

Healthcare expenditures for males with haemophilia and employer-sponsored insurance in the United States, 2008

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Summary. Although hemophilia has a potentially high economic impact, published estimates of health care costs for Americans with hemophilia are sparse and non-specific as to the non-bleeding complications of the disease. The objective of this study is to estimate average annual health care expenditures for people with hemophilia covered by employer-sponsored insurance, stratified according to the influence of age, type of hemophilia [A (factor VIII deficiency) versus B (factor IX)], presence of neutralizing alloantibody inhibitors and exposure to blood-borne viral infections. Data from the MarketScan[®] Commercial and Medicare Research Databases were used for the period 2002–2008 to identify cases of hemophilia and to estimate mean and median medical expenditures during 2008. A total of 1,164 males with hemophilia were identified with continuous enrollment during 2008, 933 with hemophilia A and 231 with hemophilia B. Mean health care expenditures were

\$155,136 [median \$73,548]. Mean costs for 30 (3%) males with an inhibitor were 5 times higher than for males without an inhibitor, approximately \$697,000 [median \$330,835] and \$144,000 [median \$73,321], respectively. Clotting factor concentrate accounted for 70%–82% of total costs. Average costs for 207 adults with HCV or HIV infection were 1.5 times higher than those for adults without infection. Hemophilia treatment is costly, particularly for individuals with neutralizing alloantibody inhibitors who require bypassing agents. Efforts to understand the cause of inhibitors are needed so that prevention strategies can be implemented and the excess costs resulting from this serious complication of hemophilia care can be avoided.

Keywords: claims data, cost of care, employer-sponsored insurance, haemophilia, inhibitor, MarketScan Commercial and Medicare databases

Introduction

Haemophilia is a rare bleeding disorder, affecting approximately 1 in 5000–10 000 live-born males, that can require regular treatment with clotting factor concentrate [1–3]. Bleeding typically occurs into soft tissues and joints, with repeated haemorrhage leading to pain, deformity and disability [1,4]. Despite the relatively small number of affected individuals, an estimated 20 000 individuals in the United States, haemophilia has a large impact on individuals, health care systems, and society [5,6].

Published estimates suggest that average (mean) healthcare costs for Americans with haemophilia are approximately \$100,000 to \$150,000 per year [7].

Inhibitors are antibodies that render the treatment

products ineffective in controlling bleeding and have been reported to occur in 10–15% of people with haemophilia. Approximately 4% of haemophilia patients receive bypassing agents to manage haemophilia [8]. Previous studies have found that the mean healthcare costs of treating people with bypassing agents for inhibitors can be 2–3 times higher than those of people without inhibitors [9–11,12 excluding outliers]. In addition, one study found that the presence of HIV or HCV infection resulted in 59% greater healthcare costs compared with costs for haemophilia alone among adults [8].

Previous estimates of haemophilia costs were based on relatively small numbers of patients, which may lead to biased estimates of cost since a small sample is less likely to be representative of the whole population. The purpose of this study was to estimate average annual costs of health care for people with haemophilia enrolled in employer-sponsored insurance

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by age, type of haemophilia, inhibitor status, and viral infection status using US health insurance claims data.

Methods

Data

The data for this study were obtained from the MarketScan® Commercial and Medicare Supplemental and COB databases (Thomson Reuters Inc., New York, NY, USA) for the period 2002–2008. Between them, the databases provided data on approximately 37 million active employees, early retirees, COBRA participants (Commercial database), and Medicare-eligible retirees (Medicare database) and their dependents in 2008. Both groups are insured by employer-sponsored plans.

The databases comprised four sources: outpatient drug claims, outpatient service claims, inpatient service claims and inpatient admission claims. The data use three types of medical codes: (i) International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM); (ii) healthcare common procedure codingsystem (HCPCS); and (iii) National Drug Code

(NDC). Demographic information on gender, age and annual enrolment, as well as information on medical costs is provided for all insurance enrollees who are assigned a unique identification code that allows tracking of individuals over time.

Sample selection criteria

Figure 1 presents the process used to identify people with haemophilia. People with haemophilia were identified if they met three criteria: (i) had an insurance claim during the years 2002–2008 with an ICD-9 code for haemophilia (286.0 or 286.1); (ii) were male; and (iii) had records between 2002 and 2008 with either anti-haemophilia drug claims or haemophilia-specific procedure codes (see Table S1 of Appendix). The criteria were developed to minimize coding errors. For example, many females had haemophilia ICD-9 codes. As true haemophilia is rare in females, it is likely that most females coded in this way in the database were either carriers of the haemophilia gene or had another coagulation disorder, but were miscoded.

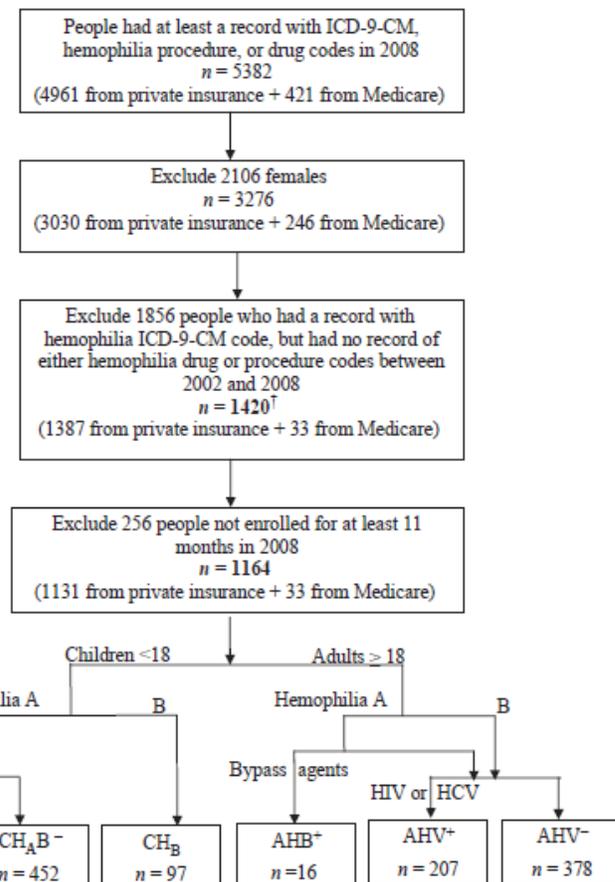


Fig. 1. Flowchart of sample selection.

Note: C = child; HA = haemophilia A;

HB = haemophilia B;

B⁺ = treatment for an inhibitor with bypassing agents;

B⁻ = no treatment for an inhibitor with bypassing agents;

A = adult; H = haemophilia; V⁺ = with blood-borne viral

infection; V⁻ = without blood-borne viral infection.

†About 17.9 million males were enrolled in private health plans and Medicare, on average, for 10 months in 2008.

Prevalence based on claims data was calculated by dividing the number of males with haemophilia by the number of males in employer-sponsored plans, including Medicare Supplemental plans paid by employers. For the purpose of estimating expenditures, the sample was further restricted to individuals with at least 11 months of coverage during 2008 because inclusion of enrollees with partial-year coverage and annual medical expenditures could lead to underestimates of annual costs.

People who were treated for inhibitors to factor VIII with certain anti-haemophilia products referred to as bypassing agents were identified using outpatient visit claims, outpatient drug claims (for home infusion), or inpatient procedure codes for infusion with bypassing agents. As we were not able to identify people with an inhibitor who did not receive these bypassing drugs, the study sample represents a subset of people with an inhibitor.

Adults with haemophilia were determined to be HIV-or HCV-infected based on either diagnosis or specifically anti-HIV or anti-HCV medicine drug codes (Table S1 of Appendix).

Finally, we established six risk groups according to age, type of haemophilia, treatment of an inhibitor with bypassing agents (hereafter referred to as individuals with inhibitors) and infection with HIV or HCV. They are: (i) children (age <18 years) with haemophilia A and inhibitors; (ii) children with haemophilia A without inhibitors; (iii) children with haemophilia B; (iv) adults with haemophilia A or haemophilia B with inhibitors; (v) adults with blood-borne viral infection without inhibitors; and (vi) adults without viral infection or inhibitors (Fig. 1). The few adults with both viral infection and inhibitors were included in the inhibitor group for the analyses.

Outcome measures

The cost of health care was defined as the sum of expenditures by insurers and individuals during 2008. Average costs were calculated for six risk groups in terms of both the mean (total expenditures within the group divided by total number of individuals) and the

median (annual expenditure for the median individual). Significance tests are reported for group differences in mean and expenditures, but not for medians. Mean expenditures have desirable statistical properties, including the ability to aggregate by component and across individuals in the sample.

Clotting factor procedure claims from the inpatient and outpatient files were combined with outpatient drug claims to calculate total clotting factor expenditures. The inpatient claims data in particular do not provide a full breakdown of costs for each procedure code. Therefore, factor costs include the cost of inpatient administration. They also included costs for both factor concentrates and bypassing agents.

Results

All persons with haemophilia

Of the 18 million males covered in 2008, a total of 1420 persons met our criteria and were identified as having haemophilia (Table 1). The prevalence of haemophilia based on the claims data was 0.79 per 10 000 insured males. Age-specific prevalence was highest for males aged 10–19 years, after which the prevalence decreased with age. Overall, the prevalence for children (<age 18; 1.42 per 10 000 males) was significantly higher than that of adults (\geq age 18; 0.57 per 10 000 males, $P < 0.01$).

A total of 1164 (82% of 1420) males with haemophilia were enrolled for at least 11 months in 2008 (Table 2). Of the 1164 males with haemophilia, 80% ($n = 933$) had haemophilia A and 20% ($n = 231$) had haemophilia B. A total of 30 males (3%) were identified as having an inhibitor to factor VIII based on their use of bypassing agents. One-third of people with haemophilia had at least one emergency department (ED) visit and 14% had an inpatient admission. Among those with at least one ED visit or admission, the mean numbers of ED visits and admissions were 2.8 and 1.4, respectively.

Table 2 also shows that annual costs for all males with haemophilia averaged \$155,136 [median \$73,548] in 2008. Mean healthcare costs were higher for

Table 1. Number of males with haemophilia and prevalence of haemophilia by enrolment period restriction, 2008.

Age group	Without enrolment period restriction			With enrolment period restriction (\geq 11 months)		
	Total males	Males with haemophilia	Prevalence (/10 000)	Total males	Males with haemophilia	Prevalence (/10 000)
0–9	2 506 789	301	1.2	1 710 137	243	1.4
10–19	2 713 990	445	1.6	2 043 810	376	1.8
20–29	2 318 390	237	1.0	1 332 213	163	1.2
30–39	2 572 766	126	0.5	1 798 513	103	0.6
40–49	2 881 022	141	0.5	2 239 377	126	0.6
50–59	2 747 651	105	0.4	2 278 569	93	0.4
60–	2 150 167	65	0.3	1 717 371	60	0.3
Total	17 890 775	1420	0.8	13 119 990	1164	0.9

Table 2. Annual costs of care of males with haemophilia by risk group, 2008.

	N	Median	Mean	95th percentile
Healthcare utilization				
No. of admission w ≥ 1 admission	164 (14%)	1.0	1.4	4.0
No. of ED visits w ≥ 1 visit	379 (33%)	1.0	2.8	9.0
Healthcare expenditures				
All	1164	73 548	155 136	560 238
Haemophilia A [‡]	933	78 598	162 054 [†]	578 958
Haemophilia B [‡]	231	55 220	127 194	489 101
Receiving no bypassing agents [§]	903	73 321	144 306 ^{†**}	527 944
Clotting factor [†]	903	51 869	123 154 ^{†**}	489 084
Receiving bypassing agents [§]	30	330 835	696 279	2 459 207
Clotting factor [†]	30	299 651	573 760	2 434 958
Child ^{††}	563	72 374	150 680 [†]	529 024
Adult ^{††}	601	76 088	159 310	613 315

** represents a 1% level of significance.

[†] t test.

[‡] Statistical tests examine the null hypothesis that people with haemophilia A have the same costs of care as people with haemophilia B.

[§] Statistical tests examine the null hypothesis that people who receive bypassing agents have the same costs of care as people who do not receive bypassing agents.

[†] Statistical tests examine the null hypothesis that the costs of clotting factor for people who receive bypassing agents are the same as those for people who do not receive bypassing agents.

^{††} Statistical tests examine the null hypothesis that children have the same costs of care as adults.

individuals with haemophilia A (\$162,054 [median \$78,598]) than those with haemophilia B (\$127,194 [median \$55,220], $P = 0.06$).

Among people with haemophilia A, average annual total costs for people with an inhibitor were 4.8 times higher than total costs for non-inhibitor patients (\$696,279 [median \$330,835] vs. \$144,306 [median \$73,321]; $P < 0.01$). Similarly, the average annual cost for clotting factor was 4.6 times higher among people with an inhibitor (\$573,760 [median \$299,651] vs. \$123,154 [median \$51,869], $P < 0.01$). Clotting factor (including factor concentrates and bypassing agents) accounted for roughly the same proportion of total costs regardless of whether or not an inhibitor was present, 82% and 85%, respectively.

Although annual costs were similar for children and adults overall (\$150,680 [median \$72,374] vs. \$159,310 [median \$76,088], respectively, $P = 0.56$), the amounts varied by 10-year age group ($P < 0.05$; Table S2 of Appendix).

Children with haemophilia

Among 563 children, 466 (83%) had haemophilia A and 14 (3%) of them were treated with a bypassing agent for an inhibitor during 2008 (Table 3). Children with haemophilia A and an inhibitor were on average 3 years younger than those without an inhibitor ($P = 0.02$). All children with inhibitors received clotting factor compared with 85% of those without an inhibitor. Furthermore, compared with children without an inhibitor, a higher proportion of children with an inhibitor had an ED visit in 2008, (71% vs. 36%, $P < 0.01$). Also, among those with at least one ED visit, the mean number of visits was greater among children

with an inhibitor. Similarly, a higher proportion of children with an inhibitor had inpatient admissions (43% vs. 10%, $P < 0.01$).

The average annual cost for children with haemophilia A and an inhibitor was \$831,866 [median \$461,527] in 2008, which was six times higher than that for children with haemophilia A without an inhibitor (\$142,057 [median \$73,659], $P < 0.01$).

Among children without an inhibitor, there was no difference in average age between children with haemophilia A and haemophilia B. Compared with children with haemophilia B, a higher proportion of children with haemophilia A received factor during 2008 (85% vs. 64%, $P < 0.01$) and mean and median costs were 1.5 and 2.0 times higher (\$142,057 [median \$73,659] vs. \$92,546 [median \$36,177], $P < 0.001$). Conversely, a higher proportion of children with haemophilia B had at least one ED visit (49% vs. 36%, $P < 0.05$).

Adults with haemophilia

As shown in Table 4, of 601 adults with haemophilia, 207 (34%) were infected with HIV or HCV, 16 (3%) of whom also had an inhibitor. Adults with an inhibitor were more likely to use clotting factor (100% vs. 74%, $P < 0.01$), more likely to visit the ED (63% vs. 28%, $P < 0.01$) and more likely to require inpatient services (31% vs. 12%, $P < 0.05$) than those without an inhibitor.

Adults with HIV or HCV infection were on average 5 years older than those uninfected ($P < 0.01$). Compared with those without infection, a higher proportion of infected adults received clotting factor in 2008, (91% vs. 74%, $P < 0.01$) and had an inpatient admission (22% vs. 12%, $P < 0.01$). There was no significant difference

Table 3. Characteristics of children with haemophilia by risk group, 2008.

Children	Haemophilia A		
	Receiving no bypassing agents (CH _A B ⁻) ^R	Receiving bypassing agents (CH _A B ⁺) [†]	Haemophilia B (CH _B) ^{††}
No. of people	452	14	97
Age group: N (%)	P = 0.20 [§]		P = 0.21 [†]
0–4	87 (19)	6 (43)	17 (18)
5–9	112 (25)	3 (21)	22 (23)
10–14	170 (38)	3 (21)	32 (33)
15–17	83 (18)	2 (14)	26 (27)
Age (mean)	1	7 ^{*†}	10 [†]
Clotting factor			
No. of people (%)	386 (85)	14 (100) [§]	62 (64) ^{***}
Emergency department (ED) visits			
No. of people (%)	163 (36)	10 (71) ^{***}	48 (49) ^{**}
Frequency among ED visitors	2.3	5.7 ^{***}	2.1 [†]
Type of care: N (% of people who received each type of care)			
Inpatient	44 (10)	6 (43) ^{***}	16 (16) [‡]
Prescription	164 (36)	0 (0) ^{§**}	26 (27) [‡]
Total expenditures (\$)			
Median	73 659	461 527	36 177
Mean	142 057	831 866 ^{***}	92 546 ^{***}
95th percentile	527 944	4 674 076	339 790
Expenditures for clotting factor (\$)			
Median	53 287	375 384	18 996
Mean	124 752	728 737 ^{***}	77 610 ^{***}
95th percentile	489 393	4 141 157	338 048

* and ** represent a 5% and a 1% level of significance, respectively.

[†]t test.

[‡]Chi-square test.

[§]Fisher's exact test.

[†]Statistical tests examine the null hypothesis that the CH_AB⁻ group has the same characteristics as the CH_AB⁺ group.

^{††}Statistical tests examine the null hypothesis that the CH_AB⁺ group has the same characteristics as the CH_B group.

^RReference.

in the proportion of adults who visited EDs by blood-borne viral infection status.

The mean annual cost for adults with an inhibitor (\$577,640 [median \$176,218]) was 3–5 times higher than the costs for adults either with (\$188,056 [median \$116,207], $P < 0.01$) or without (\$125,861 [median \$43,968], $P < 0.01$) HIV or HCV infection. The average annual costs were \$188,056 for infected adults, which was 1.5 times higher than cost for adults without infection (\$125,861, $P < 0.01$).

The cost for clotting factors was 1.4 times (\$151,634 [median \$95,600]) for adults with HIV or HCV infection higher than the costs for adults without the infection (\$107,985 [median \$27,561], $P < 0.01$). Among adults with HIV or HCV infection, clotting factors accounted for 81% of total costs, while the cost of antiviral treatment accounted for 7% (\$13,501). There is no statistically significant difference in total costs or costs for clotting factors among three different blood-borne viral infection groups (HIV only, HCV only, and co-infection group; see Fig. S1 of Appendix).

Discussion

This is the second published study to use US health insurance claims data to identify insured persons with

haemophilia and to investigate their use of health services and associated expenditures. Compared with the first study, which identified just 173 adults with haemophilia from approximately 21 million males enrolled in commercial health plans [8], we identified 601 adult males with haemophilia from among 9.7 million adult males enrolled in employer-sponsored health insurance plans. Tencer *et al.* [8] restricted their analysis to individuals who had at least one primary diagnosis of haemophilia or other bleeding disorder (ICD-9 286.xx) and at least one prescription for a haemophilia drug. Our criteria included ICD-9 codes specific to haemophilia (286.0–286.1), regardless of whether it was a primary diagnosis, and we did not require a prescription claim for a haemophilia drug. Based on prevalence estimates, our sample appears to be fairly representative of privately insured males with haemophilia.

We found that the annual healthcare cost in 2008 averaged \$155,136 [median \$73,548] (\$150,680 [median \$72,374] for children and \$159,310 [median \$76,088] for adults). Healthcare costs were particularly elevated for people who were treated with bypassing agents for inhibitors, 4–6 times higher on average, depending on age group. Our estimates are consistent with one set of results from one study [12 including

Table 4. Characteristics of adults with haemophilia by risk group, 2008.

Adults	Receiving no bypassing agents		Receiving bypassing agents (AHB ⁺) ^{††}
	w/o HIV or HCV infection (AHV ⁻) ^R	w HIV or HCV infection (AHV ⁺) [†]	
No. of people	378	207	16
HIV only	–	48	–
HCV only	–	94	–
HIV and HCV	–	65	–
Age group: N (%)		P < 0.01 [†]	P = 0.02 [†]
18–29	187 (49)	31 (15)	2 (13)
30–39	42 (11)	58 (28)	3 (19)
40–49	52 (14)	70 (34)	4 (25)
50–59	48 (13)	43 (21)	3 (19)
60–69	33 (9)	4 (2)	2 (13)
70–79	8 (2)	–	1 (6)
80–	8 (2)	1 (0.5)	1 (6)
Age (mean)	37	42 ^{†***}	48 [†]
Clotting factor			
No. of people (%)	281 (74)	188 (91) ^{***}	16 (100) ^{§**}
Emergency department (ED) visits			
No. of people (%)	107 (28)	64 (31) [‡]	10 (63) ^{†***}
Frequency among ED visitors	1.7	2.0 [†]	2.3 [†]
Type of care: N (% of people who received each type of care)			
Inpatient	47 (12)	46 (22) ^{***}	5 (31) ^{**}
Prescription	121 (32)	64 (31) [‡]	5 (31) [‡]
Total expenditures (\$)			
Median	43 968	116 207	176 218
Mean	125 861	188 056 ^{***}	577 640 ^{†***}
95th percentile	520 976	620 918	2 459 207
Expenditures for clotting factor (\$)			
Median	27 561	95 600	111 147
Mean	107 985	151 634 ^{†***}	438 155 ^{†***}
95th percentile	440 717	542 318	2 434 958

* and ** represent a 5% and a 1% level of significance, respectively.

[†]t test.

[‡]Chi-square test.

[§]Fisher's exact test.

^{††}Statistical tests examine the null hypothesis that the AHV⁻ group has the same characteristics as the AHV⁺ group.

^{†††}Statistical tests examine the null hypothesis that the AHB⁺ group has the same characteristics as the AHV⁻ group.

^RReference.

outliers], but the cost ratio appears high relative to the results of other studies, all of which reported that annual costs for inhibitor patients were 2–3 times higher than those without inhibitors [9–11,12 excluding outliers, 13]. However, other studies for the most part were not restricted to inhibitor patients receiving bypassing agents and were not based on US data.

In our data, the average cost differed by 10-year age group, tending to increase with age until the age of 49 and then to decrease. Two possible explanations for why people with haemophilia who remained on employer-sponsored insurance incurred lower costs after age 49 are (i) that as people aged, they became less physically active and hence had fewer bleeds and (ii) older people were more likely to use plasma products, which are less expensive than recombinant products. However, another reason for the decrease in costs after age 49 in our data could be that people with haemophilia who had higher health-care spending left employer-sponsored insurance and moved to public insurance. There are several possible explanations for such a shift: (i) insurance caps that cause older people to reach the

lifetime maximum on their health insurance; (ii) the exclusion of haemophilia as a pre-existing condition from health insurance coverage when people change employment (both employees and dependents); (iii) selective mortality; and (iv) the healthy worker effect (healthier people, including people with mild symptoms, are more likely to be employed and therefore remain in employer-sponsored plans). The healthy worker effect is not statistically supported as an explanation in this case as average costs were the same regardless of employment status (see Table S3 of Appendix).

The decreased prevalence of haemophilia among adults also reflects the high mortality among adults with haemophilia who developed HIV or other viral infections in the 1980s. Children in this study sample, born after 1990, have been largely unexposed to viral infection owing to the introduction of high-purity viral inactivated plasma-derived factor concentrates in the late 1980s and the development of recombinant products in the early 1990s [14]. The greater decrease in prevalence with age relative to a population-based study

of haemophilia prevalence [3] reflects factors described in the previous paragraph, which reduce the likelihood that adults with haemophilia will continue to have employer-sponsored health insurance.

Mean expenditures for privately insured adults infected with HIV or HCV were 1.5 times higher than those for adults without blood-borne viral infection. The additional costs due to blood-borne viral infection were mostly attributable to higher use of factor concentrate. Factor concentrate accounted for $\geq 79\%$ of total costs for these adults with blood-borne infection, which means that antiviral treatment for blood-borne infections does not account for their higher healthcare costs. They use more factor concentrate and therefore cost more.

The limitations of this study include, first, that the study sample is not representative of the haemophilia population as only people who were covered by employer-sponsored plans or Medicare Supplemental plans were included in the study. Second, because we required that people must have either haemophilia-related procedure or drug codes, people with mild symptoms who did not receive haemophilia-specific treatment were excluded. Therefore, our estimates of average cost apply only to people treated for haemophilia. To the extent that people with mild symptoms are under-represented in our database, our estimates would overstate average costs for the population with haemophilia as a whole. Third, a limitation of the analysis of costs associated with comorbidity from blood-borne viral infections is that we were only able to identify people who received antiviral treatments, and many HCV-infected people do not actively receive anti-HCV treatment. Fourth, costs may be understated because people may receive factor concentrate from a source other than their private plan or Medicare Supplemental plan, and these costs of care

were not included in the analysis. Fifth, information on laboratory tests for inhibitors or inhibitor status was not available, and our estimated costs for people who received bypassing agents cannot be extrapolated to people with an inhibitor in general. In particular, people with an inhibitor may instead be treated with large amounts of factor VIII or factor IX to overcome the inhibitor (immune tolerance therapy) and may have been included in the group not on bypassing agents (but on immune tolerance); therefore, the excess cost of inhibitor patients may have been underestimated.

In conclusion, we found that people with haemophilia incur substantial healthcare costs primarily due to the use of factor concentrates to control bleeding. These costs can be dramatically increased by the development of an inhibitor and for some adults with HCV or HIV infection. Although these costs are high, the costs resulting from severe complications that occur without appropriate use of factor concentrates could be far greater. Efforts to understand the cause of inhibitors are needed so that prevention strategies can be implemented and the excess costs resulting from this serious complication of haemophilia care can be avoided.

Disclosures

All of the authors except for Dr. Kessler conducted this project as part of their jobs as employees of the Centers for Disease Control and Prevention (CDC). CDC is an agency of the U.S. Department of Health and Human Services. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of CDC. The authors except for Dr. Kessler have no financial interest in this project. Dr. Kessler has received research funding (paid directly to his university with no salary set aside) from Octapharma, Baxter Immuno, Grifols, Pfizer, Bayer, and Novo Nordisk. He has received honoraria as a consultant on advisory boards for Octapharma, Baxter Immuno, Bayer, CSL Behring, Pfizer, and Novo Nordisk. SM is currently an employee of Biogen Idec.

References

- 1 Manco-Johnson MJ, Nuss R, Geraghty S, Funk S, Kilcoyne R. Results of secondary prophylaxis in children with severe hemophilia. *Am J Hematol* 1994; 47: 113–7.
- 2 Liesner RJ, Khair K, Hann IM. The impact of prophylactic treatment on children with severe haemophilia. *Br J Haematol* 1996; 92: 973–8.
- 3 Soucie JM, Evatt B, Jackson D, and the Hemophilia Surveillance System Project Investigators. Occurrence of hemophilia in the United States. *Am J Hematol* 1998; 59: 288–94.
- 4 Aledort LM, Haschmeyer RH, Pettersson HA. Longitudinal study of orthopaedic outcomes for severe factor-VIII-deficient haemophiliacs. The Orthopaedic Outcome Study Group. *J Intern Med* 1994; 236: 391–9.
- 5 Naraine VS, Risebrough NA, OH P *et al.* Health-related quality-of-life treatments for severe haemophilia: utility measurements using the Standard Gamble technique. *Haemophilia* 2002; 8: 112–20.
- 6 Escobar MA. Health economics in haemophilia: a review from the clinician's perspective. *Haemophilia* 2010; 16(Suppl.3): 29–34.
- 7 Globe DR, Curtis RG, Koerper MA, the HUGS steering committee. Utilization of care in haemophilia: a resource-based method for cost analysis from the Haemophilia Utilization Group Study (HUGS). *Haemophilia* 2004; 10(Suppl. 1): 63–70.
- 8 Tencer T, Friedman HS, Li-McLeod J, Johnson K. Medical costs and resource utilization for hemophilia patients with and without HIV or HCV infection. *J Manage Care Pharm* 2007; 13: 790–8.
- 9 Auerswald G, Von Depka Prondzinski M, Ehlen B *et al.* Treatment patterns and cost-of-illness of severe haemophilia in patients with inhibitors in Germany. *Haemophilia* 2004; 10: 499–508.
- 10 Bohn RL, Aledort LM, Putnam KG *et al.* The economic impact of factor VIII inhibitors in patients with haemophilia. *Haemophilia* 2004; 10: 63–8.
- 11 Chang H, Sher GD, Blanchette VS *et al.* The impact of inhibitors on the cost of clotting factor replacement therapy in haemophilia A in Canada. *Haemophilia* 1999; 5: 247–52.
- 12 Ullman M, Hoots WK. Assessing the costs for clinical care of patients with high responding factor VIII and IX inhibitors. *Haemophilia* 2006; 12(Suppl. 6): 74–80.
- 13 Goudemand J. Treatment of patients with inhibitors: cost issues. *Haemophilia* 1999; 5: 397–401.
- 14 Soucie JM, Richardson LC, Evatt B *et al.* Risk factors for infection with hepatitis B and hepatitis C viruses in a large cohort of hemophilic males. *Transfusion* 2001; 41: 338–43.

Supporting information

Additional Supporting Information may be found in the online version of this article:

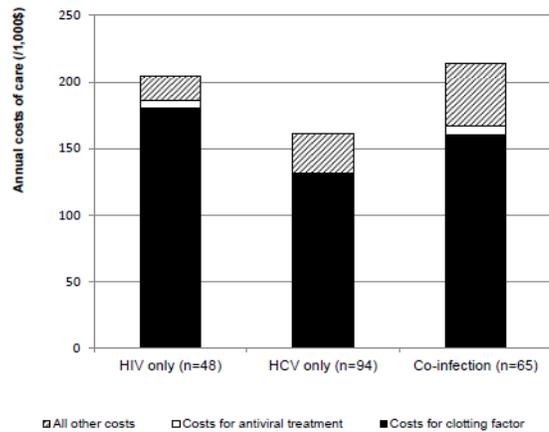


Figure S1. The annual costs of adults with blood-borne viral infection by components of health care for three different blood-borne viral infection groups.

Table S1. Identification codes for people with haemophilia, bypassing agents, HIV, or HCV.

	ICD-9-CM code	HCPCS code	Prescription drugs*
Hemophilia A	286.0	J7189; J7190; J7191; J7192; J7198; J7199; Q0187	Advate, Alphanate, Bioclote, DDAVP, Desmopressin, Factor VIII, Factor VIII:C, Factorate, Feiba-VH immune, Genarc, H.T. Factorate, Helixate, Helixate FS, Hemofil M, Hemofil T, Humate-P, Hyate: C, Koate, Koate-DVI, Koate-HP, Koate-HS, Koate-HT, Kogenate, Kogenate FS, Kogenate FS with bio-set, Kogenate FS without bio-set, Melate, Monarc-M, Monoclote-P, NovoSeven, NovoSeven RT, Profilate, Profilate HP, Profilate OSD, Profilate SD, Recombinate, Refacto, Stimate, Stimate DS, Xyntha
Hemophilia B	286.1	J7193; J7194; J7195	Alphanine, Alphanine SD, Bebulin VH, Benefix, Konyne 80, Konyne-HT factor IX complex, Mononine, Profilnine, Profilnine SD, Proflex SX-T, Proflex T, Prothar
Bypassing agents	286.0	J7189; J7198; Q0187	Autoplex; Factor VIIa, FEIBA VH, NovoSeven
HIV	042.xx; 079.53; V08		Agenerase; Aptivus; Atripla; Combivir; Crixivan; Didanosine; Didanosine DR; Emitriva; Eпивir; Eпивir A/F; Eпивir HBV; Epzicom; Fortovase; Fuzeon; Hivid; Intelence; Invirase; Isentress; Kaletra; Lexiva; Norvir; Prezista; Rescriptor; Retrovir; Reyataz; Selzentry; Stavudine; Sustiva; Trizivir; Truvada; Videx; Videx EC; Viracept; Viramune; Viramune O/S; Viread; Zerit; Ziagen; Zidovudine
Hepatitis C	070.41; 070.44; 070.51; 070.54; 070.70; 070.71		Copegus; Pegintron: Peg Intron RP; Rebetol; RibaPak; Ribasphere; RibaTab; Ribavirin; Virazole

Note: *All anti-hemophilia drugs and all anti-HIV drugs are included, because people with hemophilia were identified using the quadruple criteria and anti-HIV drugs are exclusively used only for HIV treatment. However, only the drugs that are used exclusively for HCV treatment are included, while some anti-HCV medicines also used for Hepatitis B, leukemia, melanoma, or condylomata acuminata are excluded, such as interferon alone and peginterferon Alfa-2a.

Table S2. Annual costs of care of people with haemophilia by age group (\$), 2008.

Age group	N	Median	Mean	95 th percentile
0-9	247	57,239	120,752	446,999
10-19	376	89,369	167,958	545,163
20-29	160	105,915	175,324	598,456
30-39	103	97,581	172,966	558,304
40-49	126	74,861	190,954	896,671
50-59	94	48,896	134,560	620,918
60-69	39	24,484	84,905	386,210
70-79	9	32,083	134,546	860,070
80-	10	16,170	50,201	194,596

Table S3. Annual costs of care of adults with haemophilia by age group and employment status.

Age group	N	Dependent	Employees
40-49	126	191,068 (n=29)	190,920 (n=97)
50-59	94	140,163 (n=30)	131,934 (n=64)
60-69	39	55,647 (n=11)	96,399 (n=28)

Note: Statistical tests fail to reject the null hypothesis that the costs of care are the same regardless of employment status (dependent vs. employees).