Characteristics and Treatment Patterns of von Willebrand Disease in the USA

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INTRODUCTION

- Von Willebrand disease (VWD) is the most common inherited bleeding disorder. Results from screening studies of general populations estimate the prevalence at 0.6% to 1.3% whereas results from studies of symptomatic patients seen at hemostasis centers estimate the prevalence to be much lower, from 0.0023% to 0.01%.[1] Unlike hemophilia which primarily affects males, VWD equally affects males and females.[2]
- Patients with VWD have impaired hemostasis due to a quantitative (Type 1 and Type 3) or qualitative (Type 2) deficit in von Willebrand Factor (VWF) which alters platelet adhesion and/or decreases factor VIII (FVIII) concentrations.[1] Clinical manifestations distinguishing VWD from hemophilia include mucosal bleeding, prolonged bleeding time, autosomal transmission, and normal platelet counts.[3-5] Unlike patients with hemophilia, most patients with VWD exhibit mild symptoms; these mild symptoms are often treatable without blood transfusions, factor replacement therapy, or physician office visits.[1,6]
- The CHOICE (Community Having Opportunity to Influence Care Equity) Project was conducted under a cooperative agreement between the US Centers for Disease Control and Prevention (CDC) and Hemophilia Federation of America (HFA), a non-profit, community-based advocacy organization, to survey persons with bleeding disorders, including those with VWD.
- A better understanding of the VWD population and disease burden in the US may help payers support access and improve care and treatment for this patient population.

OBJECTIVE

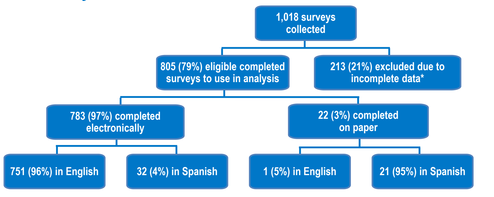
- To characterize diagnosed VWD patients in the US in terms of demographics, site of care, initial treatment, bleeds, and productivity

METHODS

Survey Methodology

- The CHOICE survey was disseminated online and in paper form from April 2013–July 2015 in the following ways, *inter alia*:
  - HFA and its 47 member organizations recruited participants at local, statewide, regional, and national meetings and via social media,
  - HFA's contracting member organizations recruited their members and family of members directly, and
  - HFA/CDC branded email/mail to 1,700+ identified hematologists identified at non-HTC facilities.
- The CHOICE survey gathered the following information from the patients:
  - Patient demographics (age, gender, income, co-morbidities, diagnoses, etc.)
  - Bleeding history (types of bleeds, number of bleeds, location of bleed, etc.)
  - Treatment (by-passing agents, non-topical, hormonal, etc.)
  - Health services utilization (physician specialty, location of treatment, hospital visits, ER visits, etc.)
- Participants were recruited to take a ~20 minute survey in English or Spanish. Survey responses were excluded from the final data set if they did not provide gender, diagnosis, and whether the person filling out the survey was a patient or patient caregiver (for children < 18 years). This selection method was approved by the CDC.
- For this analysis, respondents who had another bleeding disorder plus VWD were excluded. Surveys reporting a single diagnosis of VWD were included in the final data set.

Figure 1. Survey Data Sets Overall



*NOTE: Patients were excluded from the data if they did not provide gender, diagnosis, and whether they were a patient or patient caregiver (for those under 18 years old) filling out the survey. This selection method was approved by the CDC.

Data Analysis

- Descriptive analysis of participants reporting VWD diagnosis was performed. Patients were stratified into Treated or Non-treated cohorts. Statistical significance of differences between cohorts was assessed using t-tests for continuous measures or chi-squared for categorical variables.

RESULTS

Demographics and Type of VWD

- A total of 807 patients were surveyed of which 94 (12%) reported a diagnosis of VWD only. The 94 VWD-only diagnosed patients were divided into Treated (n = 74) vs Non-treated Groups (n = 14).
- Treated participants were defined as using at least one medication, treatment, or surgery to treat their bleeding disorder within the last 12 months prior to participation. Non-treated participants reported they did not use any medications, treatments, nor surgeries to treat their bleeding disorder within the last 12 months prior to participation.
- Majority of survey respondents were female (N = 73, 78%) and Type 1 patients (N = 55, 59%), followed by Type 2 (N = 19, 20%), Type 3 (N = 13, 14%), and 6 (6%) with unknown type.

Figure 2. VWD-only Cohort

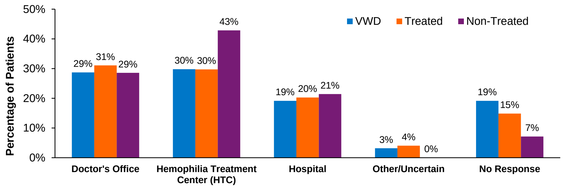
Figure 3. Summary of Characteristics of Treated vs Non-treated VWD-only Diagnosed Respondents

Treated Cohort	Non-treated Cohort
Average age: 31* (more < 18) (*p* = 0.018)	Average age: 42*
Employed full time: 16%	Employed full time: 43%
Lower annual income (*p* = 0.031)*	Higher annual income*
Fewer have health insurance (73%)	More have health insurance (86%)

*Text in magenta demotes statistical significance between cohorts, for that variable. *P*-values are reported above.

- Figure 3 summarizes patient characteristics of Treated and Non-treated respondents.
- Treated patients were significantly younger and had a higher proportion of individuals < 18 years of age compared to Non-treated patients ($p = 0.02$). However, Treated patients have a significantly lower annual income than the Non-treated patients ($p = 0.03$), although the latter cohort reported having more health insurance.

Figure 4. Reported Usual Site of Care

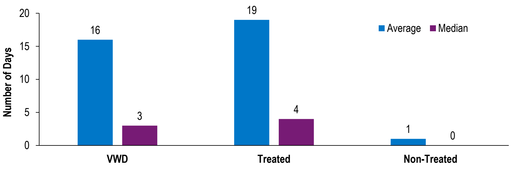


RESULTS (continued)

Site of Care and Provider Specialty

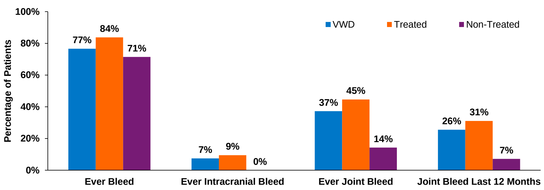
- Out of 74 who reported a usual place of care, 28 (30%) reported care at a hemophilia treatment center (HTC), 27 (29%) at a doctor's office, 18 (19%) at a hospital, and three (3%) other/uncertain. Usual place of care was defined as the type of location that a patient usually visits for care of their bleeding disorder.
- VWD patients usually go to either a doctor's office or an HTC facility to receive VWD care, while 19% report hospital as usual place of care.
- A majority (64%) of VWD patients saw a healthcare provider at least once a year for VWD care. 72% of Treated patients and 50% of Non-treated patients reported once-a-year care.
- 62% of all VWD patients usually see a hematologist for VWD care.
- Non-treated patients were more likely (43%) to seek treatment, or care, prior to a medical procedure vs Treated patients (4%); however, the difference was not statistically significant.
- Non-treated participants may receive care for their bleeding disorder by a healthcare provider but not treatment for it in the 12 months prior to completing the survey.

Figure 5. Reported Missed Days From School or Work



- Figure 5 shows that the average and median number of days patients missed from work, school, or usual activities in the last 12 months, due to VWD, was 3 days (range 1–19 days).
- VWD patients reported a diagnosis of anxiety and depression (36%/38% and 30%/43%, Treated/Non-treated, respectively).
- Among females with VWD, 87% reported ever having a heavy period with 22% (n = 16) of female respondents reporting a hysterectomy. The median age for a hysterectomy was 32 (range 30–38) years, while the mean age was 34 years.

Figure 6. Reported Bleeds Over Lifetime or Last 12 Months



- Figure 6 summarizes any bleed (Ever Bleed, Ever Intracranial bleed, Ever Joint Bleed) in lifetime, as well as over the last 12 months (Joint Bleed Last 12 Months).
- Approximately 8 out of 10 VWD patients reported a bleed at some point in their lives. Treated patients were 4 times more likely to have had a joint bleed within the last 12 months compared to Non-treated patients.
- Within the last 12 months, 26% of the total VWD cohort have had a joint bleed and 31% among the Treated cohort reported having a joint bleed.
- No significant differences were found between those Treated vs Non-treated in the Ever Bleed, Ever Intracranial Bleed, or Joint Bleeds Last 12 Months categories.

Treatment Patterns

- Of the total VWD-only diagnosed respondents, 74 patients reported receiving treatment (79%)
  - The most common treatment was plasma-derived VWF (N = 40, 54%) followed by non-plasma (ie, desmopressin) and topical products (N = 23, 31%).
  - Nearly one-third (31%) of Treated VWD patients received non-plasma and topical products within the last 12 months.

DISCUSSION

- Because VWD occurs among both genders, it is critical to examine how the disease affects both genders in terms of severity of diagnosis, treatment types, bleeds (location and frequency), usual places of care, and socio-demographic information.
- The higher bleed rates reported among Treated patients suggests that more severe patients are more likely to receive treatment. Thus, there is a need to define what is clinically severe in a VWD population.
- Questions remain about how the prevalence of heavy menses may impact quality of life and what effect improved diagnosis and early treatment would have on hysterectomy procedures, especially among women of child-bearing potential.
- Rates of both depression and anxiety, 34% and 35% respectively, among all VWD participants are well above national rates in the US. Nationally, 6.7%[7] of adults suffer from depression and 18.1%[8] from anxiety.
- Further, additional analysis and inquiry into the impact of socio-economic status is needed to understand how disease burden (bleeds, heavy menses, depression) affect employment and productivity, as a third of all VWD patients reported a household income of less than $25,000.
- Similar to hemophilia, VWD patients experience joint bleeds which may lead to arthropathy, if not properly managed. A third of patients treated reported having a joint bleed within the last year, which is higher than reported in the available literature.[1,2]

LIMITATIONS

- Results may not be generalizable beyond the population studied in this analysis.
- This sample does not necessarily represent all VWD patients as outreach by HFA member organizations in some regions may have led to over-representation of some participant characteristics.
- Data reporting was limited in this dataset and does not include prospective clinical data collection, nor adjudication to insurance medical and pharmacy claims.

CONCLUSIONS

- **Results of this analysis of initial survey data show that VWD patients are heterogeneous (both genders, all ages), experience significant clinical bleeds–including joint bleeds, and suffer humanistic burden (missed work/school days, depression/anxiety) related to their disease.**
- **Given these findings, there may be a substantial unmet need in this population (preventable bleeds, missed work/school days, depression/anxiety, hysterectomies).**
- **Further analyses are needed to understand VWD real-world clinical outcomes, treatment utilization, and quality of life compared to the general population and other bleeding disorders**.

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Academy of Managed Care Pharmacy; Oct 3–6, 2016; National Harbor, MD