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Association of overweight and obesity with the use of self and home-based infusion therapy among haemophilic men

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Summary

An elevated body mass index (BMI) may make venipuncture more difficult, potentially impacting the use of home infusion (HI) and self-infusion (SI). We sought to determine whether abovenormal BMI is associated with decreased use of HI treatment and SI of clotting factor concentrate among haemophilic persons. We analysed data from 10 814 male patients with haemophilia A and B (45% with severe disease) aged 6-79 years enrolled in the Centers for Disease Control and Prevention Universal Data Collection surveillance project between 1998 and 2008. Associations between the use of HI and SI and BMI were evaluated using logistic regression. Fifty per cent of haemophilic men were overweight or obese, similar to rates reported among the general US population by the 2007–2008 National Health and Nutrition Examination Survey [Flegal, KM et al., JAMA 2010;303:235–241;]. Twenty per cent of children and 22% of teens were obese, as were 28% of adults [Ogden, CL et al., JAMA 2010;303:235, 242]. Overall, 70% of the study sample used HI; 44% of those who used HI also used SI. Overweight and obese men were each less likely to use HI than those of normal weight [odds ratio (OR) 0.8; 95% confidence interval (CI) 0.7–1.0 and OR 0.7; 95% CI 0.6–0.8 respectively]. Obese teens and adult men were also less likely to practice SI than teens and adults of normal weight (OR 0.8; 95% CI 0.7–0.9 for each). We conclude that overweight and obese haemophilic men are less likely to use HI and obese men are less likely to use SI than their normal-weight counterparts.

Author contributions

Disclosures

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

MU, JMS and AG designed the study. MU drafted the manuscript; QCZ analysed and interpreted the data. QCZ, DB and JMS revised the draft manuscript, and DB provided clinical expertise.

The authors stated that they had no interests which might be perceived as posing a conflict or bias.

Keywords

BMI; haemophilia; home infusion; obesity; overweight; self-infusion

Introduction

Haemophilia is an X-linked genetic disorder in which a deficiency of the coagulation proteins, factor VIII or factor IX leads to episodes of bleeding. Recurrent bleeding into joint space may lead to damage of the synovium, cartilage and bone, causing pain and disability. Treatment of bleeding events requires timely administration of clotting factor concentrate to treat or prevent life-or-limb-threatening injury, preferably within 2 h [1]. Factor replacement given regularly to prevent bleeding (prophylaxis) reduces the incidence of joint disease in haemophilic boys [2]. Infusing factor at home allows haemophilic persons to treat bleeds promptly and conveniently, enhancing adherence to more intensive treatment regimens such as prophylaxis. Home therapy use is associated with decreased risk for bleeding complications, improved quality of life, fewer school and work absences, and lower unemployment and hospitalization rates [3–5]. Home infusion (HI) treatment requires that the patient or a family member become proficient in the intravenous administration of clotting factor. Venipuncture can be challenging in obese patients because veins are more difficult to visualize [6,7]. Self-infusion (SI) is usually learned in adolescence. SI promotes treatment of bleeds with minimal delay, improves adherence to prophylaxis and increases patients' independence [8].

Overweight and obesity in the US are public health concerns and continue to be a focus of public health efforts [9]. Thirty-three per cent of adult men in the general US population are obese, and 20% of boys and young men aged 6–19 [10]. A recent study found the prevalence of overweight and obesity among haemophilic men was similar to unaffected men, and the rate of loss in joint range of motion (ROM) was greater among overweight or obese men than among normal weight men [11]. European studies of haemophilic adults describe similar correlations between body mass index (BMI) and joint impairment [12,13].

Elevated body weight may decrease patients' ability to home infuse and self- infuse. No previous studies have investigated the impact of body weight on specific haemophilia treatment practices. This study examines whether overweight and obesity are associated with decreased HI or SI.

Materials and methods

The Universal Data Collection (UDC) surveillance project was conducted by the Centers for Disease Control and Prevention (CDC) and 135 federally funded Hemophilia Treatment Centers (HTCs) in the United States to collect a uniform clinical outcomes data set on persons receiving comprehensive care in these centres. More than 18 000 male patients (85% of haemophilic persons receiving care at HTCs) were enrolled between 1998 and 2011 [14,15]. From a study population of 13 037 men aged 6–79 years with haemophilia A or B, we excluded individuals with clinical or treatment characteristics having the potential to affect weight status. Exclusion criteria included a diagnosis of HIV (n = 1800) or

symptomatic liver disease (n = 236), inhibitor titre 5 Bethesda units (n = 245) and immune tolerance therapy at the time of the visit (n = 72). Individuals with incomplete height and weight data at their most recent UDC visit were also excluded (n = 133), yielding a final eligible study population of 10 814 persons enrolled from 1998 to 2008.

Demographic and clinical data were collected from UDC participants by HTC staff during annual clinic visits using a standardized data collection instrument. The registration form recorded age, gender, race, factor deficiency, diagnosis and baseline factor activity; the annual visit form collected date of visit, height, weight, insurance coverage, HI status, person performing infusion (self, family member or medical provider), central venous access device (CVAD) use and treatment regimen (episodic or prophylaxis). Data were recorded at each individual's most recent UDC visit during 1998–2008.

Definition of variables

Centers for Disease Control and Prevention guidelines were used to define categories of overweight and obesity based on measured height and weight (Fig. 1). Participants with factor activity between 6% and 49% of normal levels were considered to have mild, 1–5% moderate, and <1%, severe haemophilia [3]. Participants were grouped into three age categories: children 6–11 years; teens 12–19 years; and adults 20 years and older. Treatment type was classified as episodic if the patient received products only to treat bleeding complications since the last annual clinic visit. Individuals were considered to use prophylaxis if they received treatment products to prevent bleeding or re-bleeding either continuously or on an intermittent schedule. Persons with commercial or public health care coverage were considered to be insured. Participants who received treatment products intravenously outside the medical setting (such as an HTC or emergency department) were considered to use HI. HI was performed either by the patient, a family member, or a medical care provider, such as a home health professional. Those who infused factor without help from others, such as parents or medical care providers, were considered to use SI.

Statistical methods

The prevalence of HI and SI (among those practising HI) was calculated for each level of demographic and clinical characteristics. Pearson's chi-squared test or Fisher's exact test were used to assess the statistical significance of associations in bivariate analyses. Logistic regression was used to assess the independent association of BMI with the use of HI and SI in multivariate analyses. Adjusted odds ratios (aOR) and 95% confidence intervals were computed. All statistical analyses were based on two-sided tests with a significance level of 0.05, and conducted using SAS 9.3 (SAS Institute, Cary, NC, USA).

The analysis was conducted in four parts: (i) Frequency distributions of BMI categories and prevalence of HI and SI were calculated. (ii) Bivariate relationships of infusion use with elevated BMI and other demographic or clinical characteristics were calculated using chi-squared tests. (iii) Multiple logistic regression models were developed to describe whether overweight and obesity were associated with the likelihood of HI and SI while adjusting for seven variables that were potential confounders: age, ethnicity, insurance status, haemophilia type and severity, treatment type and CVAD use. (iv) Controlling for the same

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confounders, quartic polynomial logistic regression models using age as a continuous variable were created to illustrate the impact of BMI and advancing age on the prevalence of HI and SI. Figures based on these models illustrate the mean predicted probability of using HI and SI with advancing age among the largest subset of the sample population. This subset (n = 4721; 43% of sample population) included the most commonly occurring characteristics: white ethnicity, haemophilia A, no CVAD and having health care coverage).

Results

The sample included 10 814 male patients aged 6–79; 48% were adults aged 20–79. Seventy-six per cent had haemophilia A and 45% had severe haemophilia; 31% used prophylaxis. The mean age of the entire sample was 24; mean age of adults was 37. Sixty-nine per cent of the sample was white; Hispanics were the largest minority group (13%). Ninety-four per cent had insurance.

Increased BMI

Overall, 36% of children, 38% of teens and 63% of adults had above-normal BMI. The prevalence of obesity as compared to overweight differed among adults and youth. A larger proportion of children and teens were obese (20% and 22% respectively) than were overweight (16% in both children and teens). Overweight (35%) affected a greater proportion of adults than did obesity (28%; P < 0.0001). Hispanic participants had the highest prevalence of elevated BMI among all ages. Multiple regression analysis among adults also revealed a significant association (P = 0.0001) between increased BMI and mild haemophilic severity (Table 1).

Home infusion

Seventy per cent of male patients practised HI. Eight characteristics (Table 2) were associated (P < 0.0001) with increased HI use: age 12–19 (74%); African – American ethnicity (80%); severe haemophilia vs. moderate/mild disease (94% vs. 69% and 34%); haemophilia A vs. haemophilia B (72% vs. 65%); prophylaxis use (98% vs. 57%); CVAD use (95% vs. 68%) and normal or below-normal BMI (73%) vs. overweight (67%) and obesity (66%). These associations remained in the multivariable model. Although HI was associated with insurance coverage in the univariate analysis (P = 0.03, Table 2), this association diminished in the multivariate analysis (Table 4). Prophylaxis use is a confounder with severity, and we observed a trend effect between severity and HI use. Therefore, our analysis adjusted for both severity and treatment type; the effects of these interactions are illustrated in Figs 2 and 3.

Figures 2a and b compare the predicted probability of HI use by age and treatment regimen. Regardless of severity, HI use was more prevalent among persons using prophylaxis (Fig. 2a) than among those treating episodically (Fig. 2b). For prophylaxis users, a difference in HI use among age and BMI categories was clearly observed only among those with mild disease. Use of HI was highest among 20–29-year-olds for all BMI groups. The rate of HI use climbed steadily during childhood through the mid-20s, but fell as BMI and age increased. Among adults, HI use was highest (75%) among those of normal weight and

lowest among the obese (63%). A trend of declining HI use with increasing BMI was also observed in teens (P = 0.057) and children (P = 0.040).

Self-infusion

Self-infusion was practised by 44% of those infusing at home. Tables 2 and 3 illustrate the univariate association between demographic and clinical characteristics and prevalence of SI. Table 2 displays the prevalence of SI and HI. Table 3 highlights the reduced use of SI with increased BMI among adults and teens. This association is not apparent in Table 2 because of the inclusion of children aged 6–11, among whom there was no association between BMI and SI use. We observed a significantly higher SI prevalence (P < 0.0001, Table 2) among adults (71%); among those with severe haemophilia (vs. moderate/mild disease (47% vs. 41%, 40%); and among those using episodic vs. prophylactic treatment. The greater prevalence of SI use among persons on episodic treatment in Table 2 reflects the inclusion of children aged 6–11 (too young to self-infuse) using a prophylaxis. Table 3 demonstrates the increased prevalence of SI among teens and adults using prophylaxis compared to episodic treatment (teens: 35% vs. 27%; P < 0.0001) adults: 79% vs. 69%, P < 0.0001) There was no association between ethnicity (P = 0.13) or haemophilia type (P = 0.9) and SI use. Increased BMI was significantly associated with lower prevalence of SI among teens (P = 0.002) and adults (P = 0.005).

Self-infusion among teens—Self-infusion was practised by 32% of teens infusing at home. Use of SI in teens varied with severity (P < 0.0001): 36% of teens with severe disease used SI, compared to 27% of moderates and 20% of those with mild disease.

A significantly smaller proportion of teens with obesity used SI (P = 0.002) than did those with normal BMI (Table 3). Use of SI declined with increasing BMI. The disparity in SI prevalence among BMI categories peaked at age 16, when 39% of teens with normal or below-normal BMI used SI, compared to 27% of the overweight and 21% of the obese.

Self-infusion among adults—Self-infusion use among adults declined with decreasing haemophilic severity and was practised by 78% of those with severe disease, 66% of moderates, and 57% of those with mild disease (P < 0.0001, Table 3). A smaller proportion of obese persons used SI than those of normal weight. (P = 0.005, Table 3). The prevalence of SI among adults peaked at 76% between 30 and 39 years, declining to 36% by age 70–79.

Figures 3a and b compare the predicted probability of SI use by age and treatment regimen. The probability of SI use was highest among those with severe disease, regardless of treatment regimen, and lowest among those with mild disease treating episodically. SI use was lowest among the obese, regardless of age, severity or treatment regimen.

Table 4 illustrates the independent association (aOR) between BMI, HI and SI among the overall sample. The associations found in the bivariate analysis remained in the multiple logistic regression models. Obesity was negatively associated with HI use among adults and with SI in adults and teens after adjustment for other risk factors or confounders. Compared with persons of normal weight, overweight and obese persons were less likely to infuse at home (aOR = 0.84, 95% CI = 0.74-0.96 and aOR = 0.72; 95% CI = 0.63-0.82). Obese (but

not overweight) persons were less likely to self-infuse (aOR = 0.76, 95% CI = 0.66-0.88). Characteristics of persons with a higher probability of using HI included normal BMI, age > 19, moderate/severe disease, non-Hispanic ethnicity and prophylaxis. Characteristics of persons with a higher probability of using SI included BMI of less than 30, age > 19, moderate/severe disease, and prophylaxis.

Discussion

BMI, home infusion and self-infusion

Home treatment affords immediate access to effective treatment. The ability to access home treatment has transformed the lives of haemophilic persons by reducing time to treatment and enabling adherence to prophylactic treatment. Prophylaxis involves frequent infusion of factor concentrate (1–4 times per week) and has been demonstrated to decrease episodes of joint bleeds and chronic arthropathy [2,16]. Home treatment has been shown to reduce pain and disability, hospitalizations, time lost from work or school, and to improve patients' overall quality of life [17]. The probability graphs generated in this analysis (Fig. 2a and b) illustrate higher levels of HI use by those with moderate and severe disease and those using prophylaxis, after adjustment for other confounding variables.

Self-infusion allows patients to treat themselves conveniently at home, work, school, or while travelling. Bleeding episodes can be treated with minimal delay, a particularly important aspect of care for teenagers, who are often involved in sports and are physically very active. By facilitating timely treatment of a bleed, SI helps to preserve independence [18]. The increasing use of adult prophylactic regimens in developed countries adds to the need for SI skills [19]. We noted that SI use did not peak until 29–30 years among all severities, indicating that older teens and young adults may benefit from additional training.

This analysis suggests that obese persons with haemophilia are less likely to use HI and SI, possibly because of the increased difficulty of venipuncture caused by adiposity [6,7]. Additional studies designed to examine specific causes for the association between obesity and decreased use of HI and SI will advance our understanding of the interaction between these factors. The inability to perform HI and SI may lead to delayed treatment of bleeds, reduce the effectiveness of the treatment and place those with elevated BMI at increased risk of haemophilic complications.

Nearly 50% of haemophilic men were overweight or obese, similar to rates reported among the general US population by the 2007–2008 National Health and Nutrition Examination Survey [10,20].

Overweight and obese children are more likely to experience other poor health outcomes including high blood pressure, high cholesterol, impaired glucose tolerance, insulin resistance and type 2 diabetes, asthma, joint problems and fatty liver disease, and are at greater risk for social and psychological problems [21]. Moreover, youth with high BMI are more likely to become obese adults, a risk which increases with the degree of obesity [22,23].

Obese adults face a greater risk of hypertension, type 2 diabetes, coronary heart disease, stroke, gallbladder disease, osteoarthritis, sleep apnoea, and colon cancer [20]. Persons with bleeding disorders and elevated BMI may face unique health complications in addition to those faced by the general population. Above-normal BMI has been associated with reduced ROM in haemophilic persons in American and European studies and can increase the cost of care, as dosing of factor concentrate is based on actual body weight [11–13,24].

The increasing prevalence of obesity among young men will continue to be an issue for both the general and haemophilia populations as this cohort ages into adulthood [10,20]. NHANES data collected between 2009 and 2010 indicate that the prevalence of obesity among the general US population has now reached a plateau among most age groups except male adolescents, among whom the prevalence continues to rise [25]. The teen years are critical for haemophilic persons because during this period treatment preferences and skills (including SI) are developed. Obesity may present increasing challenges for haemophilia providers as they teach adolescents to self-infuse at an appropriate age and in the most effective way possible.

In addition, among both the sample and general US populations we note 15% of youth aged 6–19 have extreme obesity (BMI-for-age 97%), compared with only 4% of adults (BMI 40). Given our finding that obesity is strongly associated with decreased use of HI and SI and the fact that young persons with extreme obesity are likely to remain obese as adults, these individuals may, on reaching adulthood, experience even lower rates of HI and SI use than adults observed in the sample. Youth with extreme obesity may comprise a future high-risk group for whom interventions designed to increase the use of HI and SI may be beneficial.

Study limitations

Some limitations should be noted when interpreting the results of this analysis. Although we found statistically significant associations between elevated BMI, haemophilic severity and various treatments, we cannot determine from this cross-sectional data whether these associations are causal. Our sample population was derived solely from volunteer participants receiving care through federally funded HTCs, potentially limiting the application of our findings to all haemophilic persons, regardless of where they obtain care. The data reported in the UDC surveillance project were self-reported by the patient and treatment centre staff, but not confirmed with pharmacy or home care records. BMI as an indicator of obesity has limitations because it does not distinguish between fat mass and fat-free mass; however, studies demonstrate that although the association between BMI and body fat can be weak among persons with lean body mass (such as athletes), it is strong among those with higher BMI levels [26]. Small sample size may be an issue in analyses of subgroups stratified simultaneously by numerous variables, such as persons with mild disease using prophylaxis.

Conclusion

This analysis suggests that obesity is associated with a lower prevalence of HI and SI of clotting factor concentrate among haemophilic men. Persons not using HI and SI risk

delayed treatment for bleeding episodes. The decline of HI and SI use with age indicates a need for further research into possible barriers to care and the development of interventions to encourage earlier and more prolonged use of these beneficial treatment options.

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<u>Adults, ≥20 years</u>		Youths and teens, 2–19 years		
Weight (kg)/[height (m)] ² or		CDC growth charts used to calculate		
Weight (lb)/[height (in)] ² x 703		BMI-for-age percentiles		
<18.5	Underweight	<5th percentile	Underweight	
18.5 - 24.9	Normal	5th – <85th	Healthy weight	
25.0 - 29.9	Overweight	85th – <95th	Overweight	
≥30.0	Obesity	≥95th	Obesity	

Fig. 1.

Centers for Disease Control and Prevention (CDC) body mass index (BMI) categories. Sources: Adults: Flegal, KM *et al.* JAMA (2010) 303:235–241; Children: Ogden, CL *et al.* JAMA (2010) 303:242. ULLMAN et al.



(a) Predicted Probability of Home Infusion Use: Prophylactic Treatment (N = 1,386)





Fig. 2.

(a) Predicted probability of home infusion (HI) use: prophylactic treatment (N = 1386). (b) Predicted probability of HI use: episodic treatment (N = 3335). Figure 2a and b illustrate a subset of the sample population with the following characteristics: (i) hemophilia A, (ii) Caucasian ethnicity, (iii) with health care coverage and (iv) without central venous access device.

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(a) Predicted Probability of Self Infusion Use: Prophylactic Treatment (N = 1,365)

(b) Predicted Probability of Self Infusion Use: Episodic Treatment (N = 1,864)



Fig. 3.

(a) Predicted probability of self-infusion use: prophylactic treatment (N = 1365). (b) Predicted probability of self-infusion use: episodic treatment (N = 1864). Figure 3a and b illustrate a subset of the sample population with the following characteristics: (i) using home infusion, (ii) hemophilia A, (iii) Caucasian ethnicity, (iv) with health care coverage and (v) without central venous access device. The figures used in these graphs are not included in Tables 1–4.

Characteristics of sample population by body mass index.

Characteristic	Total sample no. (%) †	Normal and underweight no. $(\%)$	Over weight no. (%)	Obese no. (%)	P^*
Male patients(total sample)	10 814 (100)	5439 (50)	2745 (25)	2630 (24)	
Age					
6–11 years	2252 (21)	1430 (63)	364 (16)	458 (20)	<0.0001
12–19 years	3391 (31)	2104 (62)	554 (16)	733 (22)	
20 and older	5171 (48)	1905 (37)	1827 (35)	1439 (28)	
Ethnicity					
White	7418 (69)	3731 (50)	1961 (26)	1726 (23)	<0.0001
Hispanic	1457 (13)	682 (47)	352 (24)	423 (29)	
African American	1215 (11)	631 (52)	271 (22)	313 (26)	
Other	724 (7)	395 (55)	161 (22)	168 (23)	
Health insurance					
No	608 (6)	308 (51)	166 (27)	134 (22)	0.312
Yes	10 206 (94)	5131 (50)	2579 (25)	2496 (24)	
Haemophilia type					
Haemophilia A	8206 (76)	4145 (51)	2046 (25)	2015 (25)	0.149
Haemophilia B	2608 (24)	1294 (50)	699 (27)	615 (24)	
Severity					
Mild	3220 (30)	1447 (45)	919 (29)	854 (27)	<0.0001
Moderate	2767 (26)	1356 (49)	724 (26)	687 (25)	
Severe	4827 (45)	2636 (55)	1102 (23)	1089 (23)	
Treatment type					
Episodic	7462 (69)	3447 (46)	2109 (28)	1906 (26)	<0.0001
Prophylaxis	3352 (31)	1992 (59)	636 (19)	724 (22)	
CVAD used					
No	9932 (92)	4949 (50)	2570 (26)	2413 (24)	<0.0001
Yes	882 (8)	490 (56)	175 (20)	217 (25)	
CVAD, central venous access	device.				

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* P value calculated using chi-squared test.

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Prevalence of home and self-infusion use by demographic and clinical characteristics.

Characteristic	Home infusion no. (%)	P value*	Self-infusion no. $(\%)^{\dagger}$	P value
Male patients total ($N = 10814$)	7571 (70)		3364 (44)	
Age				
6-11 years	1530 (68)	< 0.0001	50 (3)	< 0.0001
12-19 years	2498 (74)		789 (32)	
20 and older	3543 (69)		2525 (71)	
Ethnicity				
White	5049 (68)	< 0.0001	2269 (45)	0.125
Hispanic	990 (68)		405 (41)	
African American	973 (80)		438 (45)	
Other	559 (77)		252 (45)	
Health insurance				
No	402 (66)	0.0323	210 (52)	0.001
Yes	7169 (70)		3154 (44)	
BMI status				
Normal weight or less	3994 (73)	< 0.0001	1622 (41)	< 0.0001
Overweight	1849 (67)		982 (53)	
Obese	1728 (66)		760 (44)	
Haemophilia type				
Haemophilia A	5886 (72)	< 0.0001	2617 (44)	0.933
Haemophilia B	1685 (65)		747 (44)	
Severity				
Mild	1096 (34)	< 0.0001	440 (40)	< 0.0001
Moderate	1923 (69)		798 (41)	
Severe	4552 (94)		2126 (47)	
Treatment type				
Episodic	4284 (57)	< 0.0001	2164 (51)	< 0.0001
Prophylaxis	3287 (98)		1200 (37)	
CVAD used				
No	6730 (68)	< 0.0001	3249 (48)	< 0.0001
Yes	841 (95)		115 (14)	

CVAD, central venous access device; BMI, body mass inidex.

* *P* value calculated using chi-squared test.

[†]Among persons using home infusion.

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Prevalence of home and self-infusion use by body mass index (BMI), severity and treatment type, age 12 years.

Age group	Characteristics	Total ^{\dagger} no. (%)	Self-infusion no. (%)	P value*
12-19 years		N = 2498	N = 789	
	BMI category			
	Normal weight or less	1576 (63)	535 (34)	0.002
	Overweight	406 (16)	120 (30)	
	Obese	516 (21)	134 (26)	
	Severity			
	Mild	294 (12)	58 (20)	< 0.0001
	Moderate	664 (27)	178 (27)	
20 and older	Severe	1540 (62)	553 (36)	
	Treatment type			
	Episodic	1123 (45)	306 (27)	< 0.0001
	Prophylaxis	1375 (55)	483 (35)	
		N = 3543	N = 2525	
	BMI category			
	Normal weight or less	1436 (41)	1056 (74)	0.005
	Overweight	1194 (34)	854 (72)	
	Obese	913 (26)	615 (67)	
	Severity			
	Mild	668 (19)	381 (57)	< 0.0001
	Moderate	918 (26)	609 (66)	
	Severe	1957 (55)	1535 (78)	
	Treatment type			
	Episodic	2681 (76)	1844 (69)	< 0.0001
	Prophylaxis	862 (24)	681 (79)	

* *P* value calculated using chi-squared test.

 † The percentages used in the total sample column (those on home infusion) sum to 100% by characteristic; in the self-infusion column, the denominator for each percentage is the number of home infusers in that subgroup.

Independent association of BMI status with home infusion and self-infusion.

Characteristic	Home infusion N = 10 814		Self-infusion N = 7571		
Characteristic	aOR (95% CI)*	P value	aOR (95% CI)	P value	
Age (vs. 20 and older)					
6-11 years	0.40 (0.34–0.46)	< 0.0001	0.01 (0.01-0.02)	< 0.0001	
12-19 years	0.85 (0.75-0.97)	0.013	0.15 (0.13-0.17)	< 0.0001	
Ethnicity (vs. White)					
Hispanic	0.82 (0.70-0.96)	0.015	1.17 (0.98–1.39)	0.084	
African American	1.11 (0.93–1.34)	0.256	1.16 (0.97–1.37)	0.097	
Other	1.13 (0.90–1.41)	0.300	1.12 (0.90–1.39)	0.315	
Health insurance (vs. no)					
Yes	1.18 (0.96–1.44)	0.110	1.17 (0.92–1.49)	0.190	
BMI status (vs. norma	l weight or less)				
Overweight	0.84 (0.74–0.96)	0.009	0.92 (0.80–1.06)	0.234	
Obese	0.72 (0.63-0.82)	< 0.0001	0.76 (0.66–0.88)	0.0002	
Haemophilia type (vs. haemophilia A)					
Haemophilia B	0.83 (0.74–0.94)	0.002	0.82 (0.71-0.93)	0.003	
Severity (vs. mild)					
Moderate	3.83 (3.41-4.31)	< 0.0001	1.56 (1.30–1.86)	< 0.0001	
Severe	14.41 (12.38–16.77)	< 0.0001	2.45 (2.07-2.90)	< 0.0001	
Treatment type (vs. episodic)					
Prophylaxis	12.81 (9.80–16.74)	< 0.0001	1.22 (1.06–1.39)	0.005	
CVAD used (vs. no)					
Yes	2.53 (1.75-3.65)	< 0.0001	0.32 (0.26-0.41)	< 0.0001	

CI, confidence interval; CVAD, central venous access device; BMI, body mass inidex.

* aOR, adjusted odds ratio calculated using one multivariable logistic regression that adjusted for all covariates in the table.