Subtype	Inheritance	Prevalence	Bleeding Phenotype	APTT	VIII:C	VWF:Ag	VWF:RCo	VWF:RCo/VWF:Ag ratio	FVIII Binding	RIPA - Low Dose	RIPA - High Dose	Platelet Count	PFA-100	Multimers	Comments
Normal	-	-	-	**Normal**	**Normal**	**Normal**	**Normal**	**1**	**Normal**	**Absent**	**Normal**	**Normal**	**Normal**	**Normal distribution**	
Type 1 **Partial quantitative deficiency**	Autosomal dominant	Common - accounts for 75-80% of cases of VWD. Prevalence in the general population may be as high as 1%.	Mild to moderate	May be normal or abnormal - depends upon the severity of the disorder and the level of VIII:C	Normal or ↓	↓ or ↓↓	↓ or ↓↓	1	Usually normal	Absent	Often normal	Normal	Normal or ↑	Normal distribution but reduced numbers	There are a wide spectrum of mutations associated with Type 1 VWD. Mutations include those that interfere with the intracellular transport of VWF, or which accelerate the clearance of VWF from the plasma e.g Type 1 Vicenza.
Type 2A Qualitative deficiency. Decreased VWF-dependent platelet adhesion with selective loss of HMWM	Mostly autosomal dominant [occasionally recessive]	Accounts for 10-20% of cases	Variable - usually moderate	Normal or ↑	Normal or ↓	↓	↓ ↓ or ↓↓↓	↓ [<0.7]	Normal	Absent	↓	Normal	↑↑↑	High and intermediate molecular weight multimers absent. Frequent abnormal triplet sub-bands	Type 2A VWD is due to a qualitative abnormality of VWF in which the proportion of HMW multimers is reduced. Type 2A VWD can be caused by mutations that interfere with VWF assembly or by mutations that increase its susceptibility to proteolytic cleavage in plasma. Mutations that affect multimer assembly usually lead to the secretion of multimers that are unable to bind to platelets efficiently. Homozygous mutations in the VWF prepropeptide interfere with multimer assembly within the Golgi of the cell - historically this was classified as Type IIC VWD. Heterozygous mutations within the cysteine knot region of VWF can impair dimerisation of VWF within the ER and lead to a phenotype historically known as Type IID VWD. Heterozygous mutations within the D3 domain can also impair multimer assembly leading to a phenotype historically known as Type IIE VWD.
Type 2B Qualitative deficiency Increased affinity for platelet GpIb	Autosomal dominant	Accounts for 5% of cases	Variable - usually moderate	Usually Normal or ↑	Normal or ↓	Normal or ↓	↓↓	↓ [<0.7]	Normal	↑↑↑	Usually normal	Usually ↓ but may be normal	↑↑↑	Variable loss of high-molecular weight multimers. Occasionally multimer distribution is normal with all high-molecular weight multimers present.	Type 2B VWD is caused by mutations that increase platelet-VWF binding leading to proteolytic degradation and depletion of HMW functional VWF multimers. This is similar to Platelet-type VWD in which the mutation in the GpIb receptor leads to an increased affinity for VWF leading to a depletion of the HMWM in the plasma. Type 2B mutations occur within or adjacent to Domain 1. These mutations appear to stabilise platelet-VWF interaction so enhancing platelet binding.
Type 2M Qualitative deficiency Decreased VWF-dependent platelet adhesion without selective deficiency of HMWM	Autosomal dominant	Accounts for 5% of cases	Variable - usually moderate	Usually Normal or ↑	↓↓	Usually ↓	↓↓	↓ [<0.7]	Normal	Absent	↓	Normal	↑	The full range of VWF multimers is present. Occasionally ultra-large multimers are present	Type 2M mutations reduce the interaction of VWF with platelet GpIb of with connective tissue and do not substantially impair multimer assembly. Mutations in Type 2M have been reported in the A1 domain and in the A3 domain.
Type 2N [Qualitative deficiency: Markedly decreased binding affinity for FVIII]	Autosomal recessive	Uncommon	Variable - usually moderate	↑↑	↓↓	Usually normal or slightly reduced.	Normal	1	Abnormal	Absent	Normal	Normal	Normal	Normal distribution	Type 2N VWD is due to homozygous mutations that impair binding to FVIII leading to a reduction in circulating FVIII. 2N VWD was frequently mistaken as mild-moderate haemophilia A as the VWF levels are normal but FVIII is reduced. However, the pattern of inheritance in 2N VWD is autosomal recessive whilst in Haemophilia A, it is X-linked. Most mutations causing 2N VWD lie in either the D' or D3 domain.
Type 3 Virtually complete deficiency of VWF	Autosomal recessive	Rare <1% of cases. Commoner where consanguinity is common	Severe	↑↑↑	↓↓↓	↓↓↓	↓↓↓	-	Normal	Absent	Absent	Normal	↑↑↑	No multimers visualized. May be faint low-molecular weight bands present.	No consistent genetic abnormality has been identified in Type 3 VWD. Individuals with complete gene deletions that lead to Type 3 VWD may be at risk of developing inhibitors following treatment with VWF-containing concentrates. Individuals who are heterozygous for mutations that when present either in the homozygous state or compound heterozygous state and lead to Type 3 VWD, may have only a minor bleeding phenotype or no bleeding problems.
Platelet-Type VWD A gain-of-function mutation affecting the Platelet membrane GpIb receptor	Autosomal dominant	Rare	Variable - usually moderate	Usually Normal or ↑	Normal or ↓	Normal or ↓	↓↓	↓ [<0.7]	Normal	↑↑↑		↓	↑	Reduced HMWM	Arises from a gain-of-function mutation in the GPIbα gene that encodes the platelet glycoprotein Ibα receptor, leading to an enhanced affinity for VWF. As a consequence the platelets bind spontaneously to the VWF HMW multimers and are then cleared from the circulation, leading to thrombocytopenia and the loss of VWF HMW multimers. The platelets are classically large.
Type 1C **VWD Vicenza**	Autosomal dominant	Rare	Variable - usually moderate	May be normal or abnormal - depends upon the severity of the disorder and the level of VIII:C	↓	↓	↓	1	Normal	Absent	↓	Normal	↑	Presence of ultra HMWM	A mutation [Arg1205His] leads to accelerated clearance of the variant VWF from the plasma. VWF:RCo is reduced [commonly ~15 IU/dL]. Measuring the VWFpp:VWF:Ag ratio can be of value in establishing the presence of a variant VWF with an accelerated clearance.