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Physician Trust and Depression Influence Adherence to Factor Replacement: A Single Center Cross-Sectional Study

Duc Q. Tran, MD, MSc^{*,†}, Vaughn Barry, PhD, MPH[†], Ana Antun, MD, MSc^{*}, Maria Ribeiro, MD^{*}, Sidney Stein, MD^{*}, and Christine L. Kempton, MD, MSc^{*,†}

^{*}Department of Hematology and Oncology, Emory University School of Medicine, Atlanta, Georgia, USA

[†]Department of Pediatrics, Emory University School of Medicine, Atlanta, Georgia, USA

Abstract

Introduction—Poor adherence to factor replacement therapy amongst patients with hemophilia can lead to joint bleeding and eventual disability.

Aim—The aim of this study is to determine patient-related characteristics associated with adherence to factor replacement in adults with hemophilia.

Methods—Adults with hemophilia were recruited to participate in this cross-sectional study. Adherence was measured using either the Validated Hemophilia Regimen Treatment Adherence Scale (VERITAS)-Pro or the VERITAS-PRN questionnaire. Simple and multiple regression analyses that controlled for confounding were performed to determine the association between patient-related characteristics and adherence to factor replacement therapy.

Results—Of the 99 subjects enrolled, all were men; 91% had hemophilia A and 78% had severe disease. Age ranged from 18 to 62 years. Most (95%) had functional health literacy; but only 23% were numerate. Mean adherence scores were 45.6 (SD 18) and 51.0 (SD 15) for those on a prophylactic and those on an episodic regimen, respectively, with a lower score indicating better adherence. On multivariable analysis, being on any chronic medication, longer duration followed at our hemophilia treatment center, higher physician trust, and better quality of life were associated with higher adherence. A history of depression was associated with lower adherence.

Conclusion—Two potentially modifiable characteristics, physician trust and depression, were identified as motivator and barrier to adherence to factor replacement therapy. Promoting a high

Corresponding author: Duc Q. Tran, MD, Hemostasis/Thrombosis Program, School of Medicine, Emory University, 2015 Uppergate Drive 4th floor, Atlanta, Georgia, 30322 USA, dtranjr@emory.edu, Phone: 1-404-686-3494, Fax: 1-404-727-3681.

Study Location: Comprehensive Bleeding Disorders Center at Emory University/Children's Healthcare of Atlanta, 2015 Uppergate Drive 4th floor, Atlanta, Georgia, 30322 USA

Author Contributions:

DQT and CLK designed the research study. DQT performed the research, analyzed the data, and wrote the manuscript. VB, AA, MR, SS and CLK critically reviewed and edited the manuscript.

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level of trust between the patient and the healthcare team as well as identifying and treating depression may impact adherence to factor replacement therapy and accordingly reduce joint destruction.

Keywords

adherence; physician trust; quality of life; depression; numeracy; hemophilia

INTRODUCTION

Management of hemophilia entails replacement of the deficient clotting factor. Factor replacement therapy can be prescribed through a prophylactic regimen with regular infusions [1] or through an on-demand regimen for treatment at the time of a bleed. Control of bleeding episodes ultimately decreases pain and morbidity and mortality and increases quality of life and physical activity [2, 3]. Therefore, the patient's understanding of the need for factor replacement and adherence to the regimen agreed upon by the patient and the hemophilia treatment center (HTC) are of utmost importance [4]. Adherence to factor replacement as prescribed includes treating bleeding episodes promptly and understanding different dosing for different bleeding severity, which can be complex.

Although barriers to medication adherence can vary by disease and among patients, they can conceptually be categorized into patient-related, treatment-related, provider-related, and health-system factors [5]. Studies examining the barriers to adherence to factor replacement among adults with hemophilia have been limited. One earlier study reported that 22 subjects identified that 'time constraints' was a non-modifiable barrier to adherence [6]. More recently, Llewellyn, *et al.* and DeMoerloose, *et al.* reported motivators for high adherence, namely experience of symptoms, positive belief of necessity of treatment, and a good relationship with the health care provider. Barriers to adherence to factor replacement included absence of symptoms and increasing age [7, 8].

Two patient-related factors not often considered in routine healthcare are health literacy and numeracy. Health literacy is the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions [9]. Numeracy is the ability to handle basic probability and numerical concepts like estimation and problem solving [10]. These two patient-related factors have been associated with poor adherence to medications among patients with human immunodeficiency virus (HIV) and on warfarin anticoagulation [11, 12]. Health literacy and numeracy have not been studied in patients with hemophilia but are important to understanding concepts such as total factor dose calculation from multiple vial sizes and dosing frequency. Both skills are needed to prevent adverse health outcomes including the resultant morbidities due to poor disease control. In the current study, adherence to factor replacement in patients with hemophilia and patient-related characteristics that may influence their adherence were examined. Accordingly, we included these previously unexplored components in our study of adherence. The aim of the study was to determine the association between demographic, socioeconomic, psychosocial, and health literacy, and numeracy characteristics with adherence to factor replacement therapy.

MATERIALS AND METHODS

Participants

In this cross-sectional study, after Emory University Institutional Review Board approval, patients who were 18 years old with moderate or severe hemophilia were considered potentially eligible and approached to determine eligibility during clinic at the Emory University/Children's Healthcare of Atlanta HTC between November 1st, 2012 and January 2nd, 2014. Additional eligibility criteria included current prescribed use of factor (F) VIII or FIX replacement regardless of the inhibitor titer; if prescribed an episodic regimen, subjects must have reported 3 or more hemarthroses in the past year. All self-infused or had someone in the household to infuse factor product intravenously. Lastly, as a result of limited language availability of several research tools, subjects were required to speak and read English. Patients were excluded if they had mild hemophilia, were used bypass agents, or utilized a home health care nurse or the emergency department for infusions. All subjects provided written consent to participate.

Measurements

Sources of Data

Outcome Measure: The primary outcome measure was adherence to factor replacement using the self-reported Validated Hemophilia Regimen Treatment Adherence Scale (VERITAS)-Pro and VERITAS-PRN [1, 13], completed by subjects on prophylaxis regimens and by those for episodic treatment of bleeding episodes, respectively. The range for the total score is 24 to 120, where the lower the score, the higher the adherence. In this study, the VERITAS score was treated as a continuous value as there is no validated cut-off total score to indicate adherence using the VERITAS-PRN score.

Independent Measures: Demographic and socioeconomic information collected on a self-reported questionnaire included race, ethnicity, gender, age, education level, category of annual household income level, access to a car, and employment status. Additionally, subjects self-reported current or past diagnosis of depression, presence of any joint with > 20 bleeds during a lifetime, and whether the patient was currently taking other medication(s) chronically for more than 6 months. Physician trust was measured using the 10-item Wake Forest Physician Trust Scale [14]. The total score ranges from 10 to 50 with a higher score indicating greater physician trust. Health-related quality of life was measured using the Haem-A-QoL [15] and has a total score ranging from 33-230 with a lower score indicating a higher quality of life. Health literacy was measured using the shortened Test of Functional Health Literacy in Adults (s-TOFHLA) [16]. The total score ranges from 0 to 36, and a score 23 is considered health literate. Numeracy was measured using the 3-item scale created by Schwartz & Woloshin [10]. To be considered numerate, one must answer all 3 questions correctly. The investigator was present in the room during health literacy and numeracy assessments to ensure there was no aid from others in the room or from electronic devices to complete the questionnaires. The three other questionnaires were completed by the subject during the clinic visit. Health information obtained from review of the electronic medical records included hemophilia diagnosis, severity, and presence or absence of HIV infection and Hepatitis C virus (HCV) antibody.

Statistical analysis

The pre-enrollment target sample-size was 90 individuals to have 90% power to detect an R^2 of .30 attributed to 7 independent variables of interest. Descriptive statistics were calculated for each measure. Education level was dichotomized into those that did have a bachelor's degree or higher and those that did not have a bachelor's degree. Median household income level was dichotomized at < and \$50,000 based on the median annual income in the United States of \$51,000 in 2013 [17]. Numeracy was analyzed dichotomously (all 3 questions correct vs <3 questions correct). Adherence, health literacy, physician trust, and quality of life were all analyzed as continuous variables. Adherence as measured by the VERITAS score was the outcome variable. Although patients completed one of two VERITAS questionnaires based on their factor replacement regimen, we considered any VERITAS score (whether it was VERITAS-PRO or VERITAS-prn) a measure of adherence in the regression models.

Bivariable associations between adherence and each predictor variable were assessed using simple linear regression. Variables that were significant or approaching significance ($P < .25$) in simple linear regression were included as potential exposure variables in a multivariable linear regression model. Health literacy and numeracy were also evaluated as variables in the adjusted model regardless of their P value on simple linear regression. A final adjusted model that controlled for confounding was created by using a backward step-wise model building process. Interactions between exposure variables were assessed.

All analyses were done using Statistical Analysis System (SAS) version 9.3 (SAS Institute, Cary, North Carolina). $P < .05$ was considered statistically significant.

RESULTS

Demographic and health characteristics

Of 168 potentially eligible patients identified prior to clinic, data was collected from 99 adult males (Figure 1). Complete data was collected on 91 subjects. Among the 8 subjects with missing information, physician trust, health-related quality of life, income level, employment status, insurance status, and self-reported health information were missing.

The mean age of the 99 enrolled subjects was 33 years and ranged from 18 to 62 years (Table 1). The majority were white (69%) and non-Hispanic (94%). Most had hemophilia A (91%) and severe disease (78%) with the majority reporting at least one joint with greater than 20 bleeds during their lifetime (97%). About a quarter of the study population had HIV infection (26%), and over half of the study population were HCV antibody positive (59%); depression history was reported in 21%; and half (49%) infused replacement factor prophylactically. The proportion of subjects on any chronic medications not including factor replacement was 45%. On average, patients were followed at the HTC for 16 years (SD 11). The majority on prophylaxis were adherent and adherence scores were similar between patients on prophylaxis and episodic regimens (mean VERITAS-Pro was 45 [SD 18], mean VERITAS-PRN was 51 [SD 15]) with a lower score indicating greater adherence.

Socioeconomic/Psychosocial/Health literacy measures

A substantial proportion of all subjects (42%) reported their annual household income was \$0–\$24,999; less than a third of this group was age 23 years or younger; about 75% of this group reported the highest level of education as less than a bachelor's degree. Thirty-five percent reported being unemployed or disabled; 78% owned a car. The majority (95%) had functional health literacy; but only 23% were numerate.

Characteristics associated with adherence

On bivariable analysis, the outcome of interest, adherence, was positively associated with being prescribed a prophylaxis regimen, higher physician trust, and better health-related quality of life and was negatively associated with a history of depression ($P < .05$) (Table 2). Health literacy and numeracy were not associated with adherence. On multivariable analysis, after adjusting for treatment regimen, having a history of depression was negatively associated with lower adherence ($P = .01$), whereas being on any chronic medication, longer length of time followed at HTC, higher physician trust, and better health-related quality of life were positively associated with better adherence (all $P < .01$). No effect modification was detected after assessing interaction between exposure variables and age, race, or disease severity. Health literacy, numeracy, and completed undergraduate or higher education were included in the initial multivariable model, but were neither associated with adherence ($P = .87$, $.74$ and $.24$, respectively) nor demonstrated confounding, and thus were not included in the final model (Table 3).

In a subgroup analysis, multivariable analysis was completed with subjects stratified by factor replacement regimen. Although the power was reduced due to smaller sample size, for subjects using factor replacement prophylactically, being on any chronic medication ($P < .01$) and better health-related quality of life ($P < .01$) were both associated with greater adherence, whereas history of depression ($P = .24$), longer length of time followed at HTC ($P = .16$), and higher physician trust ($P = .40$) were not associated with adherence in this subgroup. In contrast, in the subgroup of patients using on-demand therapy, history of depression ($P = .02$), longer length of time followed at HTC ($P = .04$), higher physician trust ($P = .03$), and better health-related quality of life ($P = .02$) remained associated with adherence, while being on any chronic medication ($P = .26$) was not. These differences in multivariable results were not accounted by differences between the prophylactic and on-demand groups in the proportion of subjects with history of depression (22% vs. 20%), mean health-related quality of life (98.5 vs. 96.0), mean physician trust (42.7 vs. 42.6), mean length of time followed at HTC (15.7 vs. 15.8), and subjects on a chronic medication (40% vs. 50%).

DISCUSSION AND CONCLUSION

This single center study identified several modifiable and non-modifiable characteristics associated with adherence to factor replacement in patients with moderate and severe hemophilia. Non-modifiable patient characteristics include being on any chronic medication, having been followed longer at the HTC, and better health-related quality of life. Potential

modifiable characteristics associated with adherence include high physician trust and a lack of history of depression.

The presence of a self-reported history of depression was associated with having a 7-point higher score on the VERITAS scale. Previous studies indicated depression is prevalent among patients with hemophilia [18]. Depression has been linked with poor adherence among patients with diabetes [19] and although not formally evaluated in patients with hemophilia, the negative impact of depression on adherence has been suggested in prior studies. In a qualitative study reported by Flood, *et al*, depression was related to a loss of independence with performing daily activity [18]. In a separate study, depressive symptoms were significantly associated with lack of social support and unemployment [20] as well as potentially associated with increased annual bleeding episodes which the authors surmised could be associated with failure to be adherent to anti-haemophilic factor treatment. Although history of depression was equally prevalent in both treatment regimens, it played a larger role with respect to adherence amongst patients using on-demand therapy. Since the study did not evaluate current symptoms of depression nor specify how remote or severe the depression was, it is possible that these issues are the driver of the differential significance and further investigation is needed. Alternatively, it could be that depression has more influence on adherence in patients using on-demand therapy and may in fact be a barrier to adoption of prophylactic therapy.

The association between higher adherence and better quality of life was previously reported by Duncan, *et al* [21]. She hypothesized that with higher adherence, there is improved physical functioning and therefore increased quality of life. Alternatively, higher quality of life with less psychosocial stress may facilitate adherence. The cross-sectional design of this study and the study reported by Duncan, *et al*, cannot determine the directionality of the effect.

Physician trust also influenced adherence. Every 10 points higher on the Wake Forest Physician Trust scale was associated with a 5 points decreased in the VERITAS score is expected to decrease by 5 points. The impact of physician trust on adherence to factor replacement has been previously reported. In the qualitative study by De Moerloose, *et al*, a good relationship with the health care provider was associated with adherence [8]. Although physician trust can be different than having a good relationship with the health care provider, there is some overlap in these concepts. Our study showed a positive association between the duration of time followed at our HTC and adherence to factor replacement. Similarly, De Moerloose, *et al*, did identify that the more time spent with an HTC member during a clinic visit was associated with higher adherence. This observation further emphasizes the importance of building a strong relationship with HTC patients. The positive impact of physician trust and shared decision-making on adherence to treatment has also been demonstrated in other chronic diseases such as diabetes and hypertension [22, 23]. As was the case with a history of depression, physician trust was significantly associated with adherence in patients using on-demand therapy but not in those using prophylaxis despite a similar distribution of physician trust in the two groups. Although conclusions are limited by sample size, it is also possible that physician trust is in fact more influential in patients who have yet to adopt a prophylactic regimen of factor replacement therapy.

Interestingly, the use of any chronic medication was associated with better adherence to factor replacement. Specifically, those on chronic medications were associated with a 6-point lower VERITAS score. This finding differs from two other studies that reported chronic medication use was associated with decreased adherence to oral drugs used to treat cancer and Parkinson's disease [24, 25]. We can speculate that among patients in this study, having other health conditions may be a motivator to better manage their hemophilia. Alternatively, pain medications may be a common chronic medication and pain may be a motivator for adherence to factor replacement therapy.

In contrast to other studies, neither age [26] nor disease severity [27] was associated with adherence in our study. The lack of association with age is possibly related to the fact that the majority of our patients were younger adults with only 14 subjects age 50 years or older. The ability to evaluate disease severity was limited by the necessity of having subjects who received factor replacement therapy; accordingly, the study population was fairly homogeneous in this respect with 78% having severe disease.

To date, there have been no published studies about health literacy and numeracy in the hemophilia population. There are minimal descriptions of health literacy and numeracy in any individuals with hematological disorders such as an abstract by Shook, *et al.* about health literacy in patients with sickle cell disease [28]. This area of research remains vastly underreported and understudied for those with bleeding disorders. A large majority of this single center population had functional health literacy and therefore associations with adherence to factor replacement were not able to be made. Though numeracy was not associated with adherence to factor replacement in this study, only a minority of patients were able to answer questions about probability, percentages, and proportions which may impact a patient's understanding of dose, factor pharmacokinetics, and risk.

Our study was limited by the fact that our enrollment included only those who attended their scheduled HTC appointments and were sufficiently on time to allow completion of study questionnaires. However, there was no difference in age, diagnosis, race, ethnicity, and treatment regimen between those who participated and those who were scheduled for clinic and did not show or declined to participate. Secondly, we did not evaluate more abstract patient factors such as family support, social support, social stigma, perception about the need for the medication, and perception of risk of side effects. Certain health-system factors that could influence adherence were also not evaluated including individual formularies, prior-authorization requirements, and cost-sharing. Third, we limited our enrollment to only those who read and spoke English due to the limited validated tools in other languages. This likely contributed to a study population with greater functional health-literacy than that of the population from which the study was drawn. A fourth limitation is that there is a possible misclassification of physician trust scores since patients may be less likely to report distrust while in the HTC. Nevertheless, our high participation rate provided an accurate reflection of the patient population in our single center.

In conclusion, adherence to factor replacement therapy is multifactorial and appears to be influenced by depression, physician trust, health-related quality of life, and use of chronic medications. As research continues to guide the improvement of care for patients with

hemophilia, several modifiable factors have been identified in this study such as increasing physician trust and identifying and managing depression. Since high physician trust is also associated with increased adherence to factor replacement in the hemophilia population, future research should evaluate interventions to maximize physician trust and assess its impact on adherence to factor replacement therapy.

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References

1. Duncan N, Kronenberger W, Roberson C, Shapiro A. VERITAS-Pro: a new measure of adherence to prophylactic regimens in haemophilia. *Haemophilia* : the official journal of the World Federation of Hemophilia. 2010; 16:247–55. [PubMed: 19925631]
2. Valentino LA. Secondary prophylaxis therapy: what are the benefits, limitations and unknowns? *Haemophilia* : the official journal of the World Federation of Hemophilia. 2004; 10:147–57. [PubMed: 14962203]
3. Darby SC, Kan SW, Spooner RJ, Giangrande PL, Hill FG, Hay CR, et al. Mortality rates, life expectancy, and causes of death in people with hemophilia A or B in the United Kingdom who were not infected with HIV. *Blood*. 2007; 110:815–25. [PubMed: 17446349]
4. Osterberg L, Blaschke T. Adherence to medication. *The New England journal of medicine*. 2005; 353:487–97. [PubMed: 16079372]
5. Gellad, W.; Grenard, J.; McGlynn, E. A Review of Barriers to Medication Adherence: A Framework for Driving Policy Options. Santa Monica, CA: RAND Corporation; 2009.
6. Thornburg CD, Pipe SW. Adherence to prophylactic infusions of factor VIII or factor IX for haemophilia. *Haemophilia* : the official journal of the World Federation of Hemophilia. 2006; 12:198–9. [PubMed: 16476098]
7. Llewellyn CD, Miners AH, Lee CA, Harrington C, Weinman J. The illness perceptions and treatment beliefs of individuals with severe haemophilia and their role in adherence to home treatment. *Psychol Health*. 2003; 18:185–200.
8. De Moerloose P, Urbancik W, Van Den Berg HM, Richards M. A survey of adherence to haemophilia therapy in six European countries: results and recommendations. *Haemophilia* : the official journal of the World Federation of Hemophilia. 2008; 14:931–8. [PubMed: 18684125]
9. Health literacy: report of the Council on Scientific Affairs. Ad Hoc Committee on Health Literacy for the Council on Scientific Affairs, American Medical Association. *JAMA*. 1999; 281:552–7. [PubMed: 10022112]
10. Schwartz LM, Woloshin S, Black WC, Welch HG. The role of numeracy in understanding the benefit of screening mammography. *Ann Intern Med*. 1997; 127:966–72. [PubMed: 9412301]
11. Kalichman SC, Ramachandran B, Catz S. Adherence to combination antiretroviral therapies in HIV patients of low health literacy. *J Gen Intern Med*. 1999; 14:267–73. [PubMed: 10337035]
12. Estrada CA, Martin-Hryniewicz M, Peek BT, Collins C, Byrd JC. Literacy and numeracy skills and anticoagulation control. *Am J Med Sci*. 2004; 328:88–93. [PubMed: 15311167]
13. Duncan NA, Kronenberger WG, Roberson CP, Shapiro AD. VERITAS-PRN: a new measure of adherence to episodic treatment regimens in haemophilia. *Haemophilia* : the official journal of the World Federation of Hemophilia. 2010; 16:47–53.
14. Hall MA, Zheng B, Dugan E, Camacho F, Kidd KE, Mishra A, et al. Measuring patients' trust in their primary care providers. *Medical care research and review* : MCRR. 2002; 59:293–318. [PubMed: 12205830]
15. Rentz A, Flood E, Altisent C, Bullinger M, Klamroth R, Garrido RP, et al. Cross-cultural development and psychometric evaluation of a patient-reported health-related quality of life

- questionnaire for adults with haemophilia. *Haemophilia : the official journal of the World Federation of Hemophilia*. 2008; 14:1023–34. [PubMed: 18665853]
16. Baker DW, Williams MV, Parker RM, Gazmararian JA, Nurss J. Development of a brief test to measure functional health literacy. *Patient education and counseling*. 1999; 38:33–42. [PubMed: 14528569]
 17. DeNavas-Walt, CPB. US Census Bureau: Current Population Reports. Washington, D.C: U.S. Government Printing Office; 2014. *Income and Poverty in the United States*: 2013.
 18. Flood E, Pocoski J, Michaels LA, Bell JA, Valluri S, Sasane R. Illustrating the impact of mild/moderate and severe haemophilia on health-related quality of life: hypothesised conceptual models. *European journal of haematology*. 2014; 93(Suppl 75):9–18.
 19. Krass I, Schieback P, Dhippayom T. Adherence to diabetes medication: a systematic review. *Diabetic medicine : a journal of the British Diabetic Association*. 2015; 32:725–37. [PubMed: 25440507]
 20. Iannone M, Pennick L, Tom A, Cui H, Gilbert M, Weihs K, et al. Prevalence of depression in adults with haemophilia. *Haemophilia : the official journal of the World Federation of Hemophilia*. 2012; 18:868–74. [PubMed: 22642565]
 21. Duncan N, Shapiro A, Ye X, Epstein J, Luo MP. Treatment patterns, health-related quality of life and adherence to prophylaxis among haemophilia A patients in the United States. *Haemophilia : the official journal of the World Federation of Hemophilia*. 2012; 18:760–5. [PubMed: 22548353]
 22. Bauer AM, Parker MM, Schillinger D, Katon W, Adler N, Adams AS, et al. Associations between antidepressant adherence and shared decision-making, patient-provider trust, and communication among adults with diabetes: diabetes study of Northern California (DISTANCE). *Journal of general internal medicine*. 2014; 29:1139–47. [PubMed: 24706097]
 23. Abel WM, Efrid JT. The Association between Trust in Health Care Providers and Medication Adherence among Black Women with Hypertension. *Frontiers in public health*. 2013; 1:66. [PubMed: 24350234]
 24. Verbrughe M, Verhaeghe S, Lauwaert K, Beeckman D, Van Hecke A. Determinants and associated factors influencing medication adherence and persistence to oral anticancer drugs: a systematic review. *Cancer treatment reviews*. 2013; 39:610–21. [PubMed: 23428230]
 25. Daley DJ, Myint PK, Gray RJ, Deane KH. Systematic review on factors associated with medication non-adherence in Parkinson's disease. *Parkinsonism Relat Disord*. 2012; 18:1053–61. [PubMed: 23022461]
 26. Buck D, Jacoby A, Baker GA, Chadwick DW. Factors influencing compliance with antiepileptic drug regimes. *Seizure*. 1997; 6:87–93. [PubMed: 9153719]
 27. Armstrong EP, Malone DC, Krishnan S, Wessler MJ. Adherence to clotting factors among persons with hemophilia A or B. *Hematology*. 2015; 20:148–53. [PubMed: 25001343]
 28. Shook, L.; Crosby, L.; Atweh, G. *Health Literacy and Sickle Cell Disease: An Assessment Of Adolescents, Young Adults and Caregivers*. American Society of Hematology; New Orleans, LA: 2013. p. 2251

Figure 1.
Screening and Enrollment

Table 1**Subject Characteristics (n=99)**

Characteristic	n (%)	mean (SD)
Demographics		
Age (years)		33 (18)
Male Gender	99 (100)	
Race (n=91)		
White	63 (69)	
Black	24 (27)	
Asian	3 (3)	
Other	1 (1)	
Hispanic Ethnicity (n=91)	5 (6)	
Hemophilia Measures		
Hemophilia A	90 (91)	
Severe Disease	77 (78)	
Prophylaxis Regimen	49 (49)	
Length of time seen in Emory HTC (years) (n=91)		16 (11)
Any target joint(s) (n=91)	88 (97)	
VERITAS-Pro Score (n=45) (24–120)		45 (18)
Adherent if Pro Score 57	36 (80)	
VERITAS-PRN Score (n=46) (24–120)		51 (15)
Other Health Measures		
HIV Antibody Positive (n=91)	24 (26)	
HCV Antibody Positive (n=91)	54 (59)	
Any chronic medication use (n=91)	41 (45)	
Depression History (n=91)	19 (21)	
Socioeconomic Measures		
Income Level (n=91)		
\$0 – \$24,999	38 (42)	
\$25K – \$49,999	17 (19)	
\$50K – \$99,999	25 (27)	
\$100K or more	11 (12)	
Highest Education (n=91)		
Less than a high school diploma	8 (9)	
High school diploma/GED	25 (27)	
Completed some college and/or associate's degree	25 (27)	
Bachelor's degree	23 (26)	
Graduate degree	10 (11)	
Unemployed/Disabled (n=91)	32 (35)	
Owns a car (n=91)	71 (78)	
Psychosocial Measures		
WFPTS Score (n=91) (10–50)		42.6 (6.6)

Characteristic	n (%)	mean (SD)
Haem-A-QoL Score (n=91) (33–230)		97.3 (33.2)
Literacy Measures		
s-TOFHLA Score (n=98) (0–36)		35 * (1) **
Inadequate (0–16)	2 (2)	
Marginal (17–22)	3 (3)	
Adequate (23–36)	86 (95)	
Correct Answers for the SW Numeracy Questions (n=98)		
0	13 (13)	
1	27 (28)	
2	35 (36)	
3	23 (23)	

* Median;

** Interquartile Range

SD: Standard Deviation; HTC: Hemophilia Treatment Center; VERITAS-Pro: validated hemophilia regimen treatment adherence scale (on prophylaxis); VERITAS-PRN: validated hemophilia regimen treatment adherence scale (for those who infuse only when there is a bleed); HIV: Human Immunodeficiency Virus; HCV: Hepatitis C Infection; GED: General Education Development; WFPTS: Wake Forest Physician Trust Scale; s-TOFHLA: shortened Test of Functional Health Literacy in Adults; SW: Schwartz-Woloshin

Table 2

Bivariable Linear Regression Evaluating the Association Between Adherence and Clinical and Demographic Predictors (n=91)¹

Predictor	Beta Coefficient	95% CI	P-value	R ²
Demographics				
Age	-0.05	-0.27, 0.17	0.65	0.002
White race (ref: all other)	-0.56	-6.10, 4.99	0.84	0.0004
Hispanic Ethnicity (ref: non-Hispanic)	-1.62	-12.85, 9.61	0.78	0.001
Hemophilia Measures				
Hemophilia A (ref: B)	0.86	-7.72, 9.44	0.84	0.0004
Severe Disease (ref: moderate)	-0.58	-6.56, 5.40	0.84	0.0004
Prophylaxis Regimen (ref: on-demand)	-5.49	-10.48, -0.50	0.03	0.05
Length of Time at HTC (years)	-0.20	-0.44, 0.03	0.09	0.03
Any target joints (ref: none)	4.13	-10.18, 18.45	0.57	0.004
Other Health Measures				
HIV Positive (ref: HIV negative)	-0.67	-6.48, 5.14	0.82	0.001
HCV Positive (ref: HCV negative)	-0.95	-6.16, 4.26	0.72	0.002
On chronic medication(s) (ref: none)	-3.17	-8.28, 1.93	0.22	0.02
Depression History (ref: none)	6.30	0.14, 12.46	0.04	0.04
Socioeconomic Measures				
Annual Income \$50,000 (ref: \$50,000)	-2.15	-7.37, 3.06	0.41	0.01
Completed undergrad or higher (ref: no undergrad)	-4.80	-10.03, 0.43	0.07	0.04
Unemployed/Disabled (ref: employed/retired)	2.43	-2.91, 7.77	0.37	0.01
Owns car (ref: no car)	-1.95	-8.12, 4.22	0.53	0.004
Psychosocial Measures				
WFPTS Score	-0.72	-1.08, -0.36	<0.01	0.15
Haem-A-QoL score	0.13	0.057, 0.20	<0.01	0.12
Literacy Measures				
s-TOHFLA score	-0.28	-0.76, 0.19	0.24	0.02
Numerate (ref: numeracy < 3)	0.40	-5.58, 6.39	0.89	0.0002

¹Results from simple linear regression. Adherence using VERITAS scale: The lower the VERITAS score, the higher the adherence

CI: Confidence Interval

HTC: Hemophilia Treatment Center; HIV: Human Immunodeficiency Virus; HCV: Hepatitis C Infection; WFPTS: Wake Forest Physician Trust Scale (The higher the score, the higher the physician trust); Haem-A-QoL: The lower the score, the better the quality of life; s-TOHFLA: shortened Test of Functional Health Literacy in Adults.

Table 3Multivariable Linear Regression of the Association of Adherence with Predictor Measures (n=91)[†]

Predictor	Beta Coefficient	95% CI	p-value	Partial R ²
Depression history (ref: none)	7.13	1.56, 12.69	0.01	0.11
Haem-A-QoL score (per 10 points)	1.32	0.65, 1.99	<0.01	0.11
WFPTS score (per 10 points)	-4.57	-7.81, -1.33	<0.01	0.10
Time seen at HTC (per 10 years)	-3.04	-5.04, -1.03	<0.01	0.03
On chronic medication(s) (ref: none)	-6.03	-10.5, -1.56	<0.01	0.01

[†] Adjusted model for treatment type; adjusted R² = 0.30. Adherence using VERITAS scale: The lower the VERITAS score, the higher the adherence

CI: Confidence Interval

WFPTS: Wake Forest Physician Trust Score. The higher the score, the higher the physician trust;

Haem-A-QoL: The lower the score, the better the quality of life