Supplemental figures/ tables and files

Overview:

Methods

Risk of Bias

Risk of bias was assessed using an adjusted Quality in Prognostic Studies (QUIPS)[1] checklist (see supplemental file 2 for the edited QUIPS checklist). Each article was evaluated by two reviewers and disagreements were resolved by consensus. In short, questions per domain were weighted based on relevance. A cut-off to decide whether a domain is low, moderate or high risk of bias is reported in the adjusted quips checklist. A DDAVP test is completed a few hours after administration and most studies gathered the data retrospectively. Therefore, the study attrition domain was removed from the checklist as these questions were not applicable for this review. Furthermore, sub question b and c were removed from domain Statistical analysis and reporting. These were removed as data from each study were collected and not values as calculated by statistical analysis. A study was considered as low overall risk of bias when all domain scores were rated as low or if one domain was scored moderate. We scored a study as having high overall risk of bias if two or more of the domains were judged as high. A study was scored as moderate if the criteria for 'low' or 'high' were not met.

Statistical analysis

Logistic random-effects models were applied to pool proportions of complete responders to DDAVP both pooled and separately by disease type according to the "study definition". Heterogeneity between studies was assessed by calculating I^2 and Tau^2 and by calculating a prediction interval for new studies. Forest plots were generated to show the variation between studies. Studies that could not be combined due to lack of sufficient data were assessed qualitatively. Median response in VWF levels over time in the quantitative sense (on antigen level) or in a qualitative sense (on activity level) were reported. The association between the different determinants and the response rate was assessed by performing meta-regressions; bubble plots were generated to visualize the association. As sensitivity analysis, the analyses were repeated using only low or moderate risk of bias studies. All analyses were performed using R (version 4·2·3)[2] with the packages meta (version 7·0-0), to pool the proportions and metareg to perform meta regression. The package forestplot (version 4·2·3) was used to make forest plots and ggplot2 (version 3·4·4) to make bubble plots. P-values < 0·05 were considered statistically significant.

1. Evaluation of the Quality of Prognosis Studies in Systematic Reviews. *Annals of Internal Medicine*. 2006;144(6):427-437.
2. R development Core Team. R: A language and environment for statistical computing: R foundation for statistical computing; 2024.

Supplemental file 1 – search strategy

Update 1-9-2022 - total: 591 references, of which new 21:

1. PubMed: 450 - 16 new & unique
2. Embase: 347 - 1 new & unique
3. Web of Science: 306 - 2 new & unique
4. COCHRANE Library: 62 – 2 new & unique
5. Emcare: 21 - 0 new & unique

Version 16-10-2020 - total: 570 references, taken from:

6. PubMed: 434
7. Embase: 320 - 56 unique
8. Web of Science: 293 - 45 unique
9. COCHRANE Library: 58 - 35 unique
10. Emcare: 17 - 0 unique

Pubmed

16-10-2020

(("Deamino Arginine Vasopressin"[majr] OR "Deamino Arginine Vasopressin"[ti] OR Desmopressin*[ti] OR "1-Deamino-8-D-arginine Vasopressin"[ti] OR "1-Desamino-8-arginine Vasopressin"[ti] OR "Adiuretin"[ti] OR "DDAVP"[ti] OR "Desmopressin"[ti] OR "Desmospray"[ti] OR "Minirin"[ti] OR "Minurin"[ti] OR "Octim"[ti] OR "Octostim"[ti] OR "Minrin"[ti] OR "Nocdurna"[ti]) **AND** ("Hemorrhagic Disorders"[mesh] OR "Hemorrhagic Disorders"[tw] OR "Hemorrhagic Disorder"[tw] OR "Hemorrhagic Diseases"[tw] OR "Hemorrhagic Disease"[tw] OR "Haemorrhagic Disorders"[tw] OR "Haemorrhagic Disorder"[tw] OR "Haemorrhagic Diseases"[tw] OR "Haemorrhagic Disease"[tw] OR "von Willebrand Diseases"[Mesh] OR "von Willebrand Disease"[tw] OR "von Willebrand Diseases"[tw] OR "von Willebrands Disease"[tw] OR "von Willebrand's Disease"[tw] OR "von Willebrand's Diseases"[tw] OR angiohemophil*[tw] OR "Hemophilia A"[mesh] OR "Hemophilia B"[mesh] OR hemophil*[tw] OR haemophil*[tw] OR "Factor VIII Deficiency"[tw] OR "Factor 8 Deficiency"[tw] OR "Factor IX Deficiency"[tw] OR "Afibrinogenemia"[tw] OR "Bernard-Soulier Syndrome"[tw] OR "Disseminated Intravascular Coagulation"[tw] OR "Factor V Deficiency"[tw] OR "Factor VII Deficiency"[tw] OR "Factor X Deficiency"[tw] OR "Factor XI Deficiency"[tw] OR "Factor XII Deficiency"[tw] OR "Factor XIII Deficiency"[tw] OR "Hemostatic Disorders"[tw] OR "Hemostatic Disorder"[tw] OR "Cryoglobulinemia"[tw] OR "Cryoglobulinaemia"[tw] OR "Ehlers-Danlos Syndrome"[tw] OR "Cavernous Hemangioma"[tw] OR "Cavernous Hemangiomas"[tw] OR "Cavernous Haemangioma"[tw] OR "Cavernous Haemangiomas"[tw] OR "Multiple Myeloma"[tw] OR "Multiple Myelomas"[tw] OR "Pseudoxanthoma Elasticum"[tw] OR "Hyperglobulinemic Purpura"[tw] OR "Schoenlein-Henoch Purpura"[tw] OR "Scurvy"[tw] OR "Shwartzman Phenomenon"[tw] OR "Hereditary Hemorrhagic Telangiectasia"[tw] OR "Hereditary Haemorrhagic Telangiectasia"[tw] OR "Waldenstrom Macroglobulinemia"[tw] OR "Waldenstrom Macroglobulinaemia"[tw] OR "Hypoprothrombinemias"[tw] OR "Hypoprothrombinemias"[tw] OR "Hypoprothrombinaemias"[tw] OR "Hypoprothrombinaemia"[tw] OR "Platelet Storage Pool Deficiency"[tw] OR "Hermanski-Pudlak Syndrome"[tw] OR "Idiopathic Thrombocytopenic Purpura"[tw] OR "Immune Thrombocytopenic Purpura"[tw] OR "Immune Thrombocytopenia"[tw] OR "Autoimmune Thrombocytopenia"[tw] OR "Autoimmune Thrombocytopenic Purpura"[tw] OR "Thrombasthenia"[tw] OR "Essential Thrombocythemia"[tw] OR "Vitamin K Deficiency"[tw] OR "Waterhouse-Friderichsen Syndrome"[tw] OR "Wiskott-Aldrich Syndrome"[tw]) **AND** english[la] NOT ("Animals"[mesh] NOT "Humans"[mesh]))

Embase

16-10-2020

((*"argipressin[1 deamino]"/ OR "Deamino Arginine Vasopressin".ti OR Desmopressin*.ti OR "1-Deamino-8-D-arginine Vasopressin".ti OR "1-Desamino-8-arginine Vasopressin".ti OR "Adiuretin".ti OR "DDAVP".ti OR "Desmopressin".ti OR "Desmospray".ti OR "Minirin".ti OR "Minurin".ti OR "Octim".ti OR "Octostim".ti OR "Minrin".ti OR "Nocdurna".ti) **AND** (*"Bleeding Disorder"/ OR "Hemorrhagic Disorders".ti,ab OR "Hemorrhagic Disorder".ti,ab OR "Hemorrhagic Diseases".ti,ab OR "Hemorrhagic Disease".ti,ab OR "Haemorrhagic Disorders".ti,ab OR "Haemorrhagic Disorder".ti,ab OR "Haemorrhagic Diseases".ti,ab OR "Haemorrhagic Disease".ti,ab OR *"von Willebrand Disease"/ OR "von Willebrand Disease".ti,ab OR "von Willebrand Diseases".ti,ab OR "von Willebrands Disease".ti,ab OR "von Willebrand's Disease".ti,ab OR "von Willebrand's Diseases".ti,ab OR angiohemophil*.ti,ab OR exp *"Hemophilia"/ OR hemophil*.ti,ab OR haemophil*.ti,ab OR "Factor VIII Deficiency".ti,ab OR "Factor 8 Deficiency".ti,ab OR "Factor IX Deficiency".ti,ab OR "Afibrinogenemia".ti,ab OR "Bernard-Soulier Syndrome".ti,ab OR "Disseminated Intravascular Coagulation".ti,ab OR "Factor V Deficiency".ti,ab OR "Factor VII Deficiency".ti,ab OR "Factor X Deficiency".ti,ab OR "Factor XI Deficiency".ti,ab OR "Factor XII Deficiency".ti,ab OR "Factor XIII Deficiency".ti,ab OR "Hemostatic Disorders".ti,ab OR "Hemostatic Disorder".ti,ab OR "Cryoglobulinemia".ti,ab OR "Cryoglobulinaemia".ti,ab OR "Ehlers-Danlos Syndrome".ti,ab OR "Cavernous Hemangioma".ti,ab OR "Cavernous Hemangiomas".ti,ab OR "Cavernous Haemangioma".ti,ab OR "Cavernous Haemangiomas".ti,ab OR "Multiple Myeloma".ti,ab OR "Multiple Myelomas".ti,ab OR "Pseudoxanthoma Elasticum".ti,ab OR "Hyperglobulinemic Purpura".ti,ab OR "Schoenlein-Henoch Purpura".ti,ab OR "Scurvy".ti,ab OR "Shwartzman Phenomenon".ti,ab OR "Hereditary Hemorrhagic Telangiectasia".ti,ab OR "Hereditary Haemorrhagic Telangiectasia".ti,ab OR "Waldenstrom Macroglobulinemia".ti,ab OR "Waldenstrom Macroglobulinaemia".ti,ab OR "Hypoprothrombinemias".ti,ab OR "Hypoprothrombinemias".ti,ab OR "Hypoprothrombinaemias".ti,ab OR "Hypoprothrombinaemia".ti,ab OR "Platelet Storage Pool Deficiency".ti,ab OR "Hermanski-Pudlak Syndrome".ti,ab OR "Idiopathic Thrombocytopenic Purpura".ti,ab OR "Immune Thrombocytopenic Purpura".ti,ab OR "Immune Thrombocytopenia".ti,ab OR "Autoimmune Thrombocytopenia".ti,ab OR "Autoimmune Thrombocytopenic Purpura".ti,ab OR "Thrombasthenia".ti,ab OR "Essential Thrombocythemia".ti,ab OR "Vitamin K Deficiency".ti,ab OR "Waterhouse-Friderichsen Syndrome".ti,ab OR "Wiskott-Aldrich Syndrome".ti,ab) **AND** english.la NOT (exp "Animals"/ NOT "Humans"/)) NOT (conference review or conference abstract).pt

Web of Science

16-10-2020

(ti=("argipressin[1 deamino]" OR "Deamino Arginine Vasopressin" OR Desmopressin* OR "1-Deamino-8-D-arginine Vasopressin" OR "1-Desamino-8-arginine Vasopressin" OR "Adiuretin" OR "DDAVP" OR "Desmopressin" OR "Desmospray" OR "Minirin" OR "Minurin" OR "Octim" OR "Octostim" OR "Minrin" OR "Nocdurna") **AND** ts=("Bleeding Disorder" OR "Hemorrhagic Disorders" OR "Hemorrhagic Disorder" OR "Hemorrhagic Diseases" OR "Hemorrhagic Disease" OR "Haemorrhagic Disorders" OR "Haemorrhagic Disorder" OR "Haemorrhagic Diseases" OR "Haemorrhagic Disease" OR "von Willebrand Disease" OR "von Willebrand Disease" OR "von Willebrand Diseases" OR "von Willebrands Disease" OR "von Willebrand's Disease" OR "von Willebrand's Diseases" OR angiohemophil* OR "Hemophilia" OR hemophil* OR haemophil* OR "Factor VIII Deficiency" OR "Factor 8 Deficiency" OR "Factor IX Deficiency" OR "Afibrinogenemia" OR "Bernard-Soulier Syndrome" OR "Disseminated Intravascular Coagulation" OR "Factor V Deficiency" OR "Factor VII Deficiency" OR "Factor X Deficiency" OR "Factor XI Deficiency" OR "Factor XII Deficiency" OR "Factor XIII Deficiency" OR "Hemostatic Disorders" OR "Hemostatic Disorder" OR "Cryoglobulinemia" OR "Cryoglobulinaemia" OR "Ehlers-Danlos Syndrome" OR "Cavernous Hemangioma" OR "Cavernous Hemangiomas" OR "Cavernous Haemangioma" OR "Cavernous Haemangiomas" OR "Multiple Myeloma" OR "Multiple Myelomas" OR "Pseudoxanthoma Elasticum" OR "Hyperglobulinemic Purpura" OR "Schoenlein-Henoch Purpura" OR "Scurvy" OR "Shwartzman Phenomenon" OR "Hereditary Hemorrhagic Telangiectasia" OR "Hereditary Haemorrhagic Telangiectasia" OR "Waldenstrom Macroglobulinemia" OR "Waldenstrom Macroglobulinaemia" OR "Hypoprothrombinemias" OR "Hypoprothrombinemias" OR "Hypoprothrombinaemias" OR "Hypoprothrombinaemia" OR "Platelet Storage Pool Deficiency" OR "Hermanski-Pudlak Syndrome" OR "Idiopathic Thrombocytopenic Purpura" OR "Immune Thrombocytopenic Purpura" OR "Immune Thrombocytopenia" OR "Autoimmune Thrombocytopenia" OR "Autoimmune Thrombocytopenic Purpura" OR "Thrombasthenia" OR "Essential Thrombocythemia" OR "Vitamin K Deficiency" OR "Waterhouse-Friderichsen Syndrome" OR "Wiskott-Aldrich Syndrome") **AND** la=english NOT ti=("veterinary" OR "rabbit" OR "rabbits" OR "animal" OR "animals" OR "mouse" OR "mice" OR "rodent" OR "rodents" OR "rat" OR "rats" OR "pig" OR "pigs" OR "porcine" OR "horse" OR "horses" OR "equine" OR "cow" OR "cows" OR "bovine" OR "goat" OR "goats" OR "sheep" OR "ovine" OR "canine" OR "dog" OR "dogs" OR "feline" OR "cat" OR "cats")) NOT dt=(meeting abstract)

Cochrane

16-10-2020

("argipressin[1 deamino]" OR "Deamino Arginine Vasopressin" OR Desmopressin OR Desmopressin* OR Desmopressins OR "1 Deamino 8 D arginine Vasopressin" OR "1 Desamino 8 arginine Vasopressin" OR "Adiuretin" OR "DDAVP" OR "Desmopressin" OR "Desmospray" OR "Minirin" OR "Minurin" OR "Octim" OR "Octostim" OR "Minrin" OR "Nocdurna"):ti,ab,kw

AND

(

("Bleeding Disorder" OR "Hemorrhagic Disorders" OR "Hemorrhagic Disorder" OR "Hemorrhagic Diseases" OR "Hemorrhagic Disease" OR "Haemorrhagic Disorders" OR "Haemorrhagic Disorder" OR "Haemorrhagic Diseases" OR "Haemorrhagic Disease" OR "von Willebrand Disease" OR "von

Willebrand Disease" OR "von Willebrand Diseases" OR "von Willebrands Disease" OR "von Willebrand's Disease" OR "von Willebrand's Diseases" OR angiohemophil* OR "Hemophilia" OR hemophil* OR haemophil* OR "Factor VIII Deficiency" OR "Factor 8 Deficiency" OR "Factor IX Deficiency" OR "Afibrinogenemia" OR "Bernard Soulier Syndrome" OR "Disseminated Intravascular Coagulation" OR "Factor V Deficiency" OR "Factor VII Deficiency" OR "Factor X Deficiency" OR "Factor XI Deficiency" OR "Factor XII Deficiency" OR "Factor XIII Deficiency" OR "Hemostatic Disorders" OR "Hemostatic Disorder" OR "Cryoglobulinemia" OR "Cryoglobulinaemia" OR "Ehlers Danlos Syndrome" OR "Cavernous Hemangioma"):ti,ab,kw

("Cavernous Hemangiomas" OR "Cavernous Haemangioma" OR "Cavernous Haemangiomas" OR "Multiple Myeloma" OR "Multiple Myelomas" OR "Pseudoxanthoma Elasticum" OR "Hyperglobulinemic Purpura" OR "Schoenlein Henoch Purpura" OR "Scurvy" OR "Shwartzman Phenomenon" OR "Hereditary Hemorrhagic Telangiectasia" OR "Hereditary Haemorrhagic Telangiectasia" OR "Waldenstrom Macroglobulinemia" OR "Waldenstrom Macroglobulinaemia"):ti,ab,kw

("Hypoprothrombinemias" OR "Hypoprothrombinemias" OR "Hypoprothrombinaemias" OR "Hypoprothrombinaemia" OR "Platelet Storage Pool Deficiency" OR "Hermanski Pudlak Syndrome" OR "Idiopathic Thrombocytopenic Purpura" OR "Immune Thrombocytopenic Purpura" OR "Immune Thrombocytopenia"):ti,ab,kw

("Autoimmune Thrombocytopenia" OR "Autoimmune Thrombocytopenic Purpura" OR "Thrombasthenia" OR "Essential Thrombocythemia" OR "Vitamin K Deficiency" OR "Waterhouse Friderichsen Syndrome" OR "Wiskott Aldrich Syndrome"):ti,ab,kw

):ti,ab,kw

NOT (conference abstract):pt

Emcare

16-10-2020

((*"argipressin[1 deamino]"/ OR "Deamino Arginine Vasopressin".ti OR Desmopressin*.ti OR "1-Deamino-8-D-arginine Vasopressin".ti OR "1-Desamino-8-arginine Vasopressin".ti OR "Adiuretin".ti OR "DDAVP".ti OR "Desmopressin".ti OR "Desmospray".ti OR "Minirin".ti OR "Minurin".ti OR "Octim".ti OR "Octostim".ti OR "Minrin".ti OR "Nocdurna".ti) **AND** (*"Bleeding Disorder"/ OR "Hemorrhagic Disorders".ti,ab OR "Hemorrhagic Disorder".ti,ab OR "Hemorrhagic Diseases".ti,ab OR "Hemorrhagic Disease".ti,ab OR "Haemorrhagic Disorders".ti,ab OR "Haemorrhagic Disorder".ti,ab OR "Haemorrhagic Diseases".ti,ab OR "Haemorrhagic Disease".ti,ab OR *"von Willebrand Disease"/ OR "von Willebrand Disease".ti,ab OR "von Willebrand Diseases".ti,ab OR "von Willebrands Disease".ti,ab OR "von Willebrand's Disease".ti,ab OR "von Willebrand's Diseases".ti,ab OR angiohemophil*.ti,ab OR exp *"Hemophilia"/ OR hemophil*.ti,ab OR haemophil*.ti,ab OR "Factor VIII Deficiency".ti,ab OR "Factor 8 Deficiency".ti,ab OR "Factor IX Deficiency".ti,ab OR "Afibrinogenemia".ti,ab OR "Bernard-Soulier Syndrome".ti,ab OR "Disseminated Intravascular Coagulation".ti,ab OR "Factor V Deficiency".ti,ab OR "Factor VII Deficiency".ti,ab OR "Factor X Deficiency".ti,ab OR "Factor XI Deficiency".ti,ab OR "Factor XII Deficiency".ti,ab OR "Factor XIII Deficiency".ti,ab OR "Hemostatic Disorders".ti,ab OR "Hemostatic Disorder".ti,ab OR "Cryoglobulinemia".ti,ab OR "Cryoglobulinaemia".ti,ab OR "Ehlers-Danlos Syndrome".ti,ab OR "Cavernous Hemangioma".ti,ab OR "Cavernous Hemangiomas".ti,ab OR "Cavernous

Haemangioma".ti,ab OR "Cavernous Haemangiomas".ti,ab OR "Multiple Myeloma".ti,ab OR "Multiple Myelomas".ti,ab OR "Pseudoxanthoma Elasticum".ti,ab OR "Hyperglobulinemic Purpura".ti,ab OR "Schoenlein-Henoch Purpura".ti,ab OR "Scurvy".ti,ab OR "Shwartzman Phenomenon".ti,ab OR "Hereditary Hemorrhagic Telangiectasia".ti,ab OR "Hereditary Haemorrhagic Telangiectasia".ti,ab OR "Waldenstrom Macroglobulinemia".ti,ab OR "Waldenstrom Macroglobulinaemia".ti,ab OR "Hypoprothrombinemias".ti,ab OR "Hypoprothrombinemias".ti,ab OR "Hypoprothrombinaemias".ti,ab OR "Hypoprothrombinaemia".ti,ab OR "Platelet Storage Pool Deficiency".ti,ab OR "Hermanski-Pudlak Syndrome".ti,ab OR "Idiopathic Thrombocytopenic Purpura".ti,ab OR "Immune Thrombocytopenic Purpura".ti,ab OR "Immune Thrombocytopenia".ti,ab OR "Autoimmune Thrombocytopenia".ti,ab OR "Autoimmune Thrombocytopenic Purpura".ti,ab OR "Thrombasthenia".ti,ab OR "Essential Thrombocythemia".ti,ab OR "Vitamin K Deficiency".ti,ab OR "Waterhouse-Friderichsen Syndrome".ti,ab OR "Wiskott-Aldrich Syndrome".ti,ab **OR** *"von Willebrand Factor"/ OR "Von willebrand factor".ti,ab OR "VWF".ti,ab OR "Factor VIIIR Ag".ti,ab OR "Factor VIIIR RCo".ti,ab OR "Willebrand Factor".ti,ab OR "Willebrand Protein".ti,ab OR "Factor VIII Related Antigen".ti,ab OR "Ristocetin Cofactor".ti,ab OR "Plasma Factor VIII Complex".ti,ab OR "Factor VIII"/ OR "Factor VIII".ti,ab OR "Factor 8".ti,ab OR "anti-hemophilic factor".ti,ab OR "anti-hemophilic factors".ti,ab OR "anti-haemophilic factor".ti,ab OR "anti-haemophilic factors".ti,ab OR "antihemophilic factor".ti,ab OR "antihemophilic factors".ti,ab OR "antihaemophilic factor".ti,ab OR "antihaemophilic factors".ti,ab OR "AHF".ti,ab OR "F8".ti,ab OR "coagulation factor VIII".ti,ab OR "coagulation factor 8".ti,ab OR exp *"Endothelium"/ OR "endothelium*".ti,ab OR exp *"Endothelium Cell"/ OR "Endothelial Cell".ti,ab OR "Endothelial Cells".ti,ab OR "Vasopressin receptor 2".ti,ab OR "V2R".ti,ab OR "arginine vasopressin receptor 2".ti,ab OR "AVPR2".ti,ab) **AND** english.la)

Supplemental file 2 – data extraction template including RoB (QUIPS)

See separate attached file.

Supplemental file 3 – Complete data extraction file

See separate attached file.

Supplemental table 1: Characteristics of the studies included in the primary analysis

See separate attached file.

Supplemental table 2: Definitions of response as mentioned by the included articles.

See separate attached file.

Supplemental table 3: Odds ratio of response per determinant from meta-regression.

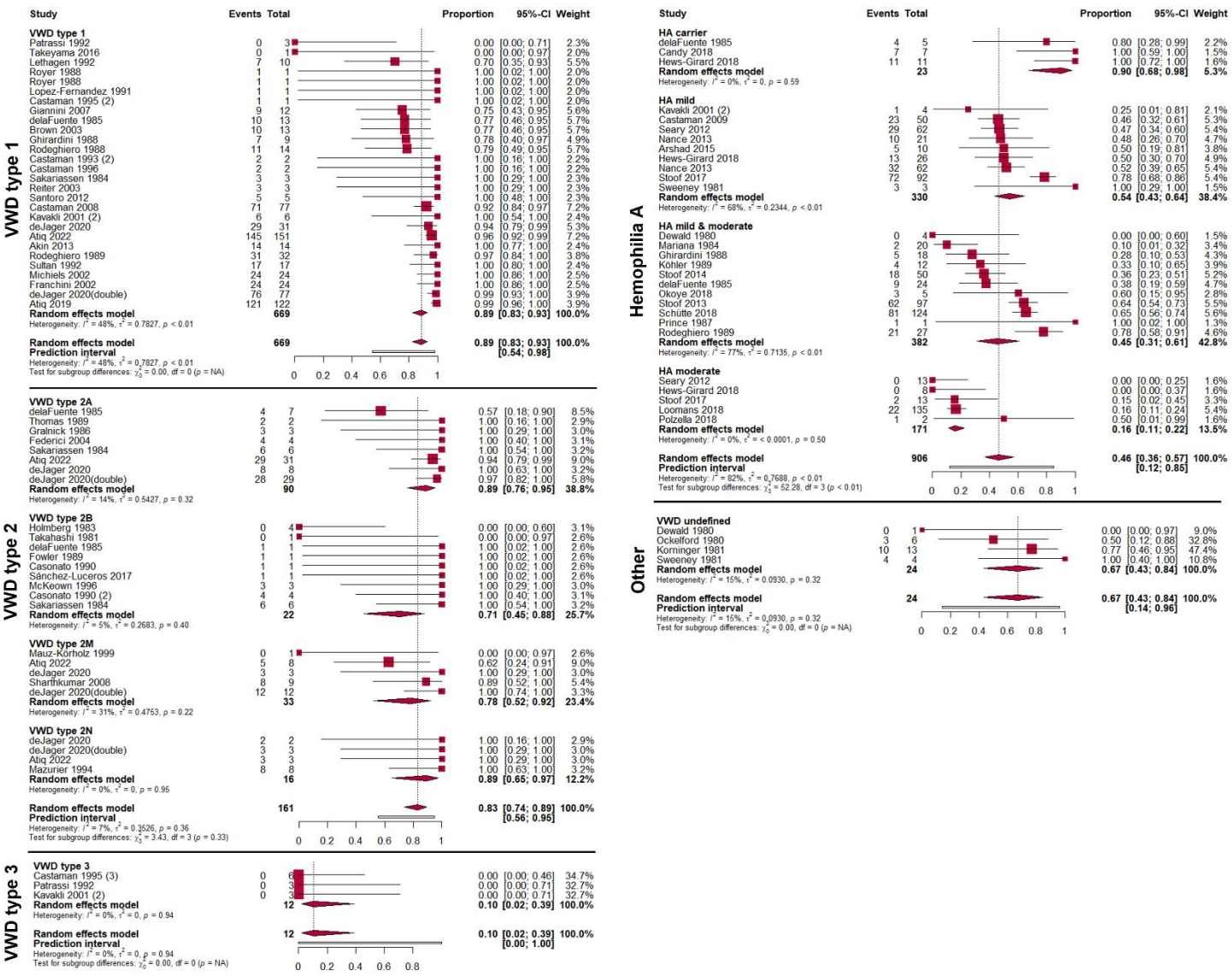
		VWD type 1			VWD type 2			Hemophilia A		
	Determinant	**OR**	**95%CI**		**OR**	**95% CI**		**OR**	**95%CI**	
	Age (years)	1,006	0,935	1,082	1,006	0,951	1,064	1,048	0,961	1,142
	Blood group non-O vs O	0,997	0,941	1,057	1,037	0,996	1,080	0,981	0,931	1,035
	Female (%)	1,003	0,976	1,030	x	x	x	1,020	1,004	1,037
Before DDAVP administration	Before DDAVP APTT (s)	0,995	0,938	1,056	x	x	x	1,010	0,706	1,446
Before DDAVP administration	Bleeding time (min)	0,917	0,759	1,109	0,946	0,822	1,090	x	x	x
Before DDAVP administration	FVIII:Ag (U/dL)	x	x	x	x	x	x	x	x	x
Before DDAVP administration	FVIII:C (U/dL)	1,023	1,002	1,045	x	x	x	1,042	0,996	1,090
Before DDAVP administration	Platelet count	0,998	0,946	1,052	1,001	0,982	1,020	x	x	x
Before DDAVP administration	VWF:Ag (U/dL)	1,055	1,016	1,093	x	x	x	1,005	0,974	1,067
Before DDAVP administration	VWF:CB (U/dL)	1,058	0,898	1,246	0,999	0,976	1,021	0,986	0,940	1,035
Before DDAVP administration	VWF:pp (U/dL)	x	x	x	x	x	x	x	x	x
Before DDAVP administration	VWF:Act (U/dL)	1,048	1,008	1,090	x	x	x	0,990	0,957	1,025
Before DDAVP administration	Bodyweight (kg)	1,044	0,974	1,119	1,033	0,982	1,086	1,120	0,983	1,276

X indicates determinants for which the meta-regression could not be performed. Abbreviations: VWD, von Willebrand Disease; OR, Odds ratio; CI, Confidence interval; DDAVP, 1-Deamino-8-D-ArgininVasoPressin; APTT, activated partial thromboplastin time; Ag, antigen; CB, Collagen Binding; pp, propeptide; Act, Activity.

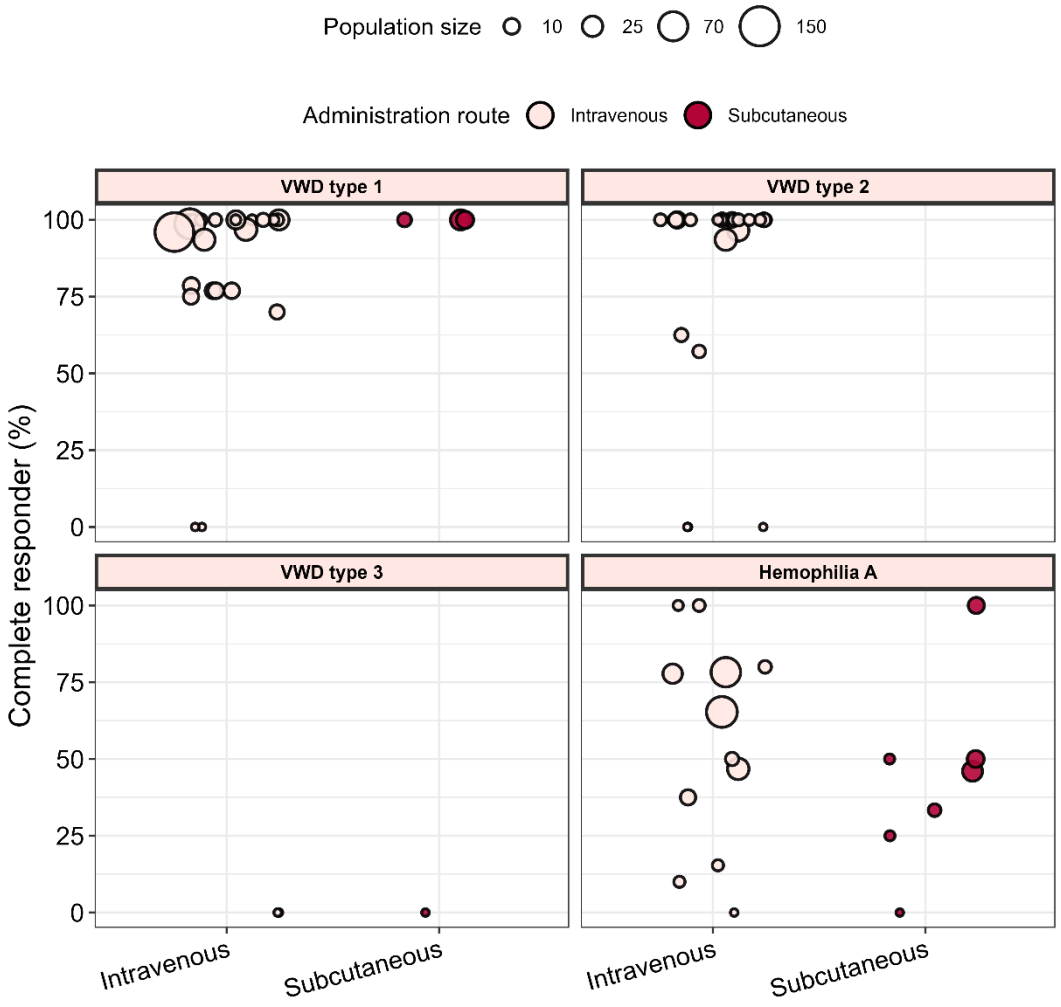
Supplemental table 4. Sensitivity analysis on Odds ratio of response per determinant

		VWD type 1			VWD type 2			Hemophilia A		
	Determinant	**OR**	**95%CI**		**OR**	**95% CI**		**OR**	**95%CI**	
	Age (years)	1,006	0,935	1,082	1,011	0,951	1,076	1,048	0,961	1,142
	Blood group non-O vs O	0,997	0,941	1,057	1,037	0,996	1,080	0,981	0,931	1,035
	Female (%)	1,003	0,976	1,030	x	x	x	1,020	1,004	1,037
Before DDAVP administration	APTT (s)	0,995	0,938	1,056	x	x	x	1,010	0,706	1,446
Before DDAVP administration	Bleeding time (min)	0,917	0,759	1,109	0,927	0,777	1,106	x	x	x
Before DDAVP administration	FVIII:Ag (U/dL)	x	x	x	x	x	x	x	x	x
Before DDAVP administration	FVIII:C (U/dL)	1,021	1,000	1,043	x	x	x	1,041	0,995	1,089
Before DDAVP administration	Platelet count	0,998	0,946	1,052	1,004	0,983	1,024	x	x	x
Before DDAVP administration	VWF:Ag (U/dL)	1,054	1,014	1,095	x	x	x	1,005	0,974	1,067
Before DDAVP administration	VWF:CB (U/dL)	1,077	0,904	1,283	0,999	0,976	1,021	0,986	0,940	1,035
Before DDAVP administration	VWF:pp (U/dL)	x	x	x	x	x	x	x	x	x
Before DDAVP administration	VWF:Act (U/dL)	1,047	1,007	1,088	x	x	x	0,990	0,957	1,025
Before DDAVP administration	Bodyweight (kg)	1,044	0,974	1,119	1,033	0,982	1,086	1,120	0,983	1,276

X indicates determinants for which the meta-regression could not be performed. Numbers in red have changed when compared to supplemental table 3. Abbreviations: VWD, von Willebrand Disease; OR, Odds ratio; CI, Confidence interval; DDAVP, 1-Deamino-8-D-ArgininVasoPressin; APTT, activated partial thromboplastin time; Ag, antigen; CB, Collagen Binding; pp, propeptide; act, Activity.



Supplemental figure 1. Complete response rate varies per disease subtype according to the study definition. Meta-analysis on response to DDAVP at one hour in patients with various bleeding disorders per subtype. Using a random effect model the proportion of complete response per study, divided by subtype, are shown. Random effects are calculated per subtype of disease but also by main type of disease. The proportion of response is not zero in zero-event studies due to the continuity correction that was performed to prevent mathematical errors. Other is, everything that is not VWD type 1, 2 or 3 or Hemophilia A. Abbreviations: HA = Hemophilia, VWD = Von Willebrand Disease.



Supplemental figure 2. Response to DDAVP per disease per administration route. Response to DDAVP of patients with VWD type 1, 2 and 3 or Hemophilia A are shown per administration route of DDAVP. Intravenous is shown in light red and Subcutaneous is shown in dark red. Studies that did not clarify which route was used are excluded from this figure. Intranasal administration is not displayed in this figure as only two studies had this data. Abbreviations: VWD = Von Willebrand Disease.