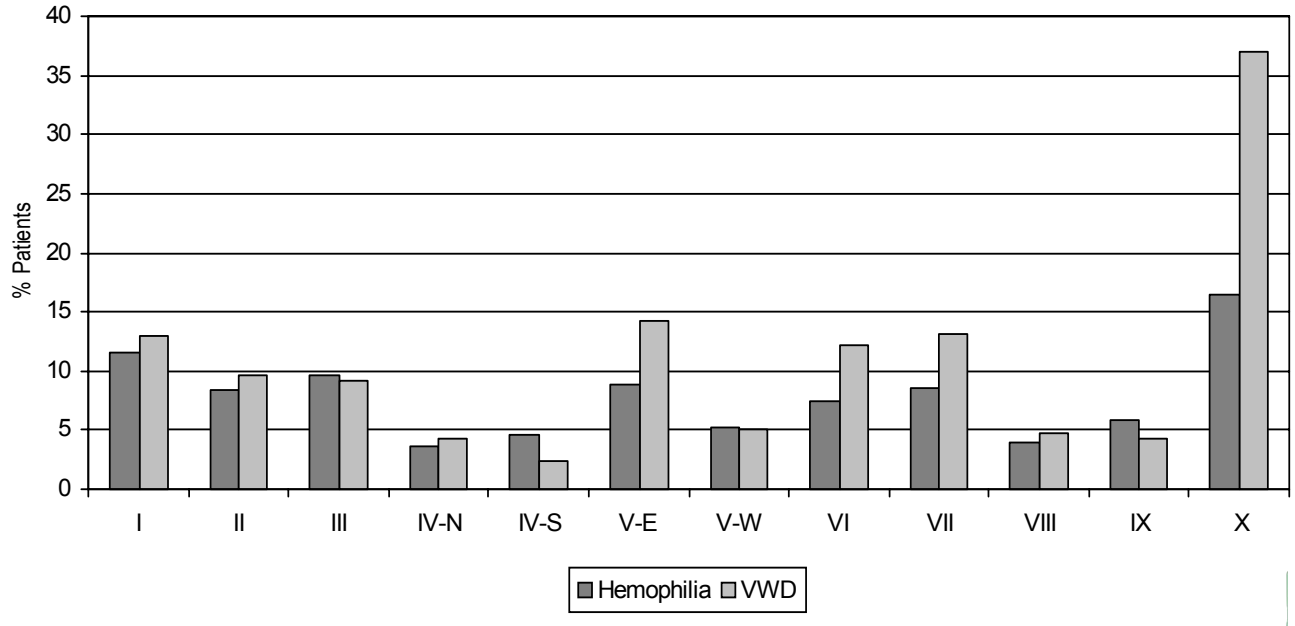


Figure 6. Refusal rates in UDC by region*, May 1998 – December 2004



*See map (page39) for regional designations.

Figure 7. Number of years of follow-up for people enrolled in UDC

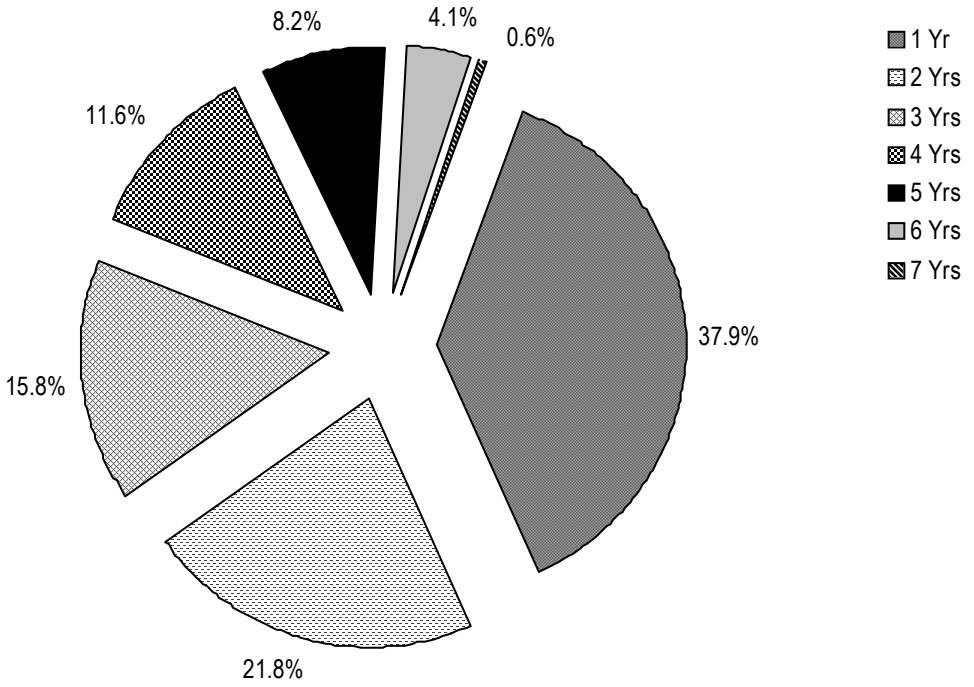


Figure 8. Visits by UDC participants through December 2004

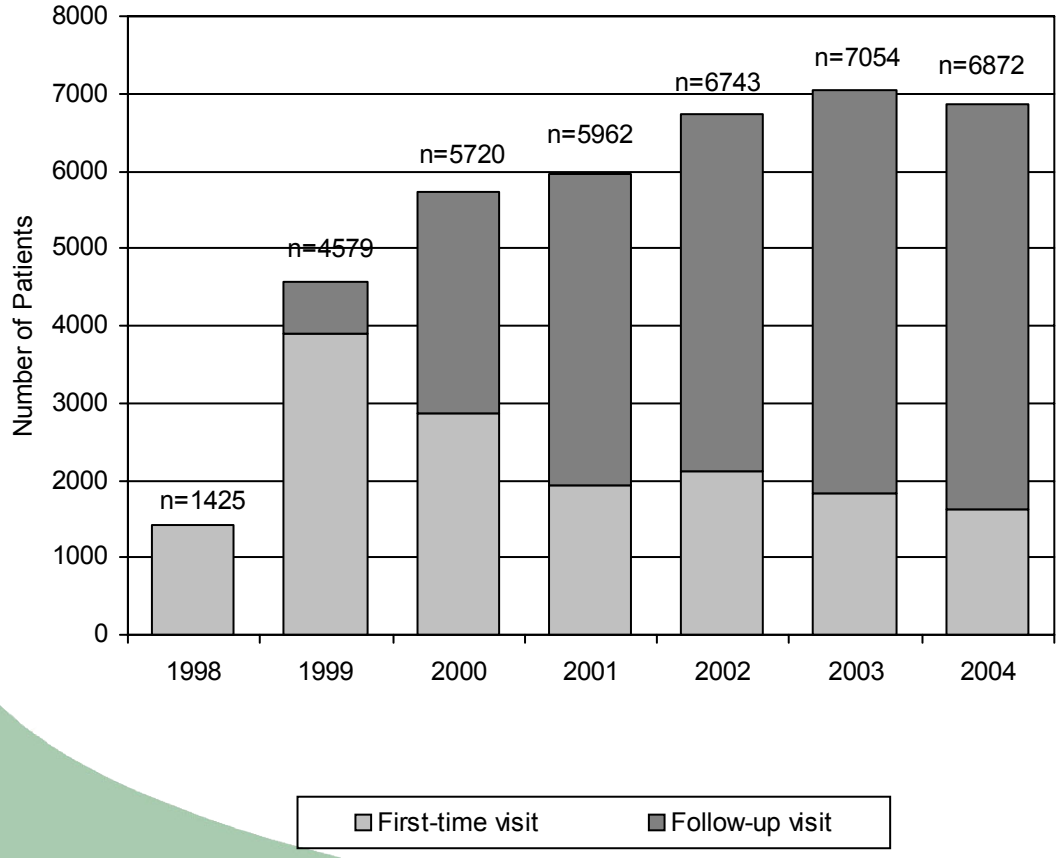


Table 1. Demographic characteristics of people* enrolled in UDC

	Hemophilia A (n =9264)		Hemophilia B (n=2526)		VWD (n = 3484)	
Characteristic	**Number**	**Percent**	**Number**	**Percent**	**Number**	**Percent**
Age Group (yrs)						
<2	52	0.6	19	0.8	2	0.1
2-10	2344	25.3	594	23.5	891	25.6
11-20	2900	31.3	725	28.7	1289	36.4
21-40	2408	26.0	635	25.1	687	19.7
41-60	1284	13.8	431	17.1	479	13.8
>60	276	3.0	122	4.8	156	4.5
Race/Ethnicity						
White	6281	67.8	1891	74.9	2599	74.6
African American	1139	12.3	274	10.8	208	6.0
Hispanic	1244	13.4	245	9.7	419	12.0
Asian/Pacific Islander	266	2.9	37	1.5	94	2.7
Native American	87	0.9	20	0.8	19	0.5
Other	247	2.7	59	2.3	145	4.2
Sex						
Male	9054	97.7	2438	96.5	1421	40.8
Female	210	2.3	88	3.5	2063	59.2

*Seventy-there people were reported to have both hemophilia and VWD (these people are included in analyses as hemophilia patients only and not VWD patients). A total of 401people had a bleeding disorder other than hemophilia or VWD.

Table 2. Sources* of health care reimbursement listed by people enrolled in UDC

	Hemophilia (n = 11790)		VWD (n = 3434)	
Reinbursement source	**Number**	**% of Total**	**Number**	**% of Total**
Commercial Insurance	2238	19.0	774	22.2
Commercial Insurance HMO	2142	18.2	801	23.0
Commercial Insurance PPO	2435	20.7	755	21.7
Medicare	1046	8.9	176	5.1
Medicare HMO	89	0.8	32	0.9
Medicaid	2446	20.8	453	13.0
Medicaid HMO	622	5.3	256	7.4
CHAMPUS	85	0.7	45	1.3
State high risk plan	452	3.8	67	1.9
Other	1566	13.3	440	12.6
Uninsured	503	4.3	127	3.7

*Some people may have listed more than one source of reimbursement.
HMO = Health maintenance organization; PPO = Preferred provider organization

Table 3. Disease severity of people enrolled in UDC

	Number	Percent
Hemophilia	**11790**	
Mild	3041	25.8
Moderate	2683	23.0
Severe	6066	51.5
VWD	**3484**	
Type 1	2501	71.8
Type 2	370	10.6
Type 3	238	6.8
Other/Unknown	375	10.8

Table 4. Bleeding episodes among people enrolled in UDC by prophylaxis use and disease severity*

No Prophylaxis	Hemophilia			VWD		
	Mild n = 3011	**Moderate** n = 2373	**Severe** n = 3965	**Type 1** n = 2486	**Type 2** n = 370	**Type 3** n=225
Bleeding site						
Joint* *	0.6 (±2.6)	3.1 (±8.0)	8.7 (±12.5)	0.1 (±1.1)	0.2 (±1.4)	1.6 (±5.0)
Muscle**	0.3 (±1.1)	0.9 (±3.1)	2.0 (±5.3)	0.1 (±0.9)	0.1 (±0.8)	0.4 (±1.4)
Other**	0.9 (±4.2)	1.5 (±7.4)	1.8(±16.2)	3.6 (±12.2)	2.7 (±6.4)	5.9 (±15.7)
All sites						
Mean (±SD)	**1.8 (±5.6)**	**5.5 (±12.7)**	**12.5 (±16.2)**	**3.8 (±12.3)**	**3.0 (±6.6)**	**7.9 (±16.7)**
Median	**0**	**2**	**8**	**0**	**0**	**2**

Prophylaxis	Hemophilia	
	Moderate n =292	**Severe** n=2057
Bleeding Site		
Joint **	3.4 (±5.8)	3.1 (±7.2)
Muscle**	0.8 (±2.0)	0.9 (±4.6)
Other**	1.9 (±7.6)	1.2 (±4.3)
All sites		
Mean (±SD)	**6.0 (±10.0)**	**5.2(±10.7)**
Median	**3**	**2**

*Includes people 2 years of age or older

**Values are mean (±SD) number of bleeding episodes experienced during the 6-month period preceding the UDC visit

Table 5. Liver disease and intravenous access device infections among people enrolled in UDC*

	Hemophilia (n = 11719)		VWD (n = 3482)	
	Number	% of Total	Number	% of Total
Risk Factors for liver disease				
Past/present hepatitis B virus infection	656	5.6	28	0.8
Past/present hepatitis C virus infection	1435	12.3	76	2.2
History of alcohol abuse	476	4.1	19	0.6
Other	169	1.4	18	0.5
None	10084	86.0	3395	97.5
Signs or symptoms of liver disease (During the last year)				
Jaundice	78	0.7	3	0.1
Ascites	70	0.6	5	0.1
Varices	61	0.5	7	0.2
Other	98	0.8	11	0.3
None	11500	98.1	3460	99.4
Laboratory markers of liver disease				
Chronically elevated ALT/AST levels	1557	13.3	65	1.9
Elevated prothrombin time in the last year	231	2.0	62	1.8
Therapy for chronic viral hepatitis				
Any therapy	873	7.4	43	1.2
Successful therapy	271	31.3**	13	31.0**
Intravenous access devices (IVAD)				
Used an IVAD in the last year	1293	11.0	74	2.1
IVAD infection in the last year	147	11.4+	5	6.8+

*Includes people 2 years of age or older
**Proportion of people who received any therapy for chronic viral hepatitis.
+Proportion of people who used an IVAD in the last year.

Table 6. Treatment type for people with hemophilia enrolled in UDC

	Mild		Moderate		Severe	
Treatment	Number	Percent	Number	Percent	Number	Percent
Episodic care	2993	98.4	2286	85.2	3427	56.5
Intermittent Prophylaxis	26	0.9	94	3.5	478	7.9
Continuous Prophylaxis*	21	0.7	291	10.8	2056	33.9
Total number	**3041**		**2683**		**6066**	

*Prophylaxis is considered continuous when administered on a regular basis and is expected to continue indefinitely.

Table 7. Prevalence of current inhibitors by titer* among people with hemophilia enrolled in UDC

	Hemophilia A			Hemophlia B		
Severity	Number	Low titer	High titer	Number	Low titer	High Titer
Mild	2372	23 (1.0%)	4 (0.2%)	669	1 (0.2%)	0 –
Moderate	1788	59 (3.3%)	23 (1.3%)	895	1 (0.1%)	3 (0.3%)
Severe	5104	310 (6.1%)	264 (5.2%)	962	23 (2.4%)	29 (3.0%)

*Inhibitor titer is determined by the highest reported inhibitor titer for any visit.
Low titer is defined as an inhibitor level of 0.5 – 5 Bethesda units (BU).
High titer is defined as an inhibitor level of >5 BU.

Table 8. Blood and factor products used* by people enrolled in UDC

	Hemophilia A n = 9264		Hemophilia B n = 2526		VWD n = 3484	
Treatment product	Number	Percent	Number	Percent	Number	Percent
Recombinant factor	5876	63.4	1420	56.2	11	0.3
Monclonal factor VIII	1443	15.6	3	0.1	5	0.1
Other human factor VIII	191	2.1	2	0.1	641	18.4
Porcine factor VIII	12	0.1	0	--	0	--
Purified factor IX	8	0.1	483	19.1	0	--
Prothrombin complex	29	0.3	25	1.0	0	--
Activated prothrombin complex	299	3.2	22	0.9	0	--
Cryoprecipitate or FFP	55	0.6	10	0.4	52	1.5
Desmopressin	766	8.3	8	0.3	1416	40.6
None used	1108	12.0	601	23.8	1383	39.7

*Any use of the product(s) during the 12-month period preceding UDC enrollment.
NOTE: Individuals may have used more than one type of treatment product.

Figure 9. Prevalence of multiple treatment product use among people with hemophilia in UDC who use treatment products by age

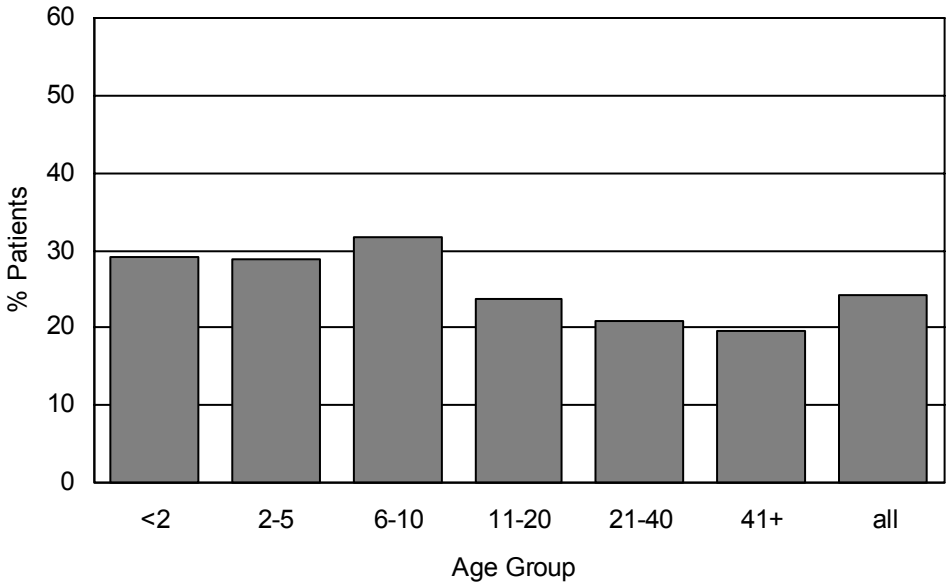


Table 9. Prevalence of multiple factor product use among people with hemophilia by treatment type

Treatment	Total using any product*	Number on Multiple Products (%)
Episodic Care	6942	1655 (23.8)
Intermittent Prophylaxis	594	133 (22.4)
Continuous Prophylaxis	2362	577 (24.4)

*Total number of people using any product is not equal to total number of people with hemophilia because people on immune tolerance are not included in this table.

Table 10. Prevalence of multiple factor product use among people with hemophilia by disease severity

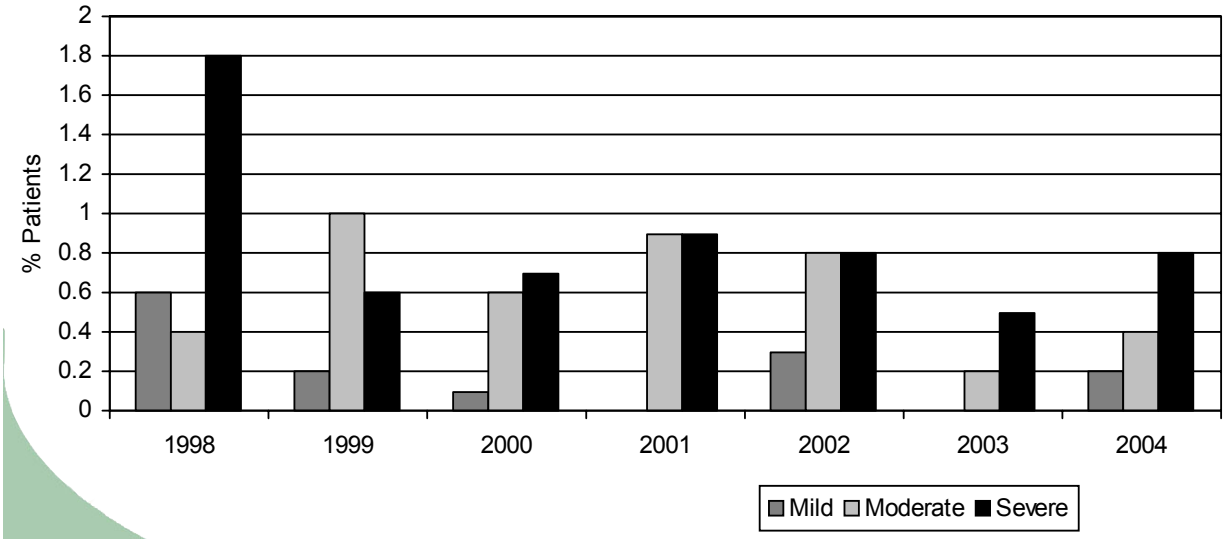
Severity	Total using any product	Number on Multiple Products (%)
Mild	1914	561 (29.3)
Moderate	2187	523 (23.9)
Severe	5915	1325 (22.4)
ALL	10016	2409 (24.1)

Table 11. Prevalence of multiple factor product use among people with hemophilia by current inhibitor titer*

Hemophilia A	Total using any product	Number on Multiple Products (%)
Negative	5261	1306 (24.8)
Low Titer	377	112 (29.7)
High Titer	284	122 (43.0)
Missing	2177	589 (27.1)
Hemophilia B	**Total using any product**	**Number on Multiple Products (%)**
Negative	1210	152 (12.6)
Low Titer	23	3 (13.0)
High Titer	31	11 (35.5)
Missing	653	114 (17.5)

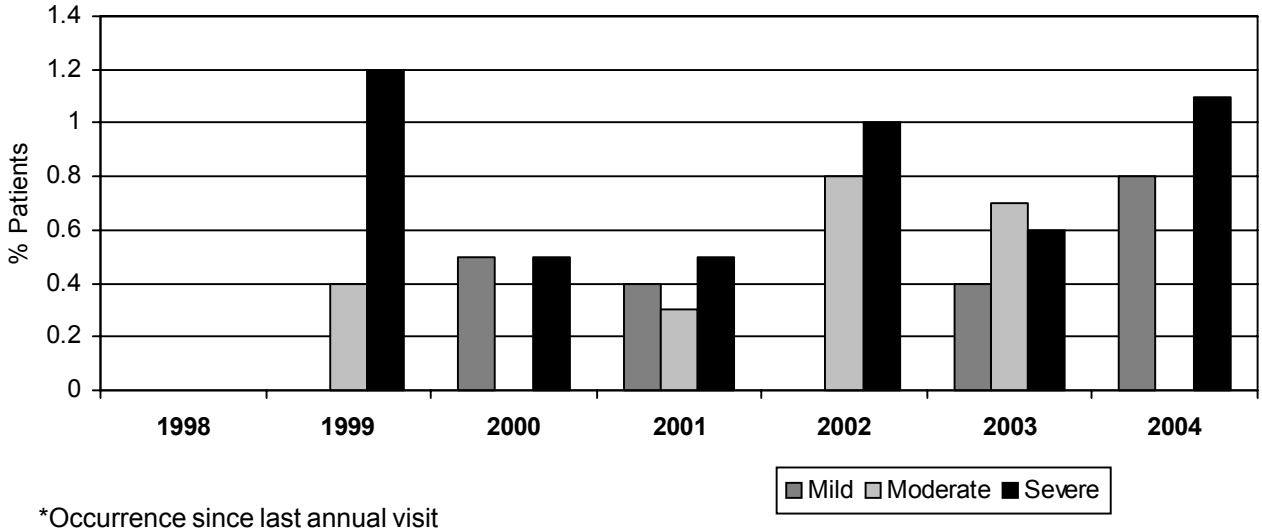
* Inhibitor titer is determined by the highest reported inhibitor titer for any visit. Low titer is defined as an inhibitor level of 0.5 – 5 Bethesda units (BU). High titer is defined as an inhibitor level of >5 BU.

Figure 10. Prevalence of intra-cranial hemorrhage* in people with hemophilia A by severity, May 1998-December 2004



*Occurrence since last annual visit

Figure 11. Prevalence of intra-cranial hemorrhage in people with hemophilia B by severity, May 1998 - December 2004



*Occurrence since last annual visit

Table 12. Joint complications among people enrolled in UDC*

	Hemophilia			VWD		
	Mild n (%)	Moderate n (%)	Severe n (%)	Type 1 n (%)	Type 2 n (%)	Type 3 n (%)
Target joint **	153 (5.0)	501 (18.8)	1991 (33.1)	35 (1.4)	4 (1.1)	33 (14.0)
Invasive procedure	70 (2.3)	84(3.2)	508(8.4)	28 (1.1)	5 (1.3)	14 (5.9)
Joint infection	23(0.8)	16 (0.6)	80 (1.3)	20 (0.8)	3 (0.8)	1(0.4)
Used cane	380 (12.5)	594 (22.3)	1798(29.9)	136 (5.4)	24 (6.4)	43 (18.2)
Used wheelchair	86 (2.8)	127(4.8)	607 (10.1)	50 (2.0)	11(2.9)	16 (6.8)
Any activity restriction	499 (16.5)	745(28.0)	2505 (41.6)	200 (8.0)	38 (10.1)	67 (28.4)

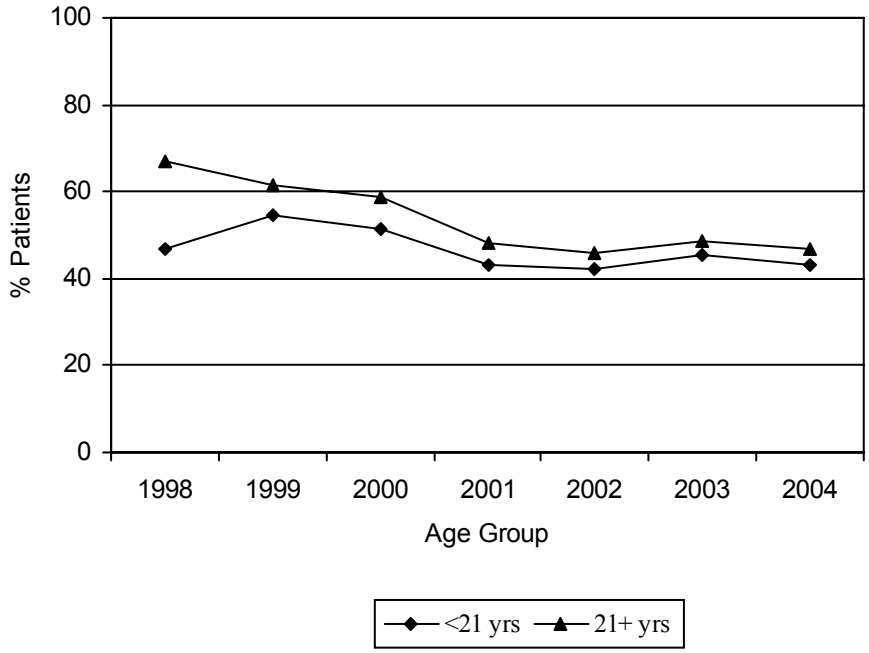
*Includes people 2 years of age or older
**Please see Technical Notes (page33) for the definition of a target joint

Table 13. Joint limitations among people enrolled in UDC*

	Hemophilia			VWD		
	Mild	Moderate	Severe	Type 1	Type 2	Type 3
Number of patients	2763	2401	5166	2324	344	214
Mean indicator* *value	55.1	87.1	148.6	17.9	27.9	70.5
Standard deviation	104.5	151.9	209.2	88.5	80.5	116.7

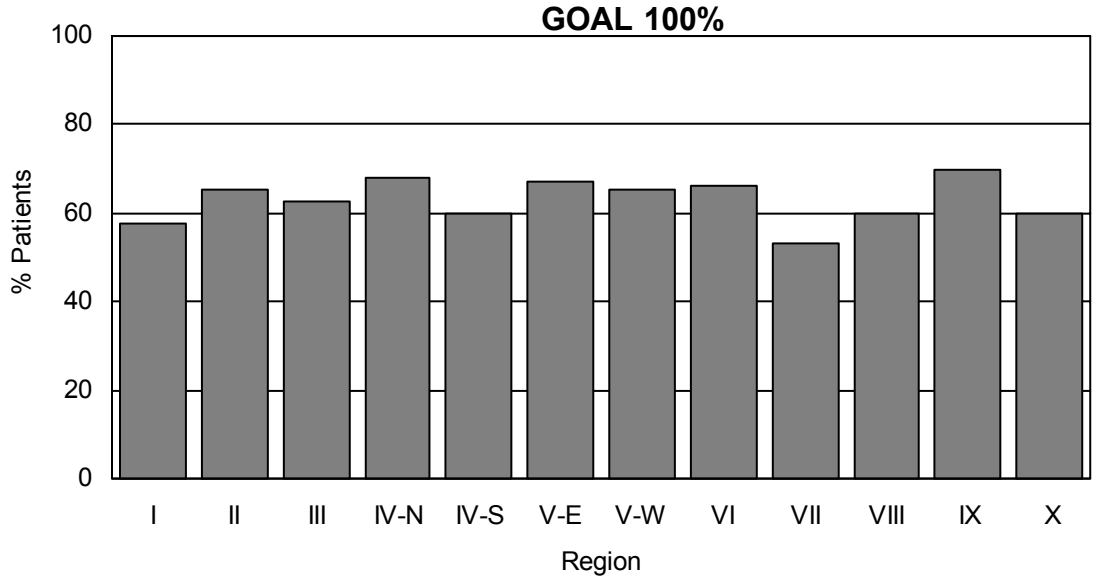
* Includes people 2 years of age or older
**Indicator is the total number of degrees of range of motion less than normal for five joints. The joint motions measured and normal values used (in parentheses) are: hip extension (30); hip flexion (120); knee flexion (135); knee extension (0); shoulder flexion (180); elbow flexion (150); elbow extension (0); elbow pronation and supination (80); ankle dorsiflexion (20); ankle plantar flexion (50). Any hyperextension of the knee or elbow is included in the calculation. In UDC, limitations in knee and elbow extension are recorded as negative numbers. Patients with missing measures for any of the joints are excluded from the analyses. As an example, patients with mild hemophilia have on average 55.6 degrees less than normal range of motion across ten joints. Because the sum of all of the normal measures is 1,690 degrees, this represents an overall 3.3% loss in range of motion.

Figure 12. Prevalence of natural or acquired immunity to hepatitis A virus over time among people with hemophilia enrolled in UDC*



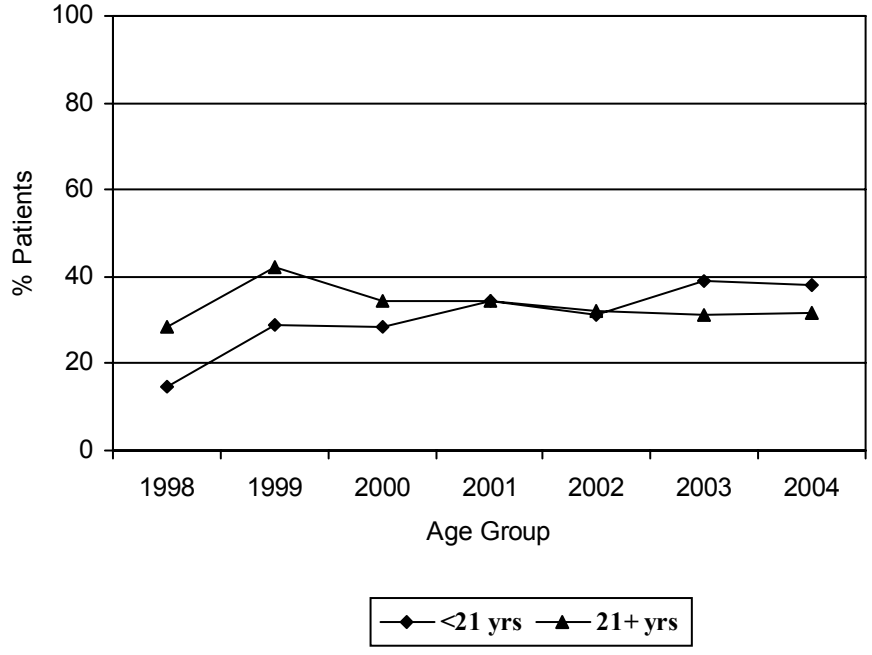
* Includes people 2 years of age or older

Figure 13. Regional distribution of natural or acquired immunity to hepatitis A virus among people with hemophilia enrolled in UDC*



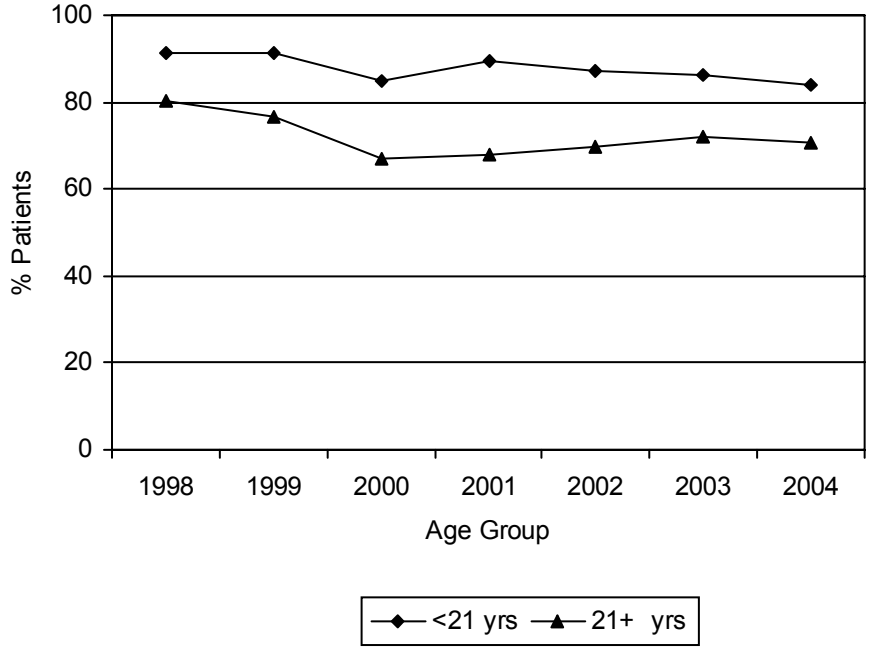
* Includes people 2 years of age or older

Figure 14. Prevalence of natural or acquired immunity to hepatitis A virus over time among people with VWD enrolled in UDC*



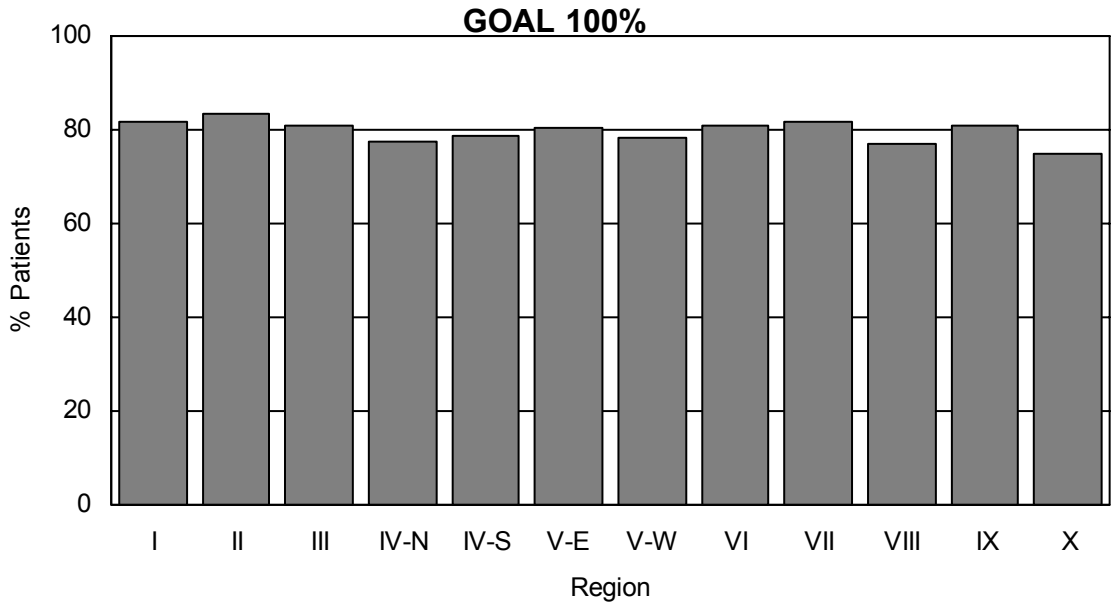
* Includes people 2 years of age or older

Figure 15. Prevalence of natural or acquired immunity to hepatitis B virus over time among people with hemophilia enrolled in UDC*



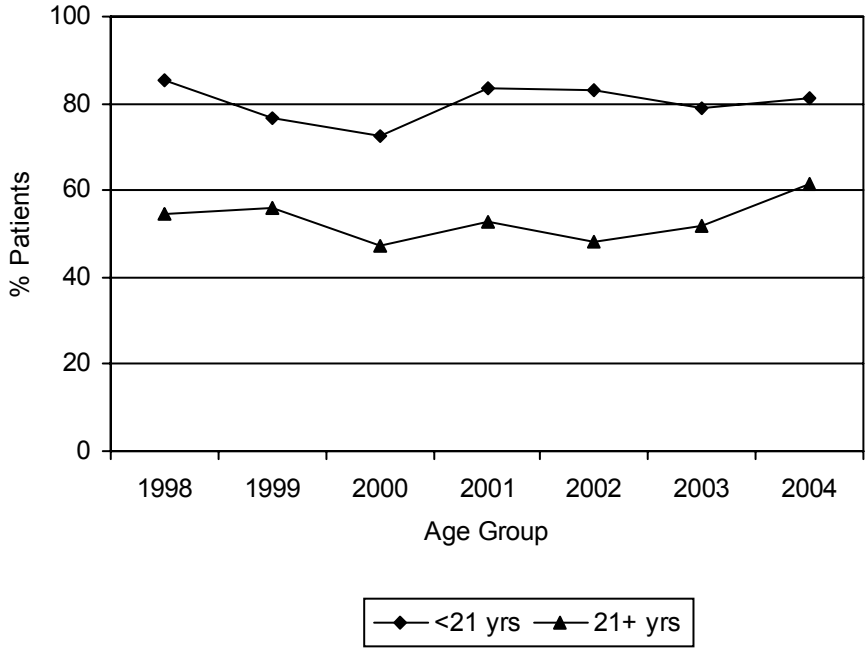
* Includes people 2 years of age or older

Figure 16. Regional distribution of natural or acquired immunity to hepatitis B virus among people with hemophilia enrolled in UDC*



* Includes people 2 years of age or older

Figure 17. Prevalence of natural or acquired immunity to hepatitis B virus over time among people with VWD enrolled in UDC*



* Includes people 2 years of age or older

Figure 18. Prevalence of hepatitis C virus infection among people with bleeding disorders enrolled in UDC

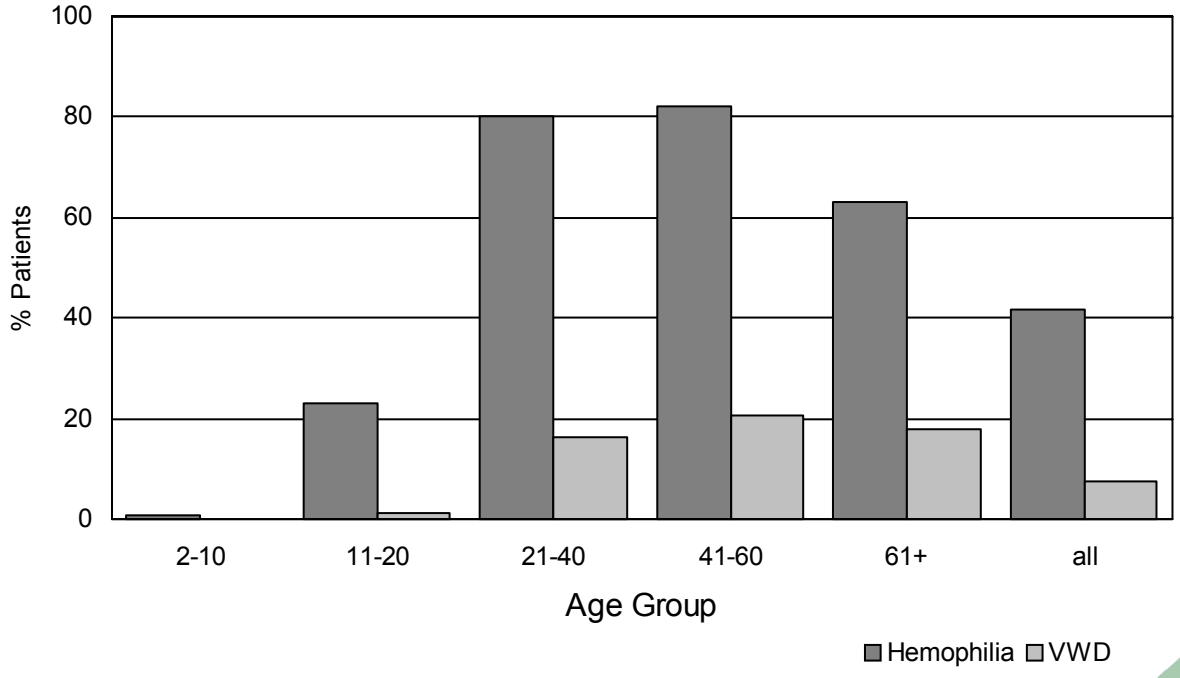
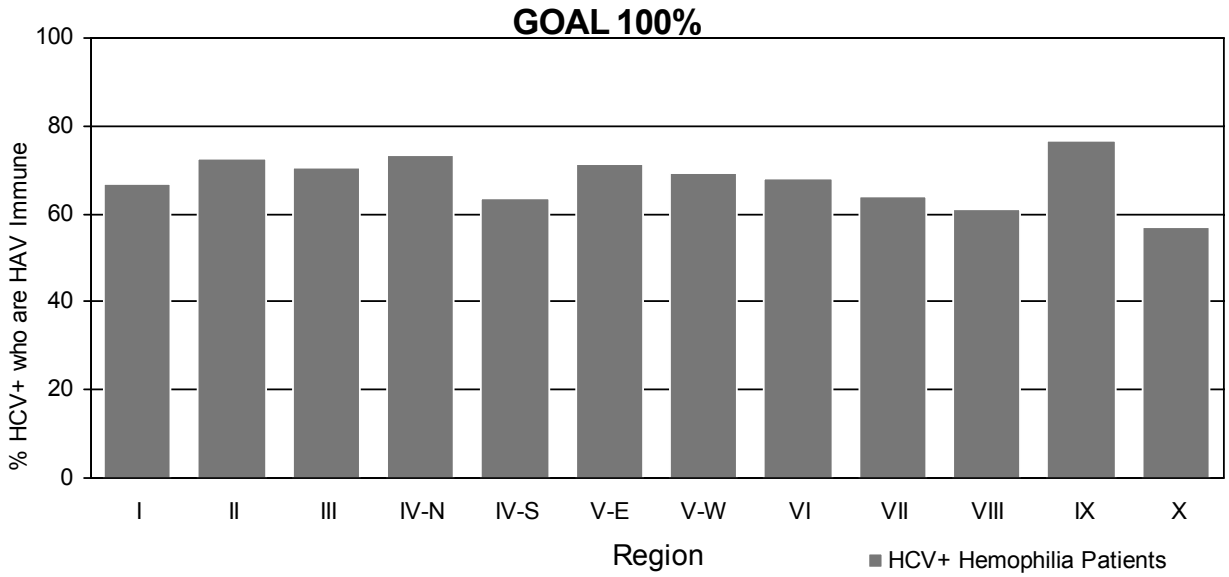


Figure 19. Prevalence of natural or acquired immunity to hepatitis A among people with hemophilia infected with hepatitis C enrolled in UDC*



* Includes people 2 years of age or older

Figure 20. Prevalence of human immunodeficiency virus infection among people with bleeding disorders enrolled in UDC

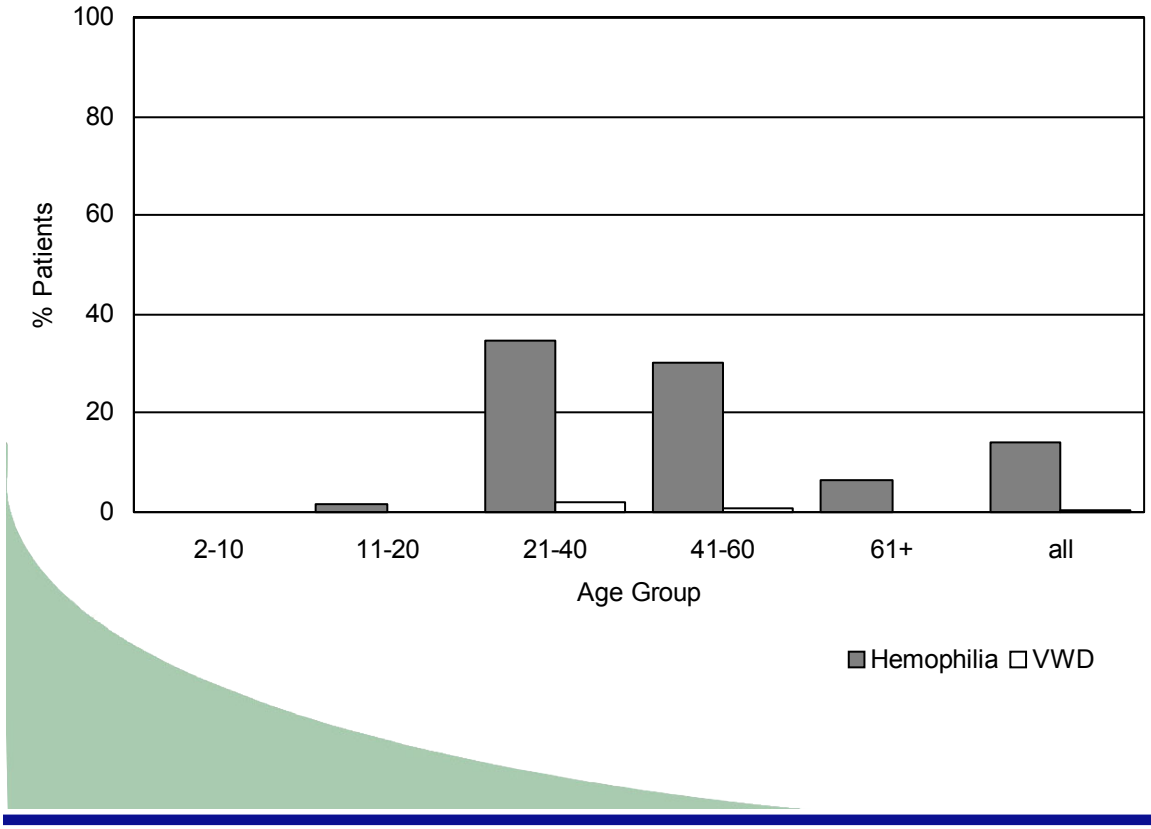


Table 14 Hemophilia A: Number of people on continuous prophylaxis

	Level of Severity					
	Mild		Moderate		Severe	
Age Group (years)	Total	N (%)	Total	N (%)	Total	N (%)
<2	7	0 (0.0)	11	1 (9.1)	34	6 (17.7)
2-5	181	3 (1.7)	171	24 (14.0)	615	328 (53.3)
6-10	320	4 (1.3)	298	62 (20.8)	759	483 (63.6)
11-15	370	4 (1.1)	299	78 (26.1)	836	469 (56.1)
16-20	347	1 (0.3)	275	42 (15.3)	773	278 (36.0)
21-25	175	0 (0.0)	148	9 (6.1)	537	105 (19.6)
31-30	119	2 (1.7)	93	2 (2.2)	315	24 (7.6)
31+	853	2 (0.2)	493	22 (4.5)	1235	112 (9.1)

Table 15. Hemophilia B: Number of people on continuous prophylaxis

	Level of Severity					
	Mild		Moderate		Severe	
Age Group (years)	Total	N (%)	Total	N (%)	Total	N (%)
< 2	2	0 (0.0)	7	1 (14.3)	10	3 (30.0)
2-5	52	0 (0.0)	87	8 (9.2)	97	45 (46.4)
6-10	84	2 (2.4)	132	14 (10.6)	142	74 (52.1)
11-15	111	1 (0.9)	149	16 (10.7)	139	56 (40.3)
16-20	76	0 (0.0)	116	8 (6.9)	134	31 (23.1)
21-25	38	0 (0.0)	71	0 (0.0)	81	15 (18.5)
31-30	32	1 (3.1)	53	3 (5.7)	58	8 (13.8)
31+	274	1 (0.4)	280	4 (1.4)	301	29 (9.6)

Table 16. Prevalence of overweight and obesity among UDC participants and the US population

Overweight

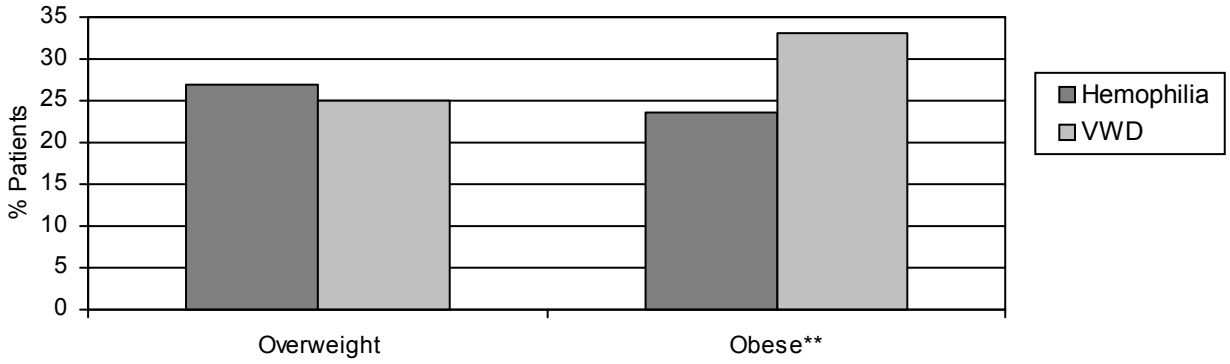
Age Group	Hemophilia	VWD	US Population*
2-12	20.6%	22.1%	13.7%
13-19	20.8%	21.1%	11.5%
20+	34.5%	30.1%	32.6%

Obese

Age Group	Hemophilia	VWD	US Population*
20+	23.5%	33.0%	22.3%

*Based on data from the third National Health and Nutrition Examination Survery

Figure 21. Prevalence of overweight and obesity among people in UDC *



* Includes people 2 years of age or older

**Proportion of people who are obese with VWD is significantly higher than the proportion of people with hemophilia who are obese ($p \geq 0.05$).

Table 17. Prevalence of overweight and obesity among UDC participants by hemophilia severity and VWD type*

Hemophilia

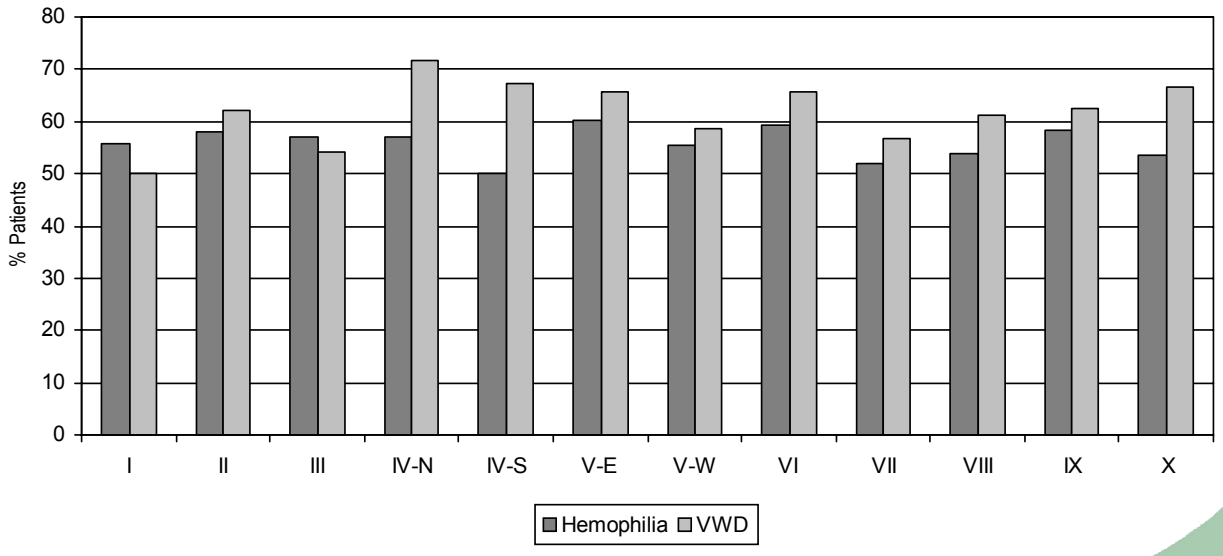
Severity	Overweight (all ages)	Obese (age 20+)
Mild	29.2%	29.2%
Moderate	29.0%	25.8%
Severe	25.0%	19.3%

VWD

Type	Overweight (all ages)	Obese (age 20+)
Type 1	24.8%	33.8%
Type 2	25.8%	27.1%
Type 3	27.5%	32.1%
Other/Unknown	24.0%	35.8%

* Includes people 2 years of age or older

Figure 22. Prevalence of overweight and obesity among people in UDC (age ≥20) by region



Technical Notes

Eligibility Requirements

To participate in UDC, patients must receive care in a federally funded HTC and meet at least one of the following criteria: (1) be 2 years of age or older with a bleeding disorder due to congenital deficiency or acquired inhibitors in which any of the coagulation proteins is missing, reduced, or defective and has a functional level of less than 50 %; or (2) be 2 years of age or older with a diagnosis by a physician of von Willebrand disease. Individuals specifically excluded from participation in UDC include persons with any of the following: (1) an exclusive diagnosis of a platelet disorder, (2) thrombophilia, or (3) coagulation protein deficiencies due to liver failure.

Data Collection

UDC data are collected during a participant's "annual visit", which ideally should occur once each calendar year (January—December), with the interval between visits as close as possible to 12 months. Data are collected according to guidelines and definitions detailed in surveillance manuals provided to HTC staff by CDC. Informed consent for participation is obtained each year. Demographic information and reasons for refusal are obtained using a patient refusal form for all eligible people who decline to participate. To protect patient confidentiality, all data sent to CDC do not contain personal identifying information, but rather use a unique 12-digit code that is generated by a computer software program supplied to HTCs by CDC.

Eligible participants are registered into UDC through a registration form completed by HTC staff; information collected on this form includes patient demographic, diagnostic, and historical information. Month and year of birth are used to calculate age on the last day of the current year. Information on race and ethnicity is obtained from clinic records and might be based either on self-report or on observations made by care providers. During the annual visit, clinical information is recorded on a standardized data collection form (annual visit form). In addition to information about education, employment status, and health insurance, data are also collected about the type of treatment (episodic vs. prophylactic), presence and treatment of inhibitors, the number of bleeding episodes experienced (based on infusion logs or patient recall), the type and brand name of all factor concentrates or other treatment products used, and whether or not clotting factor is infused at home.

Information regarding infectious diseases is also collected, including risk factors and clinical signs, symptoms, and laboratory markers of liver disease. Data are also recorded about any therapy for chronic hepatitis; the status of vaccination for hepatitis A and B viruses; and, among patients with an intravenous access device, the occurrence of a device-associated infection. People $\geq$16 years of age who are HIV-infected are asked several questions concerning risk-reduction activities, including partner testing and condom use.

Data are also collected on joint disease, including the use of walking aids, the occurrence of joint infections, and measures of impact of joint disease on daily activities. During the visit, range of motion measurements on five joints (hip, knee, shoulder, elbow, and ankle) are taken by a physical therapist or other trained health care

provider according to detailed guidelines provided in a reference manual supplied by CDC. All health care providers performing these measurements are trained and certified by regional physical therapists who have themselves received centralized training. In addition, information about whether a particular joint is a "target joint" or whether the participant has required the use of an orthopedic appliance or has undergone an invasive orthopedic procedure is collected. In UDC, a target joint is defined as a joint in which recurrent bleeding has occurred on four or more occasions during the previous 6 months.

All data collection forms are sent overnight to CDC where they are then key entered into a computer database using double-entry software to minimize data entry errors. Data are then screened for omissions, inconsistencies, and unusual values that possibly represent abstraction or data-entry errors. Error reports are generated and faxed to the HTC, where a designated UDC contact uses available information to resolve discrepancies and complete missing data items.

Laboratory Testing

During the annual visit, a blood specimen is obtained from each participant in UDC. Each specimen is processed by HTC personnel according to guidelines provided by CDC that are designed to minimize the effects of storage and shipment on subsequent analyses. Samples are shipped overnight to the CDC Serum Bank where they are aliquoted and stored. A portion of each specimen is sent to the Eugene B. Casey Hepatitis Laboratory at Baylor College of Medicine in Houston, Texas. A second portion is sent to the HIV testing laboratory at CDC. The remainder of the specimen is stored in the CDC Serum Bank for future blood safety investigations, as needed.

Testing for hepatitis A, B, and C viruses follows algorithms designed to determine with the highest probability the patient's status with regard to exposure to or infection with these viruses. Information provided by HTC staff on a Laboratory Form, including the results of previous local testing and vaccination history, is used by personnel at the testing laboratory to provide a detailed interpretation of the test results.

Testing for HIV follows algorithms designed to determine patient status with regard to infection with HIV-1 and HIV-2. The results of all laboratory testing are reported to the HTC using the CDC unique code that can be matched to the patient only by HTC staff.

Mortality Reporting

Deaths occurring among all HTC patients (regardless of whether they have been enrolled in UDC) are reported to CDC using a mortality form. Data collected include age at death, sex, race or ethnicity, type and severity of disease, and whether or not blood products had been used during the year prior to death. Additionally, information about the death, including the date, cause (primary and contributing), and whether or not an autopsy was performed, is also collected.

Tabulation and Presentation of Data

Data in this report are provisional. The data represent the most current data available from an on-going surveillance project. Future reports will include expanded data tables to cover subsequent surveillance periods and will provide the results of more detailed analyses of available data and findings from special studies.

Acknowledgements

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Yale University School of Medicine
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Maine Medical Center
Scarborough, ME
Dartmouth-Hitchcock Hemophilia Center
Lebanon, NH
Rhode Island Hospital
Providence, RI
Vermont Regional Hemophilia Center
Burlington, VT
UCONN Hemophilia Treatment Center
Farmington, CT
Boston Hemophilia Center- Children's Hospital
Boston, MA
Boston Hemophilia Center- Brigham and Women's
Boston, MA

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St. Michael's Medical Center
Newark, NJ
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SUNY Upstate Medical University-Pediatric Program
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Eastern Michigan Hemophilia Treatment Center
Flint, MI

DeVos Children's Hospital
Grand Rapids, MI
Ohio State University Medical Center
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Cincinnati Children's Hospital Medical Center
Cincinnati, OH
University of Cincinnati Medical Center
Cincinnati, OH
Forum Health, Youngstown Hemophilia Center
Youngstown, OH
Columbus Children's Hospital
Columbus, OH
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Toledo, OH
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Minneapolis, MN
Mayo Comprehensive Hemophilia Center
Rochester, MN
MeritCare Hospital DBA Roger Maris Cancer Center
Fargo, ND
Hemophilia Outreach Centre
Green Bay, WI
Gundersen Clinic
LaCrosse, WI
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Madison, WI
Sacred Heart Hospital
Eau Claire, WI
Rush Children's Hospital
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Michael Reese Hospital - Adult
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Honolulu, HI
University of California at Davis
Sacramento, CA
University of California, San Francisco
San Francisco, CA
Orthopedic Hospital of Los Angeles
Los Angeles, CA
Children's Hospital, San Diego
San Diego, CA
Children's Hospital of Orange County
Orange, CA
Children's Hospital Oakland
Oakland, CA
City of Hope National Medical Center
Duarte, CA
Hemophilia and Thrombosis Center of Nevada
Las Vegas, Nevada
Guam Comprehensive Hemophilia Care Program
Hagatna, GU
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Madera, CA
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Oregon Hemophilia Treatment Center
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Alaska Hemophilia Program
Anchorage, AK
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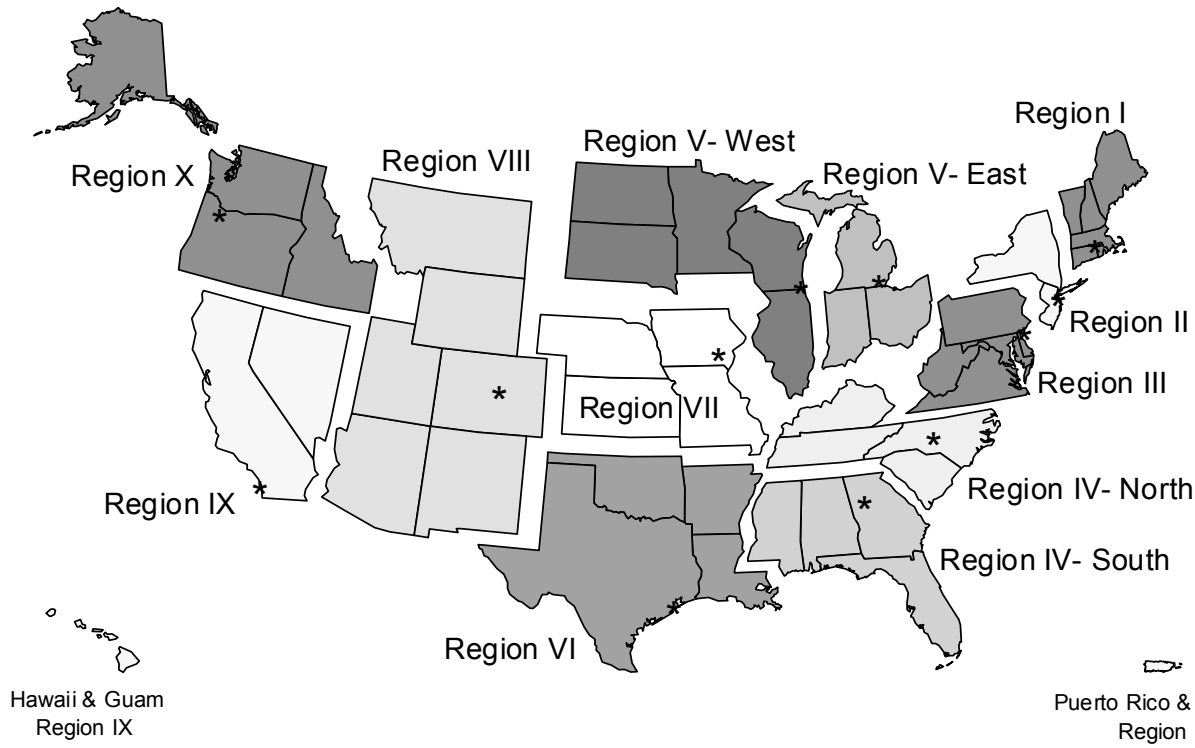
East Lansing MI

Hemophilia Treatment Center Regions



*Location of regional core center.

Department of Health and Human Services
Centers for Disease Control and Prevention