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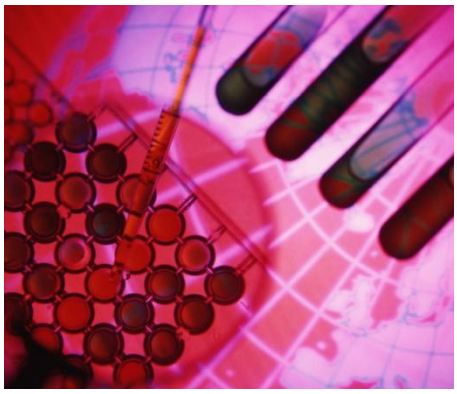

HEALTHCARE AND HUMAN SERVICES POLICY, RESEARCH, AND CONSULTING—WITH REAL-WORLD PERSPECTIVE.

Strategic Summit on Von Willebrand Disease

Prepared for: **National Hemophilia Foundation**

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March 2015

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Executive Summary

The National Hemophilia Foundation (NHF) conducted a summit meeting of stakeholders on von Willebrand disease (VWD) on November 21, 2014, in Washington, DC. The purpose of the summit was to discuss and develop a strategic approach for raising awareness of VWD and improving patient access to care in the evolving health care environment. The 38 summit participants included key figures in VWD research, care, and policy with representatives of such stakeholders as VWD patients and families, clinicians, payers, the pharmaceutical industry, and relevant federal agencies.

Following overviews of clinical and scientific aspects of VWD and patient perspectives and challenges, summit participants addressed four main issue areas: (1) recognizing and addressing stigma and marginalization, (2) clinical challenges, (3) hemophilia treatment center (HTC) and physician recognition and focus on VWD, and (4) organizational recognition and focus on VWD. For each issue area, the summit then moved to potential strategies and related next steps for NHF and VWD stakeholders to address the challenges and unmet needs. Among the key points arising in each areas are the following.

Issue 1: Recognizing and Addressing Stigma and Marginalization

- Awareness of VWD on the part of patients, families, health care providers, and others in the community is inadequate and has negative implications for patient health and quality of life.
- Patients with VWD experience externally- and internally-imposed stigma and are subject to marginalization in the health care and broader communities, all of which can have adverse impacts on their health and quality of life.
- Patients with VWD desire a stronger sense of community, with greater education and related support to empower self-advocacy in the diagnosis and management of their VWD.

Issue 2: Clinical Challenges

Clinical processes

- Physicians may be hesitant to diagnose individuals with VWD due to such factors as: lack of a well-recognized or standard diagnostic test battery, uncertain reimbursement status for a diagnostic testing battery, and uncertain or ambiguous coding and classification guidance
- An important step toward standardization of diagnosis of VWD would be to develop a protocol for the processing of certain laboratory testing variables
- Other useful steps would be to adapt such existing resources as the monograph of standards for handling blood samples for VWD testing developed by the Clinical and Laboratory Standards Institute (CLSI) and updating of diagnostic coding and accompanying terminology for VWD and certain bleeding disorders that resemble VWD.

Clinical practice guideline

- A well-qualified and authoritative organization, or a consortium of such organizations, should develop a new or updated evidence-based clinical practice guideline on VWD.

- One approach would be to update the guideline developed by the National Heart, Lung, and Blood Institute (NHLBI) that was published in 2008.
- The key organizations involved in sponsoring, developing, and or disseminating a new or updated guideline would include, though not necessarily be limited to, the NHF, NHLBI, International Society on Thrombosis and Haemostasis, and the American Society of Hematology.

Issue 3: HTC and Physician Recognition and Focus on VWD

Barriers

- Under-recognition of and under-engagement (i.e., insufficient communication and interaction) with VWD patients by HTCs and clinicians can have a negative impact on patient health and quality of life.
- Some HTCs have reportedly turned away or otherwise exhibited clinically relevant lack of engagement with patients with VWD.
- To the extent that any VWD patients have been turned away from HTCs or otherwise been discouraged from seeking care at HTCs is entirely unacceptable.

HTC-level engagement

- HTCs and the broader blood disorder community should encourage collaboration among providers through the establishment of comprehensive treatment plans and provider networks.
- Advocates should facilitate patient education and understanding of symptoms of bleeding disorders to better enable patients to describe their condition to providers and better ensure that they are appropriately evaluated at HTCs.
- HTCs should implement satellite clinics or other points of access where possible to ensure that patients in underserved areas or who are subject to other barriers to care gain adequate access; these may include, e.g., clinics for young children, adolescent clinics, and rural outreach clinics.

Organization-level engagement

- NHF or its chapters could conduct or sponsor educational events in partnership with HTCs (e.g., education in the morning, clinic in the afternoon) to improve VWD awareness and clinical care.
- NHF and other professional and advocacy groups could support provider networking to facilitate clinical referrals and multidisciplinary care of patients with VWD.

Issue 4: Organizational Recognition and Focus on VWD

- NHF should clearly re-establish its commitment as a VWD advocacy organization that sponsors and otherwise engages in collaborative, multi-stakeholder efforts to improve VWD awareness, access to care, health outcomes and quality of life, and research.
- NHF should serve as a centralized resource for information and engagement of patients with VWD, providers, HTCs, other advocacy organizations, government agencies, industry, and other VWD stakeholders.
- In collaboration with other stakeholder organizations , NHF should facilitate the development, dissemination and implementation of: a new or updated evidence-based clinical practice

guideline for VWD, standard definition and classification system for VWD, and high-quality provider and patient education materials that are appropriately tailored to the range of people with or at-risk for VWD.

Conclusion

The health care community, including providers, payers, patients, and others, has under-recognized VWD, with negative consequences for people with the disorder and their families. The summit deliberations identified potential next steps for making inroads against these deficits, including certain initiatives that can be undertaken beginning in 2015 to yield demonstrable near-term improvements. Such next steps should include some or all of improving VWD classification, VWD diagnostic criteria and testing protocols, a new or updated evidence-based clinical practice guideline, encouraging HTCs to adopt more flexible care models, and targeted educational materials to improve VWD awareness by patients, providers, payers, and other stakeholders. Pursuing these steps will require close collaboration among such organizations as NHF and other advocacy groups; such government agencies as NHLBI, HRSA, CDC, and CMS; health professional organizations; HTCs; industry; and others. As the nationally recognized patient and consumer organization for bleeding disorders, NHF should take on a more explicit, though not singular, leadership role in pursuing these next steps.

Introduction

The National Hemophilia Foundation (NHF) conducted a summit meeting of stakeholders in von Willebrand disease (VWD) on November 21, 2014, in Washington, DC. The purpose of the summit was to discuss and develop a strategic approach for raising awareness of VWD and improving patient access to care in the evolving health care environment. Participants included patients, patient advocates, clinicians, payers, treatment manufacturers, and representatives of related federal programs. NHF planned the summit in consultation with the Lewin Group, which also facilitated the event.

The summit addressed four main issues: (1) recognizing and addressing stigma and marginalization, (2) clinical challenges, (3) hemophilia treatment center and physician focus on VWD, and (4) organizational recognition and focus on VWD. This paper provides a brief background on VWD, the method of convening the meeting, an overview of the opening presentations on patient perspectives; a summary of the discussions pertaining to the four main issue areas; and summit participants' suggested next steps or other initiatives to pursue in each of the issue areas.

Background

VWD is a set of inherited bleeding disorders caused by a quantitative deficiency in von Willebrand factor (VWF), defects in VWF, or defects in the receptor sites for VWF. These problems result in slower formation of blood clots and prolonged bleeding in mucous membranes and soft tissues. The most common bleeding symptoms associated with VWD are nosebleeds, easy bruising, bleeding gums, and heavy menstrual periods. Severe bleeding into joints or other internal bleeding can occur in the rare type of VWD, and some instances can lead to internal organ damage and be life threatening.

VWD is the most common inherited bleeding disorder, with a higher prevalence than hemophilia A, hemophilia B, and deficiencies of other clotting factors. Among the challenges for managing health care for people with VWD are the inherent variability of the disease, under-reporting by patients, inconsistent approaches to defining cases in epidemiological studies, and inadequacies in the diagnosis of VWD.

VWD is classified into three main categories according to the type of deficiencies related to VWF. Type 1 is due to a quantitative reduction in VWF, type 2 is due to a qualitative deficiency in VWF, and type 3 is due to the absence of VWF. These classifications are further divided into subcategories to account for variations in those deficiencies.

Type 1 VWD is the most common form, affecting approximately 60-80% of people with the disorder, and is characterized by mild-to-moderately-severe reduction of VWF (typically defined as approximately 30-40 IU/dL). People with type 1 VWD experience limited-to-occasional bruising or bleeding after major surgery or dental work. Although people with any form of VWD can experience bleeding problems, many people with type 1 never experience severe symptoms or even realize that they have the disorder. People with type 2 VWD comprise about 15-30% of the total population with VWD, with a moderately

severe reduction of VWF (approximately 10-30 IU/dL). Depending on the variant, these patients tend to experience occasional spontaneous bleeding, with prolonged bleeding after superficial cuts or injury. People with type 3 VWD have a severe quantitative deficiency of VWF (less than 10 IU/dL) and experience spontaneous mucocutaneous bleeding and bleeding into joints and muscles. Type 3 VWD is very rare, accounting for about 5%-10% of the people with VWD.[1]

Although the genetic determinants of type 2 and type 3 VWD are well understood, those of type 1 still are not well defined and may involve any of a large number of genetic factors beyond those mediating VWF. This continues to present diagnostic challenges for identifying the most common form of VWD. The substantial variations in patient experience with VWD also increase the difficulty of diagnosing VWD and helping patients to manage their conditions effectively. In contrast to hemophilia, where there is a strong relationship between levels of factor VIII and patients' bleeding frequency and severity, the relationships between VWF deficiencies and bleeding are less clear, thereby complicating diagnosis in some VWD patients.

Less commonly, VWD can be acquired through non-heritable means arising from other medical disorders. Acquired von Willebrand syndrome is a set of rare conditions in which there are defects in the concentration, structure, or function of VWF, for example, when VWF is made normally in the body but is removed from the blood circulation more rapidly than normal. Also, certain disorders with other genetic mutations can mimic VWD.

Estimates of the prevalence of VWD vary by more than two orders of magnitude across studies, depending on such factors as the case definition used by researchers and the means of reporting affected people. Studies based on the numbers of patients with bleeding symptoms who have been seen at specialized (e.g., hemostasis) centers in various countries suggest a prevalence of roughly 23-110 cases per million population.[2,3] Other studies that are based on screening population samples using standard criteria for bleeding symptoms, family history, and laboratory values have generated prevalence estimates of about 6,000-13,000 cases per million population.[4,5,6,7,8] As opposed to VWD

[1] National Hemophilia Foundation. https://www.hemophilia.org/Bleeding-Disorders/Types-of-Bleeding-Disorders/Von-Willebrand-Disease.

[2] Nichols WL, Hultin MB, James AH, Manco-Johnson MJ. von Willebrand disease (VWD): evidence-based diagnosis and management guidelines, the National Heart, Lung, and Blood Institute (NHLBI) Expert Panel report (USA). Haemophilia 2008;14(2):171-232.

[3] Sadler JE, Mannucci PM, Berntorp E, et al. Impact, diagnosis and treatment of von Willebrand disease. Thromb Haemost 2000;84(2):160-74.

[4] Biron C, Mahieu B, Rochette A, et al. Preoperative screening for von Willebrand disease type 1: low yield and limited ability to predict bleeding. J Lab Clin Med 1999;134(6):605-9.

[5] James PD, Lillicrap D. von Willebrand disease: clinical and laboratory lessons learned from the large von Willebrand disease studies. Am J Hematol 2012;87 Suppl 1:S4-11.

[6] Rodeghiero F, Castaman G, Dini E. Epidemiological investigation of the prevalence of von Willebrand's disease. Blood 1987 Feb; 69(2):454-9.

patients with bleeding symptoms who present to treatment centers, the population-based estimates also include people with minimal or no bleeding symptoms with low VWF levels. Extrapolating from the population-based estimates, as many as 3 million people in the U.S. have some type of VWD.

VWD affects females and males about equally. However, the condition is often viewed as disproportionately affecting females, perhaps because women with VWD are more likely to experience symptoms of increased bleeding during menstrual periods (menorrhagia), as well as during pregnancy and childbirth. The identification of males and females with VWD is often age-related, as bleeding symptoms in boys are largely associated with injuries of childhood physical activity, whereas bleeding symptoms in girls most often arise with menstruation.

The three main diagnostic criteria for VWD are a personal history of mucocutaneous bleeding, results from a set of laboratory tests, and family history of the disorder. However, given the multiple forms of the disease and variation in symptoms, VWD can be difficult to diagnose accurately. In some instances this can lead to inadequate patient management and poor health outcomes.

For most patients, a personal history of bleeding prompts laboratory testing for VWD, and a family history of bleeding provides supporting evidence for VWD or another bleeding disorder.[9] The multiple diagnostic tests typically used for evaluation include hemostasis tests (ability of blood to coagulate) and assays of VWD. While these are considered to be fairly timely and accurate tests, the accuracy of VWD diagnoses can vary. The main limitations of diagnostic accuracy arise from the difficulty of quantifying bleeding reliably and categorizing individuals with low VWF and mild bleeding. Further complicating diagnosis is that VWF levels in the blood can be affected by other genetic modifiers and such non-genetic factors as hormonal fluctuations due to age, stress, pregnancy, and exercise.

Due to the complexity and variations of VWD, patients are often undiagnosed until a severe bleeding episode occurs, typically following surgery. Mild-to-moderate symptoms of VWD can go unnoticed, overlooked, or attributed to some other cause, thereby missing opportunities to identify people with the disorder. Although women are more frequently assessed for VWD due to bleeding associated with menorrhagia and other gynecological conditions, VWD in women is subject to under-diagnosis. Due to lack of awareness and stigma, women may under-report menorrhagia. Also, menorrhagia can be attributed to multiple causes that are more prevalent than VWD. VWD is typically unobserved in males except in cases of life-threatening bleeding events.

Lack of training in VWD and other bleeding disorders contributes to lack of recognition of VWD by clinicians and the hemophilia treatment centers (HTCs) that are intended to provide clinical

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[7] Werner EJ, Broxson EH, Tucker EL, et al. Prevalence of von Willebrand disease in children: a multiethnic study. J Pediatr 1993;123(6):893-8.
[8] Nichols 2008.
[9] Sadler JE, Rodeghiero F; ISTH SSC Subcommittee on von Willebrand Factor. Provisional criteria for the diagnosis of VWD type 1. J Thromb Haemost. 2005;3(4):775-7.

management of VWD. Primary care clinicians and others who do not work routinely in hematology or see patients with bleeding disorders may not be familiar with diagnostic testing protocols, increasing the likelihood of misdiagnosis.

Treatment for VWD is generally safe and very effective in preventing and managing bleeding due to VWD, and has been largely the same for more than a decade. The three main approaches to managing VWD, which can be used individually or in combination, are: increasing plasma concentration of VWF using desmopressin, a synthetic derivative of the anti-diuretic hormone, vasopressin; replacing VWF by using plasma-derived (i.e., from blood donations) concentrates of it; and promoting hemostasis.

Preventive therapy (prophylaxis) has been recommended for only a small percentage of VWD patients, particularly those with severe VWD who may be at high risk for bleeding episodes (associated with, e.g., pregnancy or major surgery). The great majority of VWD patients are not offered prophylaxis. Accurate diagnosis and classification of disease are critical for ensuring appropriate therapy, as treatment regimens will vary according to severity and subcategory of the condition.[10,11,12]

An often-cited source for information about the diagnosis, evaluation, and management of VWD, particularly in the US, is the National Heart, Lung, and Blood Institute (NHLBI) clinical practice guideline published in 2008. This guideline drew from a systematic literature search for the years 1990-2006 and was accepted for publication in October 2007. It provides detailed information on clinical and laboratory criteria used by providers to diagnose and classify patients with VWD.[13] The guideline does not address psychosocial issues or care coordination or other delivery issues involving HTCs. While some other guidelines have been published on aspects of the management of VWD, most appear to have been developed largely on expert consensus without systematic evidence reviews or similar rigorous approaches. In 2010, NHF's Medical and Scientific Advisory Council (MASAC) updated its brief set of recommendations regarding the treatment of VWD. In 2014, referring to the 2008 NHLBI guideline, NHF's MASAC called for updated guidelines for the diagnosis and management of VWD.

Patients with VWD are typically diagnosed as having a bleeding disorder following an episode of prolonged bleeding by primary care providers or, for women with menorrhagia or other gynecological-related symptoms, gynecologists. After initial evaluation, they may be referred to a hematologist, who will further diagnose and assess the severity of their condition. Patients may also receive care through a network of hematologists and other clinicians affiliated with the national network of HTCs. Although most commonly known for treating patients with hemophilia, the network of HTCs was launched in the

[10] Berntorp E, de Moerloose P, Ljung RC. The role of prophylaxis in bleeding disorders. Haemophilia 2010 Jul;16 Suppl 5:189-93.
[11] Abshire T. The role of prophylaxis in the management of von Willebrand disease: today and tomorrow. Thromb Res 2009 Nov;124 Suppl 1:S15-9.
[12] Federici AB. Prophylaxis of bleeding episodes in patients with von Willebrand's disease. Blood Transfus 2008;6 Suppl 2:s26-32.
[13] Nichols 2008.

1980s in an effort to establish a nationwide network of diagnostic and comprehensive care management centers for patients with rare bleeding disorders.[14] Approximately 140 HTCs are located across the US.

From 1996 to 2010, the reported number of VWD patients using services provided by HTCs increased by 148% (5,326 to 13,239). This number of VWD patients was comparable to the hemophilia A population seen at HTCs. The increase in VWD patients, particularly among females, was the largest source of growth of HTCs during this time. Among all females seen at HTCs in 2010, 80% were VWD patients.[15] Although the absolute number of VWD patients receiving care at HTCs has increased significantly in recent years, anecdotal reports suggest that the comprehensive care offered at HTCs does not focus sufficiently on care for patients with VWD, who may be given lower priority by clinicians than patients with hemophilia.

The aging workforce of hematologists and other clinicians involved in management of patients with blood disorders, along with migration of hematologists to other clinical areas (especially oncology), points to a shortage in the future.[16,17] To the extent that clinicians and HTCs may already focus less on VWD patients than others with bleeding disorders, these shortages may further undermine the care capacity for VWD patients.

The published evidence pertaining to psychosocial challenges experienced by people with VWD is very limited. Most of the evidence that is available has been collected from women. The published evidence and anecdotal reports gathered through patient and caregiver interviews indicate that patients with VWD experience substantial psychosocial problems and diminished health-related quality of life. For example, recent survey results for women aged 18-25 indicate that women at risk for a bleeding disorder were significantly more likely than women not at risk to report that menstruation interfered with daily activities, physical or sports activities, social activities, and school or work activities.[18]

Although it is a rare condition, hemophilia is widely understood to be a disease most commonly occurring in men. However, as another bleeding disorder that occurs equally in women and men but whose symptoms tend to be reported more often by women (particularly menorrhagia), VWD is often viewed by male patients, many clinicians, and others as a "women's disease." This disparity in understanding may contribute to the under-diagnosis and stigma associated with VWD for men.

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[14] Hemophilia treatment centers 101. USA: Hemaware, 2011. June 13, 2012. http://www.hemaware.org/story/hemophilia-treatment-centers-101

[15] Baker JR, Riske B, Drake JH, et al. US Hemophilia Treatment Center population trends 1990-2010: patient diagnoses, demographics, health services utilization. Haemophilia 2013;19(1):21-6.

[16] Marlar RA, Saenko E. Editorial: critical need for pediatric hematologists to specialize in hemostasis and thrombosis. Blood Coagul Fibrinolysis 2010 Sep;21 Suppl 1:S1-2.

[17] McCullough J, Benson K, Roseff S, Simon T. Career activities of physicians taking the subspecialty board examination in blood banking/transfusion medicine. Transfusion 2008;48(4):762-7.

[18] Rhynders PA, Sayers CA, Presley RJ, Thierry JM. Providing young women with credible health information about bleeding disorders. Am J Prev Med 2014;47(5):674-80.

Method

With input from opinion leaders and The Lewin Group, NHF developed the summit agenda (Appendix A) to reflect the major topics of strategic concern to stakeholders in the VWD community. NHF and Lewin held a series of teleconferences to gain input from certain subject matter experts and other stakeholder representatives to plan the agenda and logistics of the summit. The meeting was intended to provide new impetus for recognition and advocacy for people with VWD, as well as to identify actionable items for NHF and its stakeholders. Participants in the summit, including the presenters, were identified by NHF as key figures and organizational representatives in the VWD community (Appendix B). The summit was also attended by NHF staff and non-participating observers from some stakeholder groups.

The strategic summit was organized as follows: welcome and introductions, an overview presentation on VWD and challenges facing providers, two presentations on the patient experience with VWD, and group discussion of four pre-selected issue areas. The four main issue areas were:

1. Recognizing and addressing stigma and marginalization
2. Clinical challenges and the development of a clinical practice guideline
3. Hemophilia treatment centers (HTCs) and physician recognition and focus on VWD
4. Organizational recognition and focus on VWD

Deliberations on each of the four main topic areas were guided by a set of discussion questions that were developed by NHF and Lewin with stakeholder input prior to the summit. These questions were posed to the summit participants before launching each topic discussion.

Overview of VWD and Challenges Facing Providers

Barbara A. Konkle, MD, Director of Clinical and Translational Research at the Puget Sound Blood Center, presented an overview of VWD and its challenges to providers. Dr. Konkle's presentation spanned the first clinically recognized description of the disorder in 1926 through the recent large clinical trials in the 2000s. Among the main types of challenges she described are the complexity and variation of VWD, inconsistencies in the classification of VWD, the wide range of clinical manifestations across patients, uncertainty and variation in diagnosis and treatment, and the limited awareness of VWD and other bleeding disorders.

The particular challenges in diagnosis and treatment include, but are not limited to, the complexity of the VWF gene, VWF structure and VWF function; inherent variability in VWF levels within individual patients; challenges in defining and measuring VWF function; diagnostic criteria; variation in treatment settings and approaches; and management of patients with bleeding symptoms who do not have VWD.

The diagnostic criteria for VWD, which are commonly based on symptoms and genetics, are often ambiguous and sometimes misleading to clinicians and patients. Genetic testing of VWF presents complexity because of variability in the VWF gene that is not associated with disease. There is great variability across and within patients in VWF levels due to biologic, behavioral, and environmental

factors. Further, there are clinically important differences in the types of VWF assays used and the cutoff levels of these for defining VWF deficiency and specific types of VWD. For example, for diagnosing type 1 VWD, the NHLBI guidelines use <30 IU/dL VWF antigen and VWF ristocetin cofactor (VWF:RCo), while others use VWF:RCo (or VWF and collagen binding assay [VWF:CB]) <40 IU/dL. Others use percentile thresholds across the range of population-based VWF levels. Adding to the matters of VWF testing and thresholds for defining deficiency is the inherent variability in VWF levels, which arises from such diverse factors as blood type, race, hormone levels, menstrual cycle, stress, exercise, inflammation, age, and even time of day.

Current patterns of VWD diagnosis strongly indicate that there is under-diagnosis of people with true VWD and that some patients with other mucocutaneous bleeding and platelet disorders are incorrectly diagnosed as having VWD. Even if diagnostic criteria and protocols for VWD become more accurate, patients who have bleeding disorders other than VWD or hemophilia must gain validation of their symptoms and appropriate clinical care.

Although an increasing number of VWD patients are seen in HTCs, their services do not appear to be sufficiently available or aligned for VWD for women or men. While the awareness of bleeding disorders is increasing, recognition and management of VWD remain insufficient for many patients. Although current activities to increase awareness of bleeding disorders are largely oriented to women, awareness is still lacking among women as well as men. The limited awareness of VWD contributes to wide practice variation and lack of alignment with best practices for treatment settings, management approaches, and services offered to patients. There has been improvement in treatment options in recent years, including in such adjunctive options as oral tranexamic acid and progesterone coated IUDs, as well as new factor treatment options. Nevertheless, evidence-based clinical guidance for these treatments remains insufficient.

In summary, Dr. Konkle emphasized that VWD is a relatively common bleeding disorder that affects females and males, although women tend to experience more bleeding symptoms. The scientific and medical knowledge about the function of VWF is complex and incomplete, and current diagnostic criteria for VWD vary, therefore limiting diagnostic accuracy of VWD, particularly in type 1. Although models of care for VWD have improved in recent years, the needs of many patients are inadequately addressed. Similarly, although treatment options for VWD have improved, including in the areas of adjunctive therapies and new factor treatments, much better evidence is needed for guiding the use of these options.

Main Discussion Points

The discussion following on the overview presentation highlighted the following:

1. The VWD community should promote patient and clinician recognition of symptoms associated with bleeding disorders and standardization of processing and interpretation of laboratory samples for the diagnosis of VWD and other bleeding disorders. Better testing protocols should diminish misleading variability of testing results as well as unnecessary or duplicative testing.

2. One of the leading challenges in the VWD community is achieving accurate and reliable diagnosis of VWD. Implementing a validated bleeding score may be an important clinical improvement for diagnosis VWD; however, its usefulness will apply only to patients with an available history and may exclude some of the pediatric population.
3. Through one or more authoritative organizations, the VWD community could consider offering some form of official endorsement or other recognition to denote laboratories that use best practices and standards in testing for blood disorders.

Patient Perspectives and Challenges

Jeanette Cesta, a nationally recognized patient and family educator, shared her experiences with VWD, including those encountered in the diagnosis and management of her and her family members' VWD. Ms. Cesta highlighted in particular the lack of validation of the condition by health care providers, her late diagnosis, and the variable quality of care of care they received.

Ms. Cesta asserted that clinician acknowledgment of the presence of a bleeding disorder is an essential step in the diagnostic journey for the patient and the clinician. Even when the diagnosis of the particular bleeding disorder is still uncertain, such validation can help to assure patients that their symptoms are real, important, and recognized, and should be managed in consultation with their providers.

Although she experienced her first bleeding incident at six years old, it was not until 16 years later that Ms. Cesta was diagnosed with type 1 VWD. At the time of diagnosis, she reported that she was offered no treatment options and was instructed simply to "tell someone about it before you have surgery."

Ms. Cesta also experienced challenges in obtaining coverage for care needed following a bleeding incident. These challenges continued throughout the prenatal care and births of her children. Ms. Cesta described how, in the months leading up to her first two pregnancies, her husband donated blood to a blood bank to enable having his VWF available upon the births of their children. Following a payer-mandated switch of her obstetrics provider, she related how her new doctor reprimanded her about becoming pregnant again, causing anxiety about her survival and other serious complications, and wondering aloud whether Ms. Cesta was trying to turn her current children into "orphans." Ms. Cesta's family also met frustration obtaining emergency care following bleeding incidents, as providers were unsure of the proper care required and needed to consult the available clinical practice guidelines for hemophilia. Having traveled widely and met with many patients, families, and providers affected by VWD, Ms. Cesta emphasized that her experiences are widely shared by others. She stressed the negative implications of the lack of specific clinical guidance for the diagnosis and management of patients with VWD.

> *"You have type 1 von Willebrand disease. Just make sure you tell someone about it before you have surgery."*
> *– Diagnosing provider*

In closing, Ms. Cesta offered several suggestions to summit participants. Given the insufficient lack of national focus on VWD, she recommended that, within its organizational umbrella, NHF dedicate a distinct focus on education and resources for VWD. She also called for the improvement and standardization of VWD care in the form of updated clinical practice guidelines for VWD based on current literature and evolving research findings. Ms. Cesta also suggested the promotion and use of medical alert bracelets for patients with VWD to inform health care providers of the patient's condition when receiving emergency care. Finally, she emphasized that achieving meaningful and lasting improvements in the patient experience will require unified and concerted actions by providers, patients, and other key stakeholders.

James Hammel, MD, is a psychiatrist in private practice who was diagnosed with VWD while in medical school. He discussed his experiences with bleeding symptoms and protracted diagnosis of VWD. In relating his experience, Dr. Hammel emphasized that late diagnosis, provider confusion, and patient stigma persist in the VWD community.

Dr. Hammel described his experiences with bruising and bleeding episodes prior to his diagnosis. Following a tonsillectomy at age 27, he experienced profuse bleeding and asked his provider for a hematology consultation. He was denied and told to return home and increase his fluid intake. Upon returning home, the bleeding worsened to the point where he sought emergency services. Upon stating his concerns about having a bleeding disorder to the emergency room physician, he was informed that a diagnosis of a bleeding disorder would have already been made and that these disorders typically occurred in females. After his condition was stabilized, Dr. Hammel received the hematology consultation he had requested and was told he had a bleeding disorder, but that the diagnostic tests were not covered by his student insurance. Following this incident, Dr. Hammel described his symptoms to a medical professor who voluntarily performed tests for VWD in his laboratory and returned a diagnosis of VWD for Dr. Hammel.

> *"No, you could not have a bleeding disorder … you're not a woman and you would have been diagnosed by now"*
> *– Emergency room physician response to patient symptoms*

In conclusion, Dr. Hammel summarized the factors that contribute to the unacceptable levels of under-diagnosis in men. Recognizing challenges faced by all people with bleeding disorders, he emphasized how being male with a bleeding disorder is associated with its own particular forms of stigma and marginalization. Drawing from his training in psychiatry, he noted that many providers seem to experience counter-transference, such that when patients are confused, providers in turn experience confusion in diagnosis and treatment of the condition. This compounds frustration, stigma, and marginalization for patients and providers when confronted with VWD.

Issue Areas and Key Findings

Issue 1: Recognizing and Addressing Stigma and Marginalization

The patient experience in VWD awareness, diagnosis, and management varies. Many patients are met with confusion and uncertainty from their providers. This leads to diminished patient engagement, discouragement about the prospects for receiving care, and negative impacts on health and social outcomes for many patients. After hearing from the three opening speakers, summit participants were asked to address the following questions:

- What forms of stigma/marginalization pose the greatest barriers to patient access to care and improved health outcomes, accounting for different perspectives/needs of female and male children and adults?
- What are the best opportunities for removing these barriers?
- Are there good models/examples in practice for accomplishing this?

The multidisciplinary summit participants concurred that there is considerable frustration with the state of diagnosis and management of VWD. In contrast to their ability and confidence in managing patients with hemophilia community, many providers are less able and less confident about how to diagnose and manage patients with VWD. Augmenting points made by the initial presenters, summit participants acknowledged how physicians and other clinicians can become frustrated with the "difficult" patient who expresses symptoms and concerns about bruising and bleeding events but for whom definitive and satisfying diagnostic answers are not apparent. Frustration is also fueled by lack of readily accessible, reliable information and resources for patients, caregivers, providers, and payers. In the context of inadequate information, resources, and communication, the patient and provider frustration leaves many VWD patients discouraged and sometimes embarrassed about their condition and neglected or pushed to the margins of the health care system.

Offering focused and well-targeted educational opportunities for providers and patients is an important component of increasing awareness and reducing stigma in VWD. Providers could be far better educated on such important topics as explicit validation of patients with bleeding disorders, diagnostic criteria and protocols, evidence-based treatment and management strategies for VWD, information about evolving approaches for diagnosis and treatment, and an orientation to individualized patient treatment plans. Patients could be offered educational programs about emerging treatments, practical disease management skills, responsibilities of their providers, and other helpful tools and resources. Among the valuable skills cited for improving patient autonomy and outcomes was self-infusion of VWF when medically necessary by appropriately able and trained patients. The development of VWD materials that are endorsed by certain professional organizations could relieve stigma by educating providers and patients through sources that they trust and consider credible. Such materials should be developed for, targeted to, and delivered via media that are specific to patient subgroups along the VWD spectrum. Smart-phone and other mobile applications can strengthen patient autonomy and engagement in their care, including by facilitating patient-based reporting of symptoms, adherence to

therapeutic regimens and risk-reducing behaviors, tracking of outcomes, and other information that would support patient-centered VWD management by patients and providers.

Beyond their use for individual patient management, electronic health records and mobile "apps" would also enable VWD population-based data collection to augment the knowledge base about, for example, VWD epidemiology, health care access and utilization, treatment patterns, and health outcomes by patient subgroup, providing a more complete understanding of the VWD spectrum. Such information could support evidence-based clinical practice guidelines, innovations in VWD care and identification of research gaps. Summit participants noted that realizing benefits from electronic health records and mobile apps would depend in part on gaining improved coding and related nomenclature for VWD and other bleeding disorders.

An important aspect affecting stigma felt by patients and their marginalization in health care settings is the simplified perception that bleeding severity and consequences of VWD are not as great as those for hemophilia and, therefore, patients with VWD are routinely considered to be of lesser priority than patients with hemophilia. This type of distinction may affect allocation of scarce resources for care of people with blood disorders.

Campaigns in recent years that have focused largely on awareness of bleeding disorders in women and girls may have had unintended negative consequences for males with bleeding disorders, particularly to diminish awareness and recognition of VWD in males. Summit participants emphasized that efforts should be pursued to raise awareness of bleeding disorders in males and that doing so should have no negative impact on the continued efforts on behalf of females.

Health services marginalization also arises from ambiguities and inconsistencies in insurance coverage. Diagnostic testing for hemophilia is more standardized and consistently covered by insurance companies and other payers than is diagnostic testing for VWD. This arises largely because of the variability of VWD, the lack of well-established and standardized diagnostic testing protocols, and uncertainty in test interpretation. These sources of ambiguity may diminish some providers' willingness to order testing for VWD.

Main Discussion Points

- Awareness of VWD on the part of patients, families, health care providers, and others in the community is inadequate and has negative implications for patient health and quality of life.
- Patients with VWD experience externally- and internally-imposed stigma and are subject to marginalization in the health care and broader communities, all of which can have adverse impacts on their health and quality of life.
- Patients with VWD desire a stronger sense of community, with greater education and related support to empower self-advocacy in the diagnosis and management of their VWD.
- Recognizing the extensive variety and complexity of bleeding disorders, providers should confirm with patients the clinical presence of their bleeding disorders even when unsure of the

precise diagnosis. This will facilitate patient and provider cooperation in the development of a treatment plan.

- Among the purposes of educational materials and related means of increasing knowledge and awareness of VWD should be to decrease the stigma associated with VWD and diminish social and clinical marginalization of VWD patients.
- Any new or updated evidence-based clinical practice guideline on VWD should address the reduction of stigma and marginalization within a broader guideline orientation of patient engagement and shared decision-making.
- In addition to scientific and medical aspects, research priorities for VWD and other bleeding disorders should address means to raise awareness and reduce stigma and marginalization for people with these disorders.

Issue 2: Clinical Challenges

Providers face many clinical challenges when providing care for patients with VWD. For this discussion, summit participants were asked to consider the following:

- What process should be followed to improve diagnostic protocols, disease classification, and laboratory testing, especially for those with mild and moderate disease?
- Is a new/updated comprehensive clinical practice guideline on VWD needed? How is this best accomplished?

Clinical processes

Summit participants identified insufficient standardization of clinical protocols as a major set of clinical challenges in care of patients with VWD. Standardized protocols for blood sample collection and other aspects of pre-analytic laboratory testing processes would assist providers in making accurate diagnoses of patients with suspected VWD. Broader dissemination and implementation of laboratory testing protocols published by the Centers for Disease Control and Prevention (CDC) would promote standardized approaches. Another important resource is the monograph of standards for handling of VWD samples developed by the Clinical and Laboratory Standards Institute (CLSI, formerly the National Committee for Clinical Laboratory Standards).[19] This monograph could be reviewed, adapted as needed, and distributed to laboratories to help guide the processing of VWD samples.

Summit participants suggested that a credible organization such as NHF could implement a national laboratory endorsement program for laboratories that follow the standardized laboratory testing protocol. Each laboratory would be monitored for adherence to this protocol, which would be required for continued endorsement or recognition.

[19] National Committee for Clinical Laboratory Standards (NCCLS). Assays of von Willebrand factor antigen and ristocetin cofactor activity: approved guideline. Wayne, PA: NCCLS; 2002. H51-A.

An area of continued diagnostic ambiguity involves patients whose VWF is reduced, but not within the range for type 1 VWD. In these instances, some providers may be reluctant to assign a VWD diagnosis to avoid a potential subsequent diagnostic reversal. The summit participants called for guidance on how to diagnose patients that have a genetic mutation for VWD but not a high risk of bleeding.

Insufficient and improperly applied diagnostic coding pertaining to VWD poses clinical and administrative problems. Although terminology related to the spectrum of VWD is clinically relevant and can be useful with patients, it is less applicable for purposes of reimbursement, which generally calls for specific, well-defined classifications of diseases or disorders. Summit participants noted that, in some instances, it is difficult to translate diagnostic uncertainty about certain forms of VWD or conditions that mimic VWD into specific diagnostic classifications. They also recognized that classification of VWD and related disorders, diagnostic criteria, and diagnostic coding may evolve over time. Some suggested that using a broader "umbrella code" for "bleeding disorder" or "idiopathic bleeding" would be useful for instances in which a bleeding disorder is clinically validated but difficult to classify.

Summit participants discussed that a likely pathway for implementing any coding change would entail a recommendation from the International Society on Thrombosis and Haemostasis (ISTH). Specifically, the members of its Committee on Hematology would provide a request to the members of the American Society of Hematology (ASH), which would then provide input to the Centers for Medicare and Medicaid Services (CMS) and the CDC's coding process for the ICD-10. Such a coding change should reflect, as appropriate, any revised standardized classification or diagnostic criteria for VWD that might arise in a new or updated clinical practice guideline. Regardless of any changes in coding, summit participants emphasized that providers should be supported by current standardized coding guidance for VWD.

Clinical practice guideline

Summit participants concurred that development of a new or updated clinical practice guideline is essential for standardizing and improving the care of patients with VWD. The prevailing guideline, published by NHLBI in 2008, represented important progress toward a comprehensive guideline. However, although much of the guideline is still relevant, its scope and currency are insufficient more than six years after its publication and more than eight years after the time span of its literature review. As the guideline was published more than five years ago, the National Guideline Clearinghouse (NGC) now considers this guideline out of date and it has been archived.

ASH developed a "quick reference" pocket guide that originally summarized selected recommendations from the 2008 NHLBI guideline, then updated this guide in 2012 in cooperation with members of the NHLBI expert panel.[20] In 2010, NHF's Medical and Scientific Advisory Council (MASAC) updated its

[20] American Society of Hematology. Quick Reference: 2012 Clinical Practice Guideline on the Evaluation and Management of von Willebrand Disease (VWD). Washington, DC: ASH; 2012.

focused set of recommendations regarding the treatment of VWD. In 2014, referring to the 2008 NHLBI guideline, NHF's MASAC called for updated guidelines for the diagnosis and management of VWD.

A new or updated guideline must address a broad set of needs, including some that were not covered in the 2008 NHLBI guideline, for multiple types of users. As such, planning the approach to a new or updated guideline must consider the target populations, clinical and other scope, and depth of the guideline. The guideline should carefully examine and document the current evidentiary basis for establishing criteria for defining or classifying types of VWD, thresholds for initiative therapy, and treatment goals. While the 2008 NHLBI guideline focused on more severe forms of VWD, there is a need to devote greater attention to mild VWD and its complex mix of diagnostic and management issues.

Summit participants noted several aspects of VWD that were insufficiently or not at all addressed in the 2008 NHLBI guideline but that should be in an update, including standardized diagnostic tools, psychosocial issues, and ensuring access to appropriate care. Given the increasing cost concerns of health care providers, payers, and patients and their families and the potential impact of these concerns on their decision-making, a new or updated guideline should also address current and evolving cost and other resource implications of diagnosis, treatment, and related management of VWD. Summit participants noted that evidence-based diagnosis and management of patients with VWD may improve overall cost-effectiveness by decreasing emergency room visits and other expensive episodic care. Summit participants noted that, while guidelines do not comprise payment policies, it is important to recognize that payers increasingly cite and are otherwise influenced by evidence-based guidelines.

During the summit, NHF leadership indicated that it would accept a major role in sponsoring and coordinating the development of a new or updated VWD guideline, as it has for a hemophilia guideline currently under development. NHF concurred with summit participants that NHLBI, ISTH, and certain other groups devoted to blood disorders would be among others likely to express interest in or be approached for taking roles in the development and dissemination of the guideline. With input from others, NHF would be prepared to draft a request for proposal for a new or updated guideline.

The extent and type of any industry or other for-profit sector sponsorship or other involvement in guideline development should be considered, particularly regarding any potential or perceived conflict of interest. Some summit participants expressed that no for-profit sector sponsorship should be accepted for guideline development. Others noted the practical matter of meeting the cost of developing an evidence-based clinical practice guideline that meets the state-of-the-art quality standards, e.g., of the National Guideline Clearinghouse. They pointed out that other well-regarded guidelines have been supported in part by for-profit organizations, and that explicit requirements forbidding any link between sponsorship and development of the guideline, along with disclosure of all funding sources, would help to ensure the integrity of the guideline.

Main Discussion Points

Clinical processes

- Physicians may be hesitant to diagnose individuals due to the following:

  - Lack of a well-recognized or standard diagnostic test battery
  - Uncertain reimbursement status for a diagnostic testing battery
  - Uncertain or ambiguous coding and classification guidance
  - Potential for a reversal in diagnosis, e.g., due to increase of VWF levels with age that can lower bleeding event rates or potential future changes in criteria or classification of VWD and other bleeding disorders
- An important step toward standardization of diagnosis of VWD would be to develop a protocol for the processing of pre-analytical[21] laboratory testing variables.
- The monograph of standards for handling blood samples for VWD testing that was developed by the Clinical and Laboratory Standards Institute (CLSI) in 2002 could be adapted and disseminated to laboratories that are sanctioned or endorsed by NHF or other authoritative organizations.
- Diagnostic coding and accompanying terminology for VWD and certain bleeding disorders that resemble VWD but are difficult to diagnose should be reviewed and updated to align with improved diagnostic classifications and protocols.

Clinical practice guideline

- A well-qualified and authoritative organization, or a consortium of such organizations, should develop a new or updated evidence-based clinical practice guideline on VWD.
- One approach would be to update the guideline developed by the National Heart, Lung, and Blood Institute (NHLBI) that was published in 2008.
- The scope, depth and purpose of the new or updated guideline should be carefully delineated, including defining the target populations of the guideline.
- Drawing on the relevant peer-reviewed literature and expert consideration of qualified clinical experts and other stakeholders, including patients and families, this guideline should update the classification of VWD and standards for diagnostic criteria and testing, therapies, and management strategies in a context of shared decision-making.
- In addition to patients with definitive VWD diagnoses, the guideline should include diagnosis and treatment of patients with indeterminate diagnoses along the VWD spectrum or related yet ambiguous diagnoses.
- The guideline should support individualized, adaptable treatment plans based on shared decision-making.
- The scope of the guideline should address certain aspects of care that were not explicitly addressed in the 2008 NHLBI guideline, including but not limited to standardized diagnostic tools, psychosocial issues, access to appropriate high-quality care, and consideration of costs and other resource implications of VWD care.

[21] The pre-analytical phase of laboratory testing involves patient assessment, test request, specimen (e.g., blood) collection, transport, and receipt. Other phases are analytical (testing review and laboratory interpretation) and post-analytical (testing results transmission, clinical interpretation, follow-up, post-test specimen management).

- The key organizations involved in sponsoring, developing, and or disseminating a new or updated guideline would include, though not necessarily be limited to, the NHF, NHLBI, ISTH, and ASH.
- Evidence-based clinical practice guidelines are not the same as health care provider policies or payer coverage or reimbursement policies, although such policies may refer to or otherwise be influenced by guidelines.

Issue 3: HTC and Physician Recognition and Focus on VWD

In addition to their primary care providers, patients with VWD usually benefit from access to hematologists and other specialists, whether at hospitals, outpatient clinics, physician offices, their homes, or one of the approximately 140 HTCs in the U.S. HTCs are federally designated facilities that offer multidisciplinary care in single settings for patients with hemophilia, VWD, and other blood disorders. Their medical teams typically comprise a mix of one or more physicians, nurses, social workers, and physical therapists. Despite the training and responsibilities of hematologists and HTCs, the VWD community has expressed concerns that VWD is under-recognized and accorded secondary status to hemophilia and other conditions.

Summit participants were asked to consider the following discussion questions:

- Are HTCs under-recognizing VWD patients? Do most HTCs offer and deliver comprehensive care to VWD patients?
- Are there good models of HTCs offering responsive, comprehensive care for VWD?
- Do clinicians – primary care, OB/GYN, internal medicine – under-recognize VWD?
- What can be done to improve clinicians' ability to care for patients with VWD?

As they are intended and funded to provide care and treatment of patients with hemophilia, VWD, and other blood disorders, HTCs are obliged to properly diagnose patients at risk for VWD and provide comprehensive treatment accordingly. To help facilitate the recognition of VWD patients, the U.S. Health Resources and Services Administration (HRSA) recently expanded the explicit definition of the target population for its grant programs to "patients with hemophilia, VWD and other bleeding and clotting disorders." According to the Hemophilia Data Set, 11,954 patients with VWD (38.6% of the total patient census) were treated at HTCs in 2013 (based on the number of comprehensive annual visits conducted).

Summit participants reported that, due in part to their limited capacity, HTCs often triage incoming patients, and that care for many patients with VWD is episodic and intermittent. Limited access to care for patients with VWD may be attributable to various factors, including shortages of staff or other resources across HTCs, lack of awareness about or under-recognition of VWD, perceived lack of severity of VWD (especially in contrast to hemophilia), inadequate or ambiguous insurance coverage, and insufficient guidance about follow-up care for VWD. Summit participants emphasized that the optimal frequencies or indications for follow-up care for patients with various types and severity of VWD should be addressed in a new or updated guideline.

A pointed matter of discussion concerned reported instances in which patients with VWD who had been referred to HTCs were "turned away" from or otherwise neglected by these centers. According to patient advocates at the summit, patients in six states have been turned away by HTCs, reportedly due to such factors as perceived lack of severity of VWD and inadequate or ambiguous insurance coverage (e.g., Medicaid). Summit participants suggested that the reported problem of turning away VWD patients could be addressed in cooperation with HRSA. A primary goal of the HRSA grant is maintaining full access to quality care and appropriate hematologic, genetic, and social services through regional and HTC cooperation and collaboration for individuals with hemophilia and other bleeding disorders including VWD. Summit participants suggested that NHF or other patient advocacy groups could offer education to patients with VWD on how to describe their symptoms to help ensure that they "get in the door" of HTCs and are evaluated appropriately.

HTCs and the broader VWD community are undertaking some new approaches to improve access and efficiency of care delivery. The Foundation for Women & Girls with Blood Disorders reported that it has implemented a provider network to increase collaboration and communication between pediatric hematologists at HTCs and gynecologists. This recently formed and rapidly growing network evolved from an unmet need for better coordination of these medical specialties for women with the VWD provider community. Other promising approaches include a flexible HTC and satellite clinic model in which nurse practitioners manage clinics that share consulting hematologists. Pilot programs of this model appear to be succeeding, relieving some of the staffing challenges experienced by HTCs.

Summit participants emphasized that patient engagement is critical for providing high-quality care for many VWD patients, enabling ongoing comprehensive care and adherence to treatment plans. Inconsistent or limited contact with providers, as well as other patients, can diminish patient outcomes. Toward improving ongoing patient engagement, focusing on individualized contacts may be beneficial. Even a quick phone call or email can distinguish between patients who are pleased with their care and those who are not. Summit participants reported that instituting these direct individualized contacts at the time of initial treatment planning can improve patient satisfaction. Also, mobile applications for recording symptoms and other events can provide the basis for more objective patient-provider communications and shared decision-making. Among the examples given were a "sisterhood app" to track menstrual cycles and "PatientsLikeMe" apps for VWD and hemophilia that collect current and longitudinal patient data that also can be rolled up for community-level health and experience statistics. Recognizing that rural HTCs face particular challenges to regular patient follow-up, summit participants suggested that some of these challenges can be surmounted with satellite clinics and other care delivery models and with available and emerging tools for patients to maintain contact with their providers.

Reflecting on successful marketing approaches, a few HTC leaders described how making a favorable impression for patients' initial encounters at HTCs increases patient "capture" and contributes to retaining patients for ongoing multidisciplinary care. Recognizing the need for appropriate marketing of HTC services, a provider from a regional HTC described the "selling" of services for VWD by developing patient-centered comprehensive treatment plans and drawing attention to the benefits to patients of

using the range of available services at the HTC. This HTC provider reported a marked increase in the use of the HTC's services by VWD patients.

Summit participants noted that HTCs' ability to improve quality of care could be enhanced by systematic entry of HTC visit data into databases for tracking services utilization, care patterns, patient outcomes, and other aspects of HTC care. Examples of topics for further research are comparing alternative approaches to improving the effectiveness of patient engagement and the scientific and clinical implications of longitudinal follow-up of VWF levels.

Main Discussion Points

Barriers

- Under-recognition of and under-engagement (i.e., insufficient communication and interaction) with VWD patients by HTCs and clinicians can have a negative impact on patient health and quality of life.
- Some HTCs have reportedly turned away or otherwise exhibited clinically relevant lack of engagement with patients with VWD. Some potential reasons include perceptions of VWD as a lesser priority than hemophilia, limited HTC resources, and perceptions of inadequate insurance status of some VWD patients.
- To the extent that any VWD patients have been turned away from HTCs or otherwise been discouraged from seeking care at HTCs is entirely unacceptable.

HTC-level engagement

- HTCs and the broader blood disorder community should encourage collaboration among providers through the establishment of comprehensive treatment plans and provider networks.
- HTCs should establish procedures to make a favorable impression at the time of any patient's first encounter, including describing and promoting the appropriate range of multidisciplinary services and making follow-up contacts toward improving and maintaining patient engagement.
- Advocates should facilitate patient education and understanding of symptoms of bleeding disorders to better enable patients to describe their condition to providers and better ensure that they are appropriately evaluated at HTCs.
- HTCs should actively solicit and incorporate patient feedback on their services and areas for improvement.
- HTCs should implement satellite clinics or other points of access where possible to ensure that patients in underserved areas or who are subject to other barriers to care gain adequate access; these may include, e.g., small children clinics, adolescent clinics, and rural outreach clinics.
- Among the instances of successful alternative approaches are a flexible HTC and satellite clinical model in which at least one nurse practitioner provides full-time care for bleeding disorders with a shared consulting hematologist and other staff, such as one or more of a psychosocial service provider, physical therapist, orthopedist, or dentist.

Organization-level engagement

- NHF could conduct or sponsor educational events in partnership with HTCs (e.g., education in the morning, clinic in the afternoon) to improve VWD awareness and clinical care.
- NHF and other professional and advocacy groups could support provider networking to facilitate clinical referrals and multidisciplinary care of patients with VWD.
- In collaboration with other professional and advocacy groups and health information experts, NHF could develop a smart phone software application ("app") for patients to communicate with their providers and track information about their care and health status. Any such application must meet appropriate standards for patient privacy and security.

Issue 4: Organizational Recognition and Focus on VWD

Toward strengthening organizational advocacy for pursuing next steps to improve care for people with VWD, summit participants were asked to consider the following:

- What are the strengths of the current organizational advocacy for the VWD community?
- What are the weaknesses of the current organizational advocacy for the VWD community?
- What practical steps can be taken to strengthen organizational advocacy for the VWD community?

Summit participants generally concurred that a more explicit organizational identify for VWD is needed for gaining differentiation from hemophilia and a greater national focus on the disorder across the VWD population. Participants noted that, by virtue of their names, NHF and the HTCs are inherently "branded" as being focused on hemophilia care, although their respective roles do involve VWD. This is also true of certain other organizations involved in advocacy for people with bleeding disorders.

According to its mission statement, the NHF is "dedicated to finding better treatments and cures for inheritable bleeding disorders and to preventing the complications of these disorders through education, advocacy and research." The Hemophilia Federation of America describes itself as "address[ing] the evolving needs of the bleeding disorders community." The Foundation for Women & Girls with Blood Disorders describes a broad scope of interest including VWD, other factor deficiencies, thrombophilias, sickle cell disease, hemoglobinopathies, immune thrombocytopenic purpura, and anemias.

HTCs that receive HRSA grant funding are expected to provide optimal care using a multi-disciplinary team approach that provides accessible, family-centered, continuous, comprehensive, coordinated, and culturally effective care for individuals with hemophilia and other bleeding disorders. The CDC's web page about HTCs refers to hemophilia but not to other bleeding or clotting disorders. However, the CDC's web page about VWD includes a section about treatment that states: "Often the best choice is a comprehensive hemophilia treatment center (HTC). Although it is called a *hemophilia* treatment center, HTCs provide care to address all issues related to VWD." The Hemophilia Alliance states that "HTCs provide multidisciplinary care … in treating individuals with bleeding disorders."

Given its prominence and standing in the blood disorders community, summit participants generally indicated that NHF should take on a more explicit, enhanced role in VWD. Summit participants discussed pros and cons of changing the name of NHF to encompass VWD or all bleeding and clotting disorders. The pros include being explicit to stakeholders and the public about being an organization that serves VWD as part of a broader patient population. The cons for a name change for a more inclusive organizational orientation could be interpreted as reducing or diluting the NHF brand equity or focus. Some participants noted that "National Hemophilia Foundation" and "NHF" are well-recognized brand names in the blood disorders community that, at least to those familiar with its activities, do not necessarily connote a focus on hemophilia only. Also, any name disruption could at least temporarily diminish organizational recognition and would have attendant costs and administrative burdens.

A suggestion that NHF could add a tagline such as "the organization for the treatment of bleeding disorders," which would be consistent with its currently stated mission, appeared to be well received by some participants. The addition of such a tagline for NHF could be timed to coincide with taking on one or more new initiatives in support of VWD. Any form of rebranding must be done strategically to maintain a balance between the organization's connotation for representing the interests of people with particular bleeding disorders and for the shared interests of people across bleeding disorders.

On an organizational level, there are several next steps that could be implemented to improve focus on VWD. As noted above, one would be sponsorship by one or more organizations of a new or updated clinical practice guideline for diagnosis and management of VWD. A related effort, which could be incorporated into a guideline, would be development of standardized criteria and classification of VWD.

An important initiative for organizational advocacy would be sponsorship of educational programs for patients and providers on VWD. As described above, these efforts should be targeted for types of VWD, younger and older patients, and female and male patients, respectively. Educational programs could include such topics as emerging therapies and management strategies for VWD, developing personalized treatment plans, and the identification of other VWD tools and resources.

A more explicit organizational focus for VWD advocacy would provide a locus for partnerships with other organizations to be a centralized source for development and dissemination of patient and provider educational materials and other high-quality resources. NHF and partner advocacy organizations could also convene meetings with stakeholders such as federal agencies, public and private payers, researchers, and industry to identify further developments in the VWD community as well as to identify and gain support for research needs in the field.

Main Discussion Points

- An explicit organizational identify for VWD is needed to help gain differentiation from hemophilia and a greater national focus on the priorities of VWD.
- NHF should clearly re-establish its commitment as a VWD advocacy organization that sponsors and otherwise engages in collaborative, multi-stakeholder efforts to improve VWD awareness, access to care, health outcomes and quality of life, and research.

- While retaining its strongly established identify with hemophilia, NHF should consider rebranding the organization to be more explicitly inclusive of VWD and other bleeding and clotting disorders. This might involve, e.g., a tag-line to NHF that encompasses VWD or other bleeding and clotting disorders.
- NHF should serve as a centralized resource for information and engagement of patients with VWD, providers, HTCs, other advocacy organizations, government agencies, industry, and other VWD stakeholders.
- In collaboration with other appropriate organizations, NHF should implement activities that target underserved VWD populations, including certain subgroups of men, adolescents, and young adults.
- NHF and other well-qualified and authoritative organizations should develop and convey educational materials on VWD that are targeted appropriately to patients and their families, providers, payers, industry, and others in the VWD community.
- In collaboration with other stakeholder organizations , NHF should facilitate the development, dissemination and implementation of the following:
    - A new or updated evidence-based clinical practice guideline for VWD
    - Standard definition and classification system for VWD
    - High-quality provider and patient education materials that are appropriately tailored (by content, format, and means of dissemination) to the range of people with or at-risk for VWD (e.g., by type of VWD, age, and sex).

Conclusion

The health care community, including providers, payers, patients, and others, has under-recognized VWD, with negative consequences for people with the disorder and their families. The summit deliberations identified potential next steps for making inroads against these deficits, including certain initiatives that can be undertaken beginning in 2015 to yield demonstrable near-term improvements. Such next steps should include some or all of improving VWD classification, VWD diagnostic criteria and testing protocols, a new or updated evidence-based clinical practice guideline, encouraging HTCs to adopt more flexible care models, and targeted educational materials to improve VWD awareness by patients, providers, payers, and other stakeholders. Pursuing these steps will require close collaboration among such organizations as NHF and other advocacy groups; such government agencies as NHLBI, HRSA, CDC, and CMS; health professional organizations; HTCs; industry; and others. As the nationally recognized patient and consumer organization for bleeding disorders, NHF should take on a more explicit, though not singular, leadership role in pursuing these next steps.

Appendix A. Summit Agenda

NATIONAL HEMOPHILIA FOUNDATION

www.hemophilia.org

Strategic Summit on Von Willebrand Disease
November 20 – 21, 2014
Phoenix Park Hotel, Washington, DC

AGENDA

November 20, 2014 – 6:30 PM – 9:00 PM - Welcoming Reception – Powers Court Room

November 21, 2014 7:30 AM – 5:00 PM Strategic Summit - Ballroom

7:30 AM – Breakfast

8:00 – 8:10 Welcome and Meeting Objectives – Val Bias

8:10 – 9:00 Introductions and Outline for Day – Cliff Goodman, Facilitator
Affiliations of participants, areas of expertise, and anticipated contribution

9:00 – 9:30 Overview of VWD and Challenges Facing Providers – Barbara Konkle, MD

9:30 – 10:00 Patients' Perspectives and Challenges – Jeanette Cesta and James Hammel, MD

10 – 10:15 Break

10:15 – 11:15 First Issue Area – Recognizing and Addressing Stigma and Marginalization

- What forms of stigma/marginalization pose the greatest barriers to patient access to care and improved health outcomes, accounting for different perspectives/needs of female and male children and adults
- What are the best opportunities for removing these barriers?
- Are there good models/examples in practice for accomplishing this?

11:15 – 12:30 Second Issue Area – Clinical Challenges

- What process should be followed to improve - diagnostic protocols, disease classification, and laboratory testing, especially for those with mild and moderate disease?

- Is a new/updated comprehensive clinical practice guideline on VWD needed? How is this best accomplished?

12:30 – 1:30 Lunch

1:30 – 2:30 Third Issue Area – HTC and Physician Recognition and Focus on VWD

- Are HTCs under-recognizing VWD patients? Do most HTCs offer and deliver comprehensive care to VWD patients?
- Are there good models of HTCs offering responsive, comprehensive care for VWD?
- Do clinicians – primary care, OB/GYN, internal medicine - under-recognize VWD?
- What can be done to improve clinicians' ability to care for patients with VWD?

2:30 – 3:30 Fourth Issue Area – Organizational Recognition and Focus on VWD

- What are the strengths of the current organizational advocacy for the VWD community?
- What are the weaknesses of the current organizational advocacy for the VWD community?
- What practical steps can be taken to strengthen organizational advocacy for the VWD community?

3:30 – 3:45 Break

3:45 – 4:45 Summary of Day's Discussion – Cliff Goodman

4:45 – 5:00 Closing Remarks – Val Bias

Appendix B. Summit Participants

NATIONAL HEMOPHILIA FOUNDATION
www.hemophilia.org

Von Willebrand Disease Strategic Summit Participant List

November 20 – 21, 2014

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