

## » Abstract

### Introduction and Objectives:

People with bleeding disorders often require regular intravenous infusions of clotting factor to prevent or treat bleeding episodes in the home. Although the ideal method of administration is via peripheral IV access, some may require placement of a central venous access device (CVAD) to facilitate treatment, especially with frequent administration. Central venous line infections represent potentially life-threatening complications that are the most common cause of hospitalization in children with hemophilia. In addition to antibiotic treatment, replacement of the CVAD may be required.

### Materials and Methods:

A retrospective, longitudinal analysis of central venous line (CVL) infections among hemophilia patients receiving intravenous clotting factor dispensed through Accredo home healthcare services was conducted. Patients were included based on the presence or placement of a CVAD for at least 15 days in a study year and a diagnosis of coagulation defects using ICD-9 diagnostic codes. Patients were identified in the study years 2009 through 2013. The patient-reported infection rate was defined as the number of bloodstream infections per 1,000 patient catheter days.

### Results:

The sample consisted of 777 hemophilia patients that met all inclusion criteria. The sample was predominantly male (90.4%) with an average age of 19.9 years (SD 19.3). This population encompassed 763,017 catheter days during the 2009-2013 study period, with an average yearly number of catheter days of 196.4 days. The yearly infection rate ranged from 0.121 to 0.281 per 1000 catheter days in 2012 and 2010 respectively. The overall infection rate was 0.194 per 1000 catheter days.

### Conclusion:

Infusion by CVAD is an important option for patients with bleeding disorders and requires strict attention to sterile technique. This is the largest sample size published to date and overall low rate of infection indicates that factor infusions can be managed safely in the homecare setting.

## » Background

Prophylaxis has become the recommended treatment regimen for people with severe hemophilia. The Medical and Scientific Advisory Council of the National Hemophilia Foundation recommends that prophylaxis be started prior to the onset of frequent bleeding due to the demonstrated benefit on joint health.<sup>1</sup> This requires frequent intravenous infusions in the very young who have small vasculature.<sup>2</sup> Reliable venous access is crucial to the success of prophylaxis, and while peripheral access is the preferred route of administration, it may require placement of a central venous access device for reliable venous access.<sup>3</sup> In addition, the development of an inhibitor and its recommended treatment with immune tolerance induction make reliable venous access even more critical in some patients.<sup>4</sup> Placement of central venous access devices eases the burden of prophylaxis and immune tolerance therapy.<sup>3</sup>

Potential complications include thrombosis, infection and malfunction and can lead to significant long term problems including progressive joint damage and failure of immune tolerance therapy.<sup>5</sup>

Rates of infection are overall relatively low in people with bleeding disorders, but they vary from one area to another. In the meta-analysis by Valentino and colleagues, the incidence of infection was 0.66 infections per 1000 CVAD days.<sup>6</sup>

## » Methods

### Objective:

The objective of this study is to evaluate the rate of infection in a large population receiving clotting factor intravenously through a central venous access device in the home care setting.

### Patient Sample:

A retrospective, longitudinal analysis of central venous line (CVL) infections among hemophilia patients receiving intravenous clotting factor dispensed through Accredo home healthcare services was conducted. Patients were included based on the presence or placement of a CVAD for at least 15 days in a study year and a diagnosis of coagulation defect using ICD-9 diagnostic codes. Patients were identified in the study years 2009 through 2013. The patient-reported infection rate was defined as the number of bloodstream infections per 1,000 patient catheter days. Infection rates are reported across study years.

Patients who were enrolled as Express Scripts' clients that did not allow their data to be used for research were excluded from the final sample, leaving a study sample of 777 people with bleeding disorders and central venous access device in place for at least 15 days.

## » Results

The sample consisted of 777 hemophilia patients that met all inclusion criteria. The sample was predominantly male (90.7%) with an average age of 19.9 years (SD 19.4). This population encompassed 763,017 catheter days from January 1, 2009 through December 31, 2013.

The majority of the population had hemophilia A (75%) with 12% having hemophilia B, 9% von Willebrand disease and 4% other coagulation difficulties.

There were 670 patients who did not have an inhibitor with 687,635 line days with a cumulative central line infection rate of 0.16/1000 catheter days. While the cumulative rate of infection for the 107 patients who had an inhibitor was 0.36/1000 catheter days.

## » Discussion

The patients in this study provide a nationwide sample and therefore represent clinical practices of many hemophilia treatment centers. Accredo's specialty clinical care service model is consistent across the country and serves to reinforce the teaching of the individual centers.

The cumulative rate of infection was 0.19 per 1000 catheter days compared to 0.66 per 1000 catheter days in the large meta-analysis.<sup>4</sup> People who did not have an inhibitor had a CVL infection rate 51% lower than people who had an inhibitor.

The yearly and overall rate of infection in people with inhibitors in this study compares favorably with those from the International Immune Tolerance study (yearly 0.36/1000 catheter days compared to 0.94/1000 catheter days).<sup>7</sup>

Limitations include that it is retrospective and that patient-reported data may be incomplete.

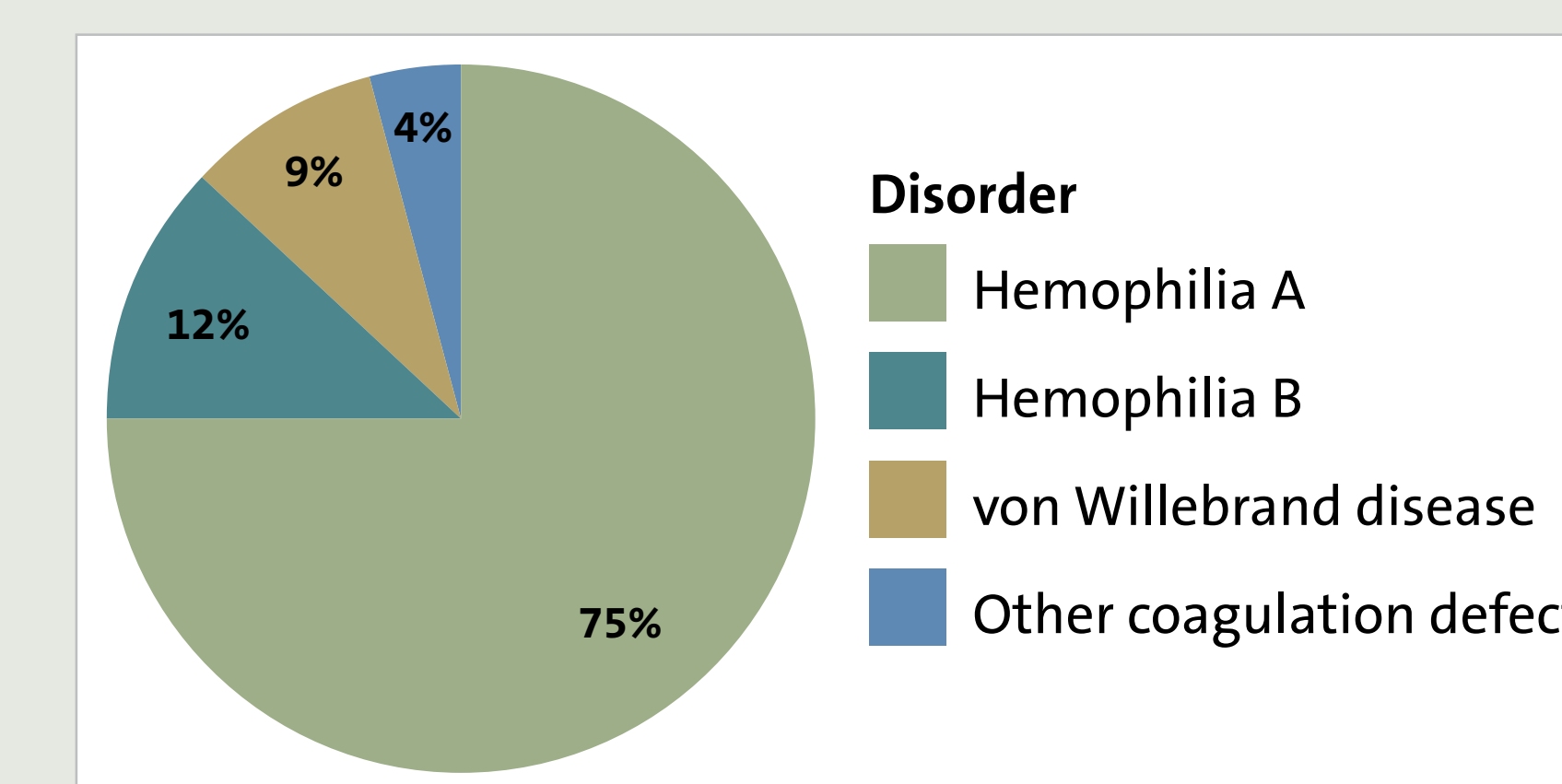
## » Conclusion

The study confirms the central venous access devices can be safely used to ease factor infusions in patients who require frequent intravenous infusions in the home care setting.

## » References

- 1 Medical and Scientific Advisory Council (MASAC). Document 241. MASAC recommendation concerning prophylaxis (regular administration of clotting factor concentrate to prevent bleeding). New York, NY: National Hemophilia Foundation; February 2016.
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- 3 Santogostino E, Mancuso ME. Venous access in haemophilic children: choice and management. *Haemophilia*. 2010;16(Suppl 1):20-24.
- 4 Valentino LA, Kawji M, Grygotis M. Venous access in the management of hemophilia. *Blood Rev*. 2011;25:11-5.
- 5 Carcao MD. Side effects and venous access issues with immune tolerance therapy. *Haemophilia*. 2009;15:494-500.
- 6 Valentino LA, Ewenstein B, Navickis RJ, Wilkes MM. Central venous access devices in haemophilia. *Haemophilia*. 2004;10:134-46.
- 7 Rodriguez V, Mancuso ME, Warard D, Hay CRM et al. Central venous access device (CVAD) complications in haemophilia with inhibitors undergoing immune tolerance induction: lessons from the international immune tolerance study. *Haemophilia*. 2015;21:e369-74.

Characteristic	Average (StdDev)/Pct.	Median
Age (years)	19.9 (19.4)	12
Pct. Male	90.7%	



Inhibitor Status	n	Year	Active days	Infections	Rate/1000 days
Negative	670	2009	99742	16	0.16
		2010	129904	36	0.28
		2011	145044	27	0.19
		2012	148800	15	0.10
		2013	164145	27	0.16
		Total	687635	121	0.18
Positive	107	2009	9398	6	0.64
		2010	12673	4	0.32
		2011	14490	4	0.28
		2012	16677	5	0.30
		2013	22144	8	0.36
		Total	75382	27	0.36
Total Population	777	2009	109140	22	0.20
		2010	142577	40	0.21
		2011	159534	31	0.19
		2012	165477	20	0.12
		2013	186289	35	0.19
		Total	763017	148	0.19

