

CLOTTING FACTOR UTILIZATION AND BLEEDING RATES AMONG PERSONS WITH HEMOPHILIA A FROM A LONGITUDINAL STUDY

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BACKGROUND

- Approximately 80% of children and 42% of adults with hemophilia A in developed countries treat their disorder using a prophylactic regimen, which is known to improve health outcomes.
- There are few longitudinal studies assessing prophylaxis regimen use over time.
- This evidence gap limits understanding of how prophylaxis utilization is associated with bleeding rates over time, especially across age groups.

OBJECTIVES

- We compared study participants' characteristics between baseline of Hemophilia Utilization Group Studies part Va (HUGS-Va) and Long-Term Follow-up Study (HUGS-LTS) to investigate impacts of changes in participants' characteristics on annualized bleeding rates (ABR).

METHODS

Study Design

- HUGS-Va was a two-year observational study of persons with hemophilia A conducted from 2005-2007 at six geographically diverse hemophilia treatment centers (HTC) in the United States.
- Participants from HUGS-Va were contacted for enrollment into the HUGS-LTS in 2014.
- Study participants: 1) Were aged 2-65 years at HUGS-Va; 2) Received a majority of hemophilia care at the HTC within 2 years prior to enrollment into HUGS-Va, and continued hemophilia care at the HTC to the time of HUGS-LTS; 3) Were not judged to be cognitively impaired as determined by the clinician; 4) Did not have an additional bleeding disorder; 5) Had complete data on clotting factor dispensation and bleeding rates; and 6) Transitioned to an older age group from HUGS-Va to HUGS-LTS.

Study Variables

- Sociodemographic and clinical characteristics were collected, including age, marital status, educational attainment, employment status, insurance coverage, and household income.
- Age group was classified at baseline of HUGS-Va, children (2-11 years), adolescents (12-20 years), and adults (≥ 21 years).
- Clotting factor dispensation records were collected prospectively for two years in HUGS-Va and retrospectively for six months prior to HUGS-LTS enrollment.
- Self-reports of bleeding episodes were collected via periodic surveys for 2 years in HUGS-Va and via a one-time survey that asked about bleeding in the past 6 months in HUGS-LTS.
- Annualized factor dispensation and ABR were calculated.

Statistical Analysis

- Annualized factor dispensing and ABR were compared among age groups (children 2-11 years, adolescents 12-20 years, and adults ≥ 21 years) using analysis of variance (ANOVA), and between HUGS-Va and HUGS-LTS using paired T-tests.

RESULTS

- Sixty-nine participants completed both HUGS-Va and HUGS-LTS.
- Participants or parents of children participants had a higher rate of college education attainment (98.5% vs. 76.5%) and full-year health insurance (95.7% vs. 88.4%) in HUGS-LTS than in HUGS-Va.
- The prophylactic treatment rate in adolescents and adults increased from HUGS-Va to HUGS-LTS (60.0% to 78.6% and 30.8% to 69.2%, respectively), all $P < 0.05$ (Table 1).
- The proportion of participants reported moderate/severe joint pain increased 6.7% for adolescents to 11.6% for adults from HUGS-Va to HUGS-LTS.
- Children had the highest mean/median factor dispensation (4822 \pm 4152/3300, 5061 \pm 3764/5336 IU/kg/year) and lowest mean/median ABR (3.9 \pm 4.4/2.8, 4.9 \pm 5.3/4.0); while adults had the lowest mean/median factor dispensation (2084 \pm 1870/1582, 4612 \pm 2571/4290 IU/kg/year) and highest ABR (12.4 \pm 9.2/14.0, 13.3 \pm 21.5/6.0) in both HUGS-Va and HUGS-LTS, respectively (Table 2).
- Overall 70% of participants increased mean factor dispensation, while 51% of participants increased mean ABR from HUGS-Va to HUGS-LTS.
- The mean/median ABR was not significantly different between HUGS-Va (7.4 \pm 8.6/3.8) and HUGS-LTS (8.7 \pm 14.7/4.0), $P = 0.45$.
- Participants who used episodic treatment had higher mean ABR in HUGS-LTS (15.7) than those who used prophylactic treatment (10.0), ($P = 0.41$) in HUGS-LTS (Figure 1).

TABLE 1. PARTICIPANTS' CHARACTERISTICS IN HUGS-Va AND HUGS-LTS

Variables	HUGS-Va			HUGS-LTS		
	Children N=28 (40%)	Adolescents N=15 (22%)	Adults N=26 (38%)	Children N=28 (40%)	Adolescents N=15 (22%)	Adults N=26 (38%)
Mean age in years (SD)	8.5 (2.2)	17.3 (1.9)	30.4 (8.6)	16.8 (2.4)	26.0 (1.9)	38.9 (8.7)
Marital status †	25 (89.3)	8 (53.3)	9 (37.7)	11 (40.7)	6 (40.0)	15 (57.7)
College or above education†	26 (92.9)	8 (53.3)	18 (72.0)	27 (100.0)	14 (93.3)	25 (100.0)
Employed adults or parents†	24 (85.7)	9 (60.0)	17 (65.4)	16 (59.3)	10 (71.4)	17 (65.4)
Entire year health insurance	28 (100.0)	14 (93.3)	19 (73.1)	26 (92.9)	15 (100.0)	25 (96.2)
Private health insurance	22 (78.6)	5 (33.3)	13 (61.9)	23 (85.2)	8 (53.3)	14 (56.0)
Public health insurance	6 (21.4)	10 (66.7)	8 (30.8)	4 (14.3)	7 (46.7)	11 (37.7)
Household income > \$75,000	16 (57.1)	3 (20.0)	2 (8.0)	13 (48.2)	1 (7.7)	6 (26.1)
Severe hemophilia‡	26 (92.9)	11 (73.3)	19 (73.1)	-	-	-
Prophylactic treatment	22 (81.5)	9 (60.0)	8 (30.8)	23 (85.2)	11 (78.6)	18 (69.2)
Moderate/severe joint pain	8 (28.6)	6 (40.0)	19 (73.1)	11 (39.3)	7 (46.7)	22 (84.6)

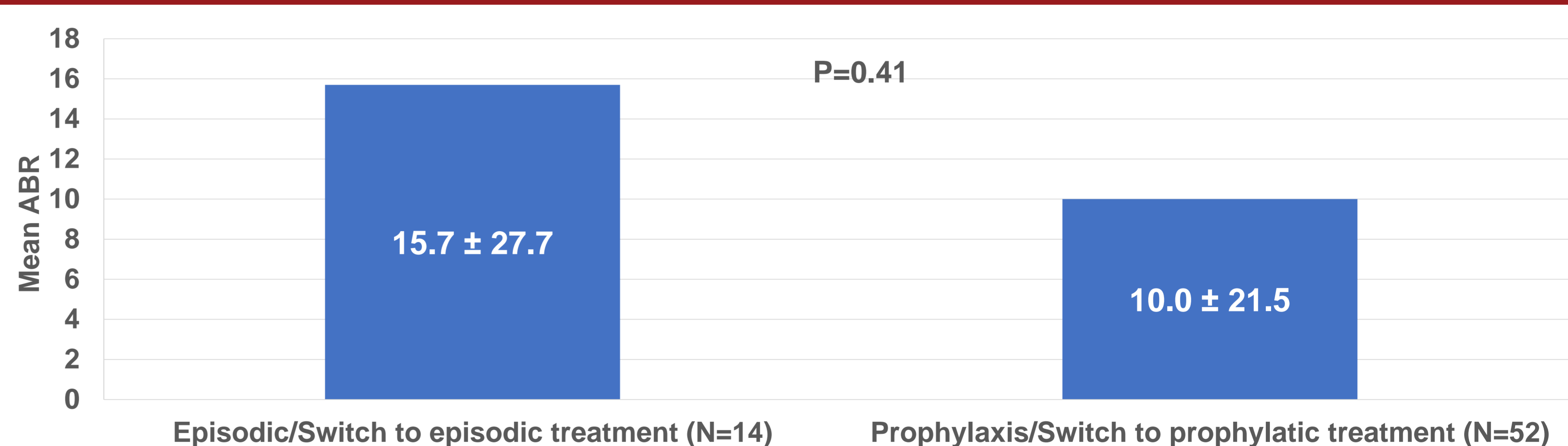
Abbreviations: HUGS-Va=Hemophilia Utilization Group Studies part Va; LTS=Long-Term Study; N=number; SD=standard deviation. Note: Data are presented as frequency (column percentage) except for age. Age was classified into three groups at enrollment of HUGS-Va: children (aged 2-11 years), adolescents (aged 12-20 years), and adults (aged ≥ 21 years). * P values were calculated from Chi-square tests to compare the proportion differences across the three age groups for categorical variables. † Variable applied to adults ≥ 18 years or parents of children <18 years. ‡ Hemophilia severity was assessed at HUGS-Va.

TABLE 2. FACTOR UTILIZATION AND ANNUALIZED BLEEDING RATES

Age Group or Treatment Regimen	HUGS-Va		HUGS-LTS		P†
	Mean (SD)	Median (min,max)	Mean (SD)	Median (min,max)	
Annual Factor Dispensation, IU/kg					
Children (N=28, 40%)	4822 ^a (4152)	3300 (0, 13998)	5061 ^a (3764)	5336 (0, 18567)	0.75
Adolescents (N=15, 22%)	2983 ^{a,b} (2507)	2203 (0, 7183)	4886 ^a (3043)	4953 (457, 10756)	0.03
Adults (N=26, 38%)	2084 ^b (1870)	1582 (0, 7015)	4612 ^a (2571)	4290 (620, 11101)	<0.0001
TOTAL (N=69)	3391 (3310)	2203 (0, 13998)	4854 (3162)	4952 (0, 18567)	<0.001
P‡	<0.01	-	0.88	-	
Prophylaxis	4970 (3497)	4252 (626, 13998)	5778 (3409)	5304 (0.4, 11101)	
Episodic	1899 (2042)	1121 (0, 7183)	2293 (1792)	2003 (234, 6665)	
Annualized Bleeding Rate					
Children (N=28, 40%)	3.9 ^a (4.4)	2.8 (0, 15.5)	4.9 ^a (5.3)	4.0 (0, 24)	0.43
Adolescents (N=15, 22%)	5.4 ^a (9.9)	1.5 (0, 39.5)	8.3 ^a (11.3)	2.0 (0-40)	0.41
Adults (N=26, 38%)	11.9 ^b (9.3)	13.5 (0, 31.0)	18.5 ^a (34.0)	6.0 (0, 150)	0.36
TOTAL§ (N=68)	7.4 (8.6)	3.8 (0, 39.5)	8.7 (14.7)	4.0 (0, 108)	0.45
P‡	<0.01	-	0.07	-	
Prophylaxis	5.0 (6.6)	3.0 (0, 31.0)	10.0 (21.5)	5.0 (0, 150)	
Episodic	10.5 (10.0)	7.5 (0, 39.5)	14.8 (27.0)	4.0 (2.0, 108)	

Abbreviations: IU/kg=international units per kilogram; max=maximum; min=minimum; N=number; SD=standard deviation. Note: Age was classified into three groups at enrollment of HUGS-Va: children (aged 2-11 years), adolescents (aged 12-20 years), and adults (aged ≥ 21 years). † P values were calculated from paired T-tests to compare the differences between HUGS-Va and HUGS-LTS. ‡ P values were calculated from ANOVA to compare mean differences across three age groups for continuous variables. For each column, means with different symbols (a, b) across the age groups are statistically significantly from one another using Tukey multiple comparison procedure ($P < 0.05$). § One adult who had a 150/year bleeding rate difference between the two studies was excluded.

FIGURE 1. MEAN ANNUALIZED BLEEDING RATE IN HUGS-LTS



Note: The numbers in the bar represent mean \pm standard deviation. The treatment regimens refer to participants that were either on that regimen throughout HUGS-Va and HUGS-LTS or had switched to the regimen in HUGS-LTS. Sixteen (23%) participants switched from episodic treatment to prophylactic treatment from HUGS-Va to HUGS-LTS; of those, 13% were children, 18% were adolescents, and 69% were adults.

CONCLUSIONS

- As compared to adults, children and adolescents had higher rate of prophylactic treatment and higher amount of factor dispensation, but they had lower ABRs. Prophylaxis should be continued in adulthood.
- Mean ABR did not significantly changed with aging.
- Higher rates of college education and health insurance may be associated with increased use of prophylactic treatment and factor dispensation, which is associated with lower ABR.

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