COMPARISON OF HEALTH UTILITIES IN PERSONS WITH HEMOPHILIA B

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INTRODUCTION

- Preference-based health state utility measures provide a single index score ranging from 0.0 (death) to 1.0 (perfect health) which can be used to calculate the quality-adjusted life year (QALY), commonly used as the denominator in cost-effectiveness analysis.
- Studies with health utility measures are particularly needed for rare, life-long and costly disorders to adequately inform economic analyses of treatment options.

OBJECTIVES

- 1) To compare different health utility measurement methods among persons with hemophilia B (HB).
- 2) To compare health utilities between parent-proxy reported for children and adults.

METHODS

- **Study Design**
  - The Hemophilia Utilization Group Study Part Vb (HUGS Vb) is a prospective, longitudinal, multicenter cohort study completed between June 2009 and April 2013.
  - Data were collected from HB patients residing in 11 geographically diverse US states. All obtained comprehensive hemophilia care at 10 federally supported hemophilia treatment centers (HTCs).
  - An initial interview collected data based on adults' self-reported or parent-proxy reported for their children less than 18 years. Data included socio-demographics, health insurance status, co-morbidities, access to care, hemophilia treatment regimen (use factor prophylactic or on-demand), factor utilization, and self-reported joint pain and motion limitation.
  - Following the initial patient interview, clinical data were collected by HTC staff through chart review using standardized clinical data collection forms. Data abstracted included body weight, height, HB severity level, current and historic inhibitor levels, history of immune tolerance therapy, hepatitis and HIV serology, infusion method and treatment regimen.
- **Study Sample**
  - *Inclusion Criteria*
    - Age 2–64 years with blood factor IX level ≤30%;
    - Received 90% of hemophilia care at a participating HTC;
    - Obtained care at the HTC within 2 years prior to enrollment;
    - Spoke English or Spanish.
  - *Exclusion Criteria*
    - Cognitive impairment as determined by the physician; or
    - Additional bleeding disorder, or
    - Children who self-reported their health utility measures (N=7); or
    - The patients did not complete hemophilia-specific utility using paper based standard gamble (PSG) (N=10).
- **Health Utility Measurements**
  - Preference-based health utility measures were collected at the initial patient interview.
  - The Short Form Health Survey Version 1 (SF-12) was administered to adult patients, and was used to estimated a preference-based single index via SF-6D health state classification.
  - The EQ-5D-3L was collected from both parent-proxy reported for children and adults patients. The EQ-5D-3L serves three functions: 1) descriptive system of health state; 2) visual analog scale (VAS); and 3) EQ index of time-trade-of utility derived from the US population-based preference weight.
  - Paper Standard Gamble (PSG) method was used to collect hemophilia-specific utilities from both parent-proxy reported for children and adult patients within 2 weeks of completion of initial interview.
- **Statistical Analysis**
  - Health utilities were compared by age group, instrument, hemophilic severity, joint pain and motion limitation.
  - The degree of agreement for each paired utility was examined by calculating the intraclass correlation coefficient (ICC).

Table 1. Patients Characteristics

Variable	Total (n=130)	Children (n=60)	Adults (n=70)	P-value*
Age, Mean (standard deviation)	24.8 (18.2)	9.2 (3.9)	38.2 (14.8)	<0.0001
Married/with a partner†	85 (66.4)	46 (76.7)	39 (57.4)	0.02
Education >12 years†	88 (67.7)	38 (63.3)	50 (71.4)	0.33
Self-reported joint pain§				<0.0001
Have no pain	40 (31.0)	29 (48.3)	11 (16.0)	
Only when bleeding	49 (38.0)	26 (43.4)	23 (33.3)	
Some of the time	16 (12.4)	2 (3.3)	14 (20.3)	
Most of the time	10 (7.7)	2 (3.3)	8 (11.6)	
Severe pain all the time	14 (10.9)	1 (1.7)	13 (18.8)	
Self-reported Motion limitation§				<0.0001
No limitation	45 (35.1)	31 (51.7)	14 (20.6)	
Only when bleeding	49 (38.3)	25 (41.7)	24 (35.3)	
Affects activities	28 (21.9)	4 (6.6)	24 (35.3)	
Severe limitation	6 (4.7)	0 (0)	6 (8.8)	
Hemophilia Severity				0.98
Moderate/Mild	76 (58.5)	35 (58.3)	41 (58.6)	
Severe	54 (41.5)	25 (41.7)	29 (41.4)	
Use of clotting factor IX	124 (95.4)	55 (91.7)	69 (98.6)	0.09
Use of prophylaxis	34 (26.6)	19 (32.8)	15 (21.4)	0.15
History of inhibitors	3 (2.3)	2 (3.3)	1 (1.5)	0.60
Current inhibitors	2 (1.6)	1 (1.7)	1 (1.5)	1.00

Data were presented as frequency (column percentage) or mean (standard deviation). *P values were calculated from Chi-square (or Fisher's exact) tests for categorical variables or Student T-tests for continuous variables. †For patients or parents of age<18 years. §Data do not add up to N=130 because of missing data.

Table 2. EQ-5D Descriptive System

Variable	Total (n=130)	Children (n=60)	Adults (n=70)	P-Value*
Mobility				<0.0001
No problem	101 (77.7%)	59 (98.3%)	42 (60.0%)	
Some problem	28 (21.5%)	1 (1.7%)	27 (38.6%)	
Extreme problem	1 (0.8%)	0 (0%)	1 (1.4%)	
Self-Care				0.72
No problem	122 (93.9%)	57 (95.0%)	65 (92.9%)	
Some problem	8 (6.1%)	3 (5.0%)	5 (7.1%)	
Extreme problem	0 (0%)	0 (0%)	0 (0%)	
Usual Activities				<0.0001
No problem	106 (81.5%)	58 (96.7%)	48 (68.6%)	
Some problem	21 (16.2%)	2 (3.3%)	19 (27.1%)	
Extreme problem	3 (2.3%)	0 (0%)	3 (4.3%)	
Pain/Discomfort				<0.0001
No problem	85 (65.4%)	52 (86.7%)	33 (47.1%)	
Some problem	36 (27.7%)	7 (11.7%)	29 (41.4%)	
Extreme problem	9 (6.9%)	1 (1.6%)	8 (11.4%)	
Anxiety/Depression				0.01
No problem	101 (77.7%)	52 (86.7%)	49 (70.0%)	
Some problem	28 (21.5%)	7 (11.7%)	21 (30.0%)	
Extreme problem	1 (0.8%)	1 (1.6%)	0 (0%)	

Data are presented as frequency (column percentage).
*P values were calculated from Chi-square tests or Fisher's exact tests (if the cell numbers are less than 5).

Fig 1. Health Utilities By Joint Pain

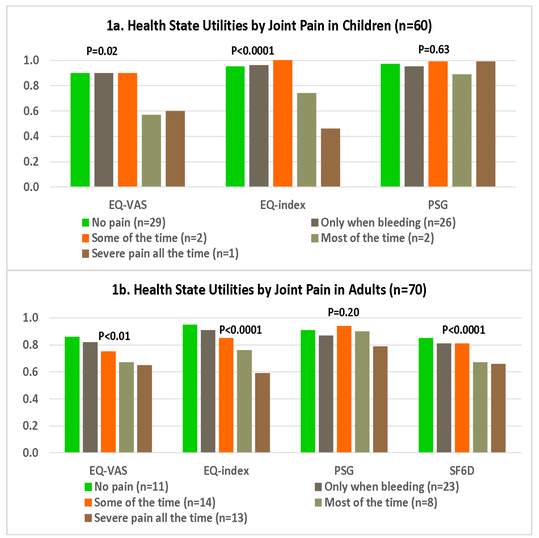
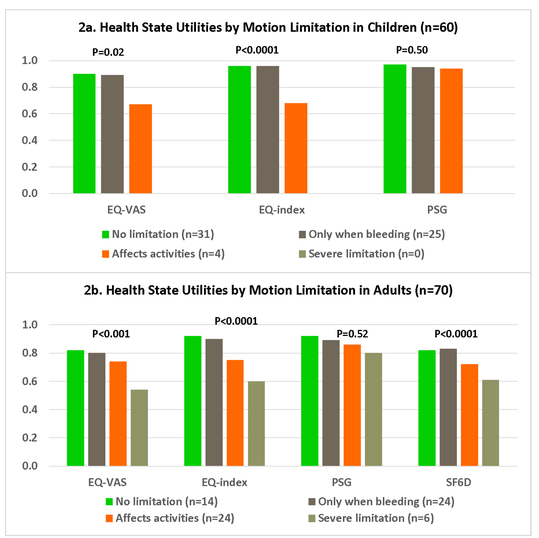


Fig 2. Health Utilities By Motion Limitation



RESULTS

- Data from 130 persons with hemophilia B were analyzed (Table 1).
- Parents of children patients were more likely to report no problem than were adult patients in describing mobility, usual activities, pain/discomfort, and anxiety/depression (Table 2).
- PSG had a low degree of agreement with EQ index (ICC=0.38 for children, ICC=0.06 for adults) and SF-6D (ICC=0.13) for adults.
- EQ-index had moderate agreement with SF-6D (ICC=0.68) in adult patients.
- None of the utility measures differed significantly by hemophilic severity.
- PSG scores did not differ significantly by joint pain (Figure 1) and motion limitation levels (Figure 2, P≥0.05). However, EQ-VAS, EQ-index, and SF-6D were significantly lower in persons with joint pain or motion limitation (Figure 1 and 2, all p<0.05).
- Mean health utilities ranged from 0.81 for EQ VAS to 0.92 for PSG (Table 3).
- Mean health utilities for parent-proxy reported for children were significantly higher than adults (EQ-VAS: 0.88±0.16 vs 0.76±0.18, P<0.0001; EQ-index: 0.94±0.11 vs 0.82±0.20, P<0.0001; PSG: 0.96±0.08 vs 0.88±0.17, P=0.001) (Table 3).

Table 3. Comparison of Utility Measurements

Utility	Total (n=130)	Children (n=60)	Adults (n=70)	P-value*
EQ VAS				<0.0001
Median	0.90	0.92	0.80	
Mean (SD)	0.81 (0.18)	0.88 (0.16)	0.76 (0.18)	
Range	0.20-1.00	0.23-1.00	0.20-1.00	
EQ-5D index				<0.0001
Median	1.00	1.00	0.83	
Mean (SD)	0.87 (0.18)	0.94 (0.11)	0.82 (0.20)	
Range	0.05-1.00	0.46-1.00	0.05-1.00	
SF-6D	N/A	N/A		N/A
Median			0.79	
Mean (SD)			0.77 (0.14)	
Range			0.46-1.00	
PSG				0.001
Median	0.98	0.99	0.96	
Mean (SD)	0.92 (0.14)	0.96 (0.08)	0.88 (0.17)	
Range	0.35-1.00	0.55-1.00	0.35-0.995	

Abbreviations: EQ VAS=EQ visual analog scale, PSG=paper standard gamble, SF-6D=Short Form 6-dimenstional health state classification, N/A=not applicable. * P values were calculated from Student T-tests to compare the mean utility differences between parent proxy report for children and adults.

CONCLUSIONS

- This study provided partial validation of health utility measurements used in HB patients.
  - EQ-5D and SF-6D can discriminate joint problems in the HB patients.
  - Hemophilia specified PSG observed health utilities were higher than the EQ index, EQ VAS, and SF-6D.
  - Hemophilia specified PSG was less sensitive in discriminating hemophilia severity and hemophilic-related joint problems than the instruments of EQ-5D and SF-6D.
- Health utilities were significantly higher among parent-proxy reported for children than adults. Further studies should explore direct administration of health utility instruments in adolescent hemophilia patients and compare to parent-proxy reported utility, which will allow us to test whether parents are not willing to trade their children's health when making treatment selection.

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