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**2020**

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**Re: Request for new ICD-10-CM codes for von Willebrand disease**

Dear Ms. Pickett and Dr. Berglund,

The American Society of Hematology (ASH) is pleased to submit this proposal to establish new ICD-10-CM diagnosis codes for von Willebrand disease (VWD).

ASH represents more than 18,000 clinicians and scientists worldwide who are committed to the study and treatment of blood and blood-related diseases. These disorders encompass malignant hematologic disorders such as leukemia, lymphoma, and multiple myeloma, as well as non-malignant conditions such as sickle cell anemia, thalassemia, bone marrow failure, venous thromboembolism, and hemophilia. In addition, hematologists are pioneers in demonstrating the potential of treating various hematologic diseases and continue to be innovators in the field of stem cell biology, regenerative medicine, transfusion medicine, and gene therapy.

Von Willebrand disease is the most common inherited bleeding disorder, in which the blood does not clot properly, with wide variability in clinical phenotype. According to the Centers for Disease Control and Prevention, about 3.2 million (or about 1 in every 100) people in the US have the disease.<sup>1,2</sup> More recent epidemiologic studies reference a prevalence of 1 in 1000.<sup>3</sup> People with VWD either have a low level of von Willebrand factor (VWF), a protein that helps the blood to clot, or the VWF protein does not work the way it should. Although VWD occurs among men and women equally, women are more likely to notice the symptoms because of heavy or abnormal bleeding during their menstrual periods and after childbirth.<sup>1</sup>

In 2006, the International Society of Thrombosis and Haemostasis (ISTH) classified VWD into six categories or subtypes, based on the difference in clinical features and therapeutic requirements. Recently, ASH in partnership with ISTH, the National Hemophilia Foundation (NHF) and the World Federation of Hemophilia (WFH), has developed clinical practice guidelines for the diagnosis and management of VWD. The guidelines will be published in *Blood Advances* in December 2020. With the upcoming publication of the guidelines, it is critically important to update the ICD-10-CM classification for VWD to allow for the adoption of the guideline recommendations and to improve best practices for clinical care.

Currently, only one ICD-10-CM code, D68.0 (Von Willebrand's disease) exists, making it difficult to accurately document, diagnose and in turn, appropriately treat the different subtypes of VWD. For this reason, ASH is requesting the addition of new ICD-10-CM diagnosis codes for VWD to better define the disease and its subtypes. Below, please find descriptions for each subtype, which provides the rationale for the newly proposed codes. Attachment 1 includes our suggested coding revisions.

In general, ASH is recommending several editorial changes to better reflect widely accepted terminology for VWD, including what is used by the World Health Organization (WHO). First, we suggest the removal of the apostrophe "s" currently included in the code descriptor in ICD-10-CM (von Willebrand's disease) and that this apply to all subsequent codes created for VWD. Second, ASH requests that the "v" in von Willebrand disease be made lowercase rather than the uppercase that is currently used. Again, this is accurate based on how VWD is written in the literature and used by the WHO. Finally, when the abbreviation for von Willebrand Disease is used, we recommend that it be in all capital letters, e.g., "VWD."

In addition to the request for the VWD codes defining subtypes, ASH is seeking the deletion of several terms currently listed under D68.0, which are no longer used in clinical practice (see attachment 1). ASH is also proposing to add the term Low von Willebrand factor to R79.1 – Abnormal Coagulation Profile (see attachment 1).

ASH recommends the following recommendations for nine new diagnosis codes for VWD subtypes in addition to three additional codes outlined in attachment 1, "von Willebrand disease, Type 2, unspecified," "von Willebrand disease, other," and "von Willebrand disease, unspecified."

- **TYPE 1 VON WILLEBRAND DISEASE:** Type 1 VWD is characterized by decreased levels (qualitative deficiency) of von Willebrand factor (VWF). The VWF that is made is functionally normal, however lower circulating levels lead to an increased risk of bleeding. Options for treatment including VWF concentrate, desmopressin to stimulate release of stored VWF, and antifibrinolytic therapy.
- **TYPE 1C VON WILLEBRAND DISEASE:** Type 1C VWD is characterized by increased clearance of VWF, leading to decreased levels. As is the case with type 1 VWD, the circulating VWF in type 1C is functionally normal, however the protein is degraded quickly and not available to participate in hemostasis, leading to increased risk of bleeding. Options for treatment include VWF concentrate in conjunction with antifibrinolytic therapy. While desmopressin will lead to a transient release of stored endogenous VWF, the effect is transient with quick return to baseline levels and increased risk of bleeding if not maintained in high risk situations such as surgery.

All forms of type 2 VWD are characterized by functional defects in VWF with subtyping based on the specific functional defect. Treatment may involve desmopressin for most subtypes (except type 2B) along with VWF concentrate and adjunctive therapy with antifibrinolytics.

- **TYPE 2A VON WILLEBRAND DISEASE:** Characterized by abnormal platelet-dependent VWF function with loss of the most hemostatically active high-molecular weight multimers of VWF.

- **TYPE 2B VON WILLEBRAND DISEASE:** Characterized by abnormal function of VWF due to a gain of function mutation that increases binding of VWF to platelet glycoprotein 1b-alpha, often leading to thrombocytopenia. Desmopressin is contraindicated due to paradoxically worsened bleeding due to increased thrombocytopenia.
- **TYPE 2M VON WILLEBRAND DISEASE:** Characterized by abnormal platelet-dependent VWF function, however multimers are preserved, a major difference between type 2A and type 2M.
- **TYPE 2N VON WILLEBRAND DISEASE:** Characterized by abnormal factor VIII binding by VWF, leading to decreased factor VIII levels and varying degree of bleeding similar to hemophilia A.
- **TYPE 3 VON WILLEBRAND DISEASE:** A qualitative form of VWD with near complete absence of circulating VWF. This is the most severe subtype, requiring use of VWF concentrate as desmopressin is not effective.<sup>4,5,6,7</sup>
- **ACQUIRED VON WILLEBRAND SYNDROME:** The acquired von Willebrand syndrome (AVWS) is a deficiency in the amount or function of von Willebrand factor (VWF) that is due to acquired rather than inherited causes. Examples of causes for AVWS include shearing and subsequent degradation of VWF across stenotic heart valves or through mechanical circulatory support circuits such as left-ventricular assist devices or via extracorporeal membrane oxygenation. AVWS may arise due to autoantibody formation such as that seen in immune dysregulation disorders or VWF may be directly adsorbed onto malignant cells as observed in patients with Wilms tumors or Waldenstrom macroglobulinemia. Treatment consists of supportive therapy with VWF concentrate, desmopressin, and/or antifibrinolytic therapy along with correction of the underlying cause (e.g. valve replacement therapy or immunosuppression).<sup>8,9</sup>
- **PLATELET-TYPE VON WILLEBRAND DISEASE:** Platelet-type von Willebrand disease is due to a functional defect in the platelet receptor for von Willebrand factor. Often misdiagnosed as type 2B von Willebrand disease, treatment consists of platelet transfusions in addition to standard VWD therapies such as VWF concentrate or antifibrinolytic therapy.<sup>10</sup>

Thank you for your consideration. Please contact Leslie Brady, Policy and Practice Manager, at [lbrady@hematology.org](mailto:lbrady@hematology.org) or 716-361-2764 (cell) with any questions.

Sincerely,



Stephanie J. Lee, MD, MPH  
President

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- <sup>1</sup> Centers for Disease Control and Prevention. October 2020. What is von Willebrand Disease? November 23, 2020. <https://www.cdc.gov/ncbddd/vwd/facts.html>
- <sup>2</sup> Rodeghiero, F, Castaman, G, Dini, E. Epidemiological Investigation of the Prevalence of von Willebrand's Disease. *Blood*, Vol 69, No 2, 1987: pp 454-459.
- <sup>3</sup> Bowman, M, et al. The Prevalence of symptomatic von Willebrand disease in primary care practice. *J Thromb Haemost* 2010; 8: 213-6.
- <sup>4</sup> Sadler JE, et al. Update on the pathophysiology and classification of von Willebrand disease: a report of the Subcommittee on von Willebrand Factor. *J Thromb Haemost*. 2006 Oct;4(10):2103-14.
- <sup>5</sup> Ng C, Motto DG, Di Paola J. Diagnostic approach to von Willebrand disease. *Blood*. 2015 Mar 26;125(13):2029-37.
- <sup>6</sup> James P, et al. ASH ISTH NHF WFH 2020 Guidelines on the Diagnosis of von Willebrand Disease. *Blood Adv*. In Press 2020.
- <sup>7</sup> Connell N and Flood VH, et al. ASH ISTH NHF WFH 2020 Guidelines on the Management of von Willebrand Disease. *Blood Adv*. In Press 2020.
- <sup>8</sup> Franchini M, Mannucci PM. The acquired von Willebrand syndrome focused for hematologists. *Haematologica*. 2020.
- <sup>9</sup> Nascimbene, A. et al. Acquired von Willebrand syndrome associated with left ventricular assist device. *Blood*, 23 June 2016, Vol 127 (25).
- <sup>10</sup> Othman M, Gresele P. Guidance on the diagnosis and management of Platelet- type von Willebrand Disease: a communication from the platelet physiology subcommittee of the ISTH. *J Thromb Haemost*. 2020.

## Attachment 1

### Current Coding Structure for VWD

#### D68 Other coagulation defects

**Excludes1:** abnormal coagulation profile (R79.1)  
coagulation defects complicating abortion or ectopic or molar pregnancy (O00-O07, O08.1)  
coagulation defects complicating pregnancy, childbirth and the puerperium (O45.0, O46.0, O67.0, O72.3)

#### D68.0 Von Willebrand's disease

Angiohemophilia  
Factor VIII deficiency with vascular defect  
Vascular hemophilia

**Excludes1:** capillary fragility (hereditary) (D69.8)  
factor VIII deficiency NOS (D66)

**Commented [ASH]:** ASH Recommends deleting these terms as they are no longer used in clinical practice

### Proposed Coding Structure for VWD

#### D68.01 von Willebrand disease, Type 1 - partial quantitative deficiency of von Willebrand factor (VWF)

**D68.01x** - von Willebrand disease, **Type 1C** - partial quantitative deficiency of VWF characterized by rapid, increased clearance from circulation

**Commented [ASH]:** Type 1 is distinct from Type 1C

#### D68.02 von Willebrand disease, Type 2 - qualitative defects of von Willebrand factor (VWF)

**D68.02A** - von Willebrand disease, **Type 2A**- qualitative defects of VWF includes variants with decreased platelet adhesion characterized by selective deficiency of high-molecular-weight VWF multimers

**D68.02B** - von Willebrand disease, **Type 2B** - qualitative defects of VWF that identifies “hyper-adhesive” VWF forms also usually associated with high-molecular-weight VWF loss (includes variants with increased affinity for platelet glycoprotein 1b)

**D68.02M** - von Willebrand disease, **Type 2M** - qualitative defects of VWF includes variants with markedly defective platelet adhesion with a normal size distribution of VWF multimers

**D68.02N** - von Willebrand disease, **Type 2N** - qualitative defects of VWF includes variants with markedly decreased affinity for factor VIII. (identifies defective VWF:FVIII binding)

**D68.02x** - von Willebrand disease, **Type 2, unspecified** - qualitative defect in VWF function, not meeting criteria for further subtyping

**Commented [ASH]:** Four subtypes recognized for type 2 – all type 2 should be able to be classified into one of these four – there are technically other type 2 variants that are very rare but none that are officially recognized. No one should get a diagnosis of “type 2” – it should be one of the subtypes.

**Commented [ASH]:** Type 2: unspecified – clear the patient has a type 2 variant but testing is inconclusive or additional testing is needed, not all testing complete, etc.

#### D68.03 von Willebrand disease, Type 3 - total quantitative deficiency of VWF (complete or near complete absence of VWF)

#### D68.04 von Willebrand disease, Platelet-type

#### D68.05 Acquired von Willebrand syndrome

**Commented [ASH]:** Could be an inclusion term under D69 Platelet Disorders or a separate VWD code.

**Commented [ASH]:** Not an inherited abnormality of VWF, a problem acquired at some point in life with VWF. Acquired problem due to non-genetic causes. Other term – acquired von Willebrand disease

Acquired von Willebrand disease

D68.08 von Willebrand disease, other

D68.09 von Willebrand disease, unspecified

Proposed Edit to R-Code

R79.1 – Abnormal Coagulation Profile

Low von Willebrand factor (add term to code)

**Commented [ASH]:** The term low VWF reflects an abnormal lab test not a diagnosis. VWF levels between 30-50% of normal. Recommend that this be a term under r-code (R79.1).