

Appendix

Appendix 1: Search strategies

Searches Strategy for VWD Management guidelines

1. Umbrella search for all questions

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to October 2019

1. exp von Willebrand Diseases/ or VWD.mp. or (von willebrand adj4 (disease or disorder)).mp.
2. exp Hemophilia A/ or exp Hemophilia B/ or h?emophilia.mp. or angioh?emophilia.mp.
3. exp Blood Coagulation Disorders, Inherited/ or inherited bleeding disorders.mp. or exp Blood Platelet Disorders/ or platelet function disorders.mp. or h?emophillia carrier*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
4. prophylaxis.mp.
5. von willebrand factor.mp. or von Willebrand Factor/
6. 4 and 5
7. (prophyla* adj3 von Willebrand).mp.
8. 6 or 7
9. 1 and 8 [PICO 1]
10. Deamino Arginine Vasopressin/ or desmopressin.mp. or DDAVP.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
11. (challenge or trial).mp.
12. 10 and 11
13. 1 and 12 [PICO 2]
14. cardiovascular disease.mp. or exp Cardiovascular Diseases/
15. anticoagula*.mp. or exp Anticoagulants/
16. exp Platelet Aggregation Inhibitors/ or antiplatelet*.mp.
17. 1 and 14 and (15 or 16) [PICO 3]
18. Surgical Procedures, Operative/
19. major.mp.
20. (major adj4 surg*).mp.
21. (18 and 19) or 20

22. (1 or 2) and 21 [PICO 4]
23. exp Menorrhagia/
24. heavy menstrual bleeding.mp.25. hypermenorrhea.mp.
26. 23 or 24 or 25
27. (1 or 2 or 3) and 26 [PICO 5]
28. exp ANESTHESIA, EPIDURAL/ or exp ANALGESIA, EPIDURAL/
29. ((epidural or peridural or extradural) and (anesthesia or analgesia or block*)).mp.
30. (1 or 2 or 3) and (28 or 29) [PICO 6]
31. (postpartum or puerperium).mp. or exp Postpartum Period/
32. (1 or 2 or 3) and 31 [PICO 7]
33. 18 and minor.mp.
34. (minor adj4 surg*).mp.
35. exp Dental Care/
36. (dental treatment or dental procedure* or dental surg* or t??th extraction or dental clean* or oral surg*).mp.
37. exp Dermatologic Surgical Procedures/
38. exp BIOPSY/ or biopsy.mp.
39. joint aspiration.mp.
40. CIRCUMCISION, MALE/ or circumcision.mp.
41. Cataract Extraction/ or Lens Implantation, Intraocular/ or cataract surgery.mp.
42. colposcopy.mp. or exp COLPOSCOPY/
43. Intrauterine Devices/ or intrauterine device plac*.mp.
44. endoscopy.mp. or exp ENDOSCOPY/
45. or/33-44
46. (1 or 2) and 45 [PICO 8]
47. 9 or 13 or 17 or 22 or 27 or 32 or 46
48. (randomized controlled trial or controlled clinical trial).pt. or (randomized or placebo).ab. or drug therapy.fs. or (randomly or trial or groups).ab.
49. epidemiologic studies/ or exp case control studies/ or exp cohort studies/ or Cross-sectional studies/
50. case control.tw.
51. (cohort adj (study or studies)).tw.
52. cohort analy\$.tw.
53. (Follow up adj (study or studies)).tw.
54. (Observational adj (study or studies)).tw.
55. (longitudinal or retrospective or cross sectional).tw.
56. or/49-5557. (registr* or database).mp.
58. 48 or 56 or 57
59. 47 and 58

EMBASE (OVID) 1974 to 2019 October 10

1. exp von Willebrand Disease/ or VWD.mp. or (von willebrand adj4 (disease or disorder)).mp.

2. exp hemophilia/ or h?emophilia.mp. or angioh?emophilia.mp.
3. blood clotting disorder/ or (inherited bleeding disorder or hemophilia carrier).mp.
4. exp prophylaxis/ or prophylaxis.mp.
5. von willebrand factor.mp. or exp von Willebrand factor/
6. 4 and 5
7. (prophyla* adj3 von Willebrand).mp.
8. 6 or 7
9. 1 and 8 [PICO 1]
10. "argipressin[1 deamino]"/ or desmopressin.mp. or DDAVP.mp.
11. (challenge or trial).mp.
12. 10 and 11
13. 1 and 12 [PICO 2]
14. cardiovascular disease/ or cardiovascular disease*.mp.
15. exp anticoagulant agent/ or anticoagula*.mp.
16. exp antithrombocytic agent/ or antiplatelet*.mp.
17. 1 and 14 and (15 or 16) [PICO 3]
18. exp major surgery/
19. (major adj4 surg*).mp.
20. (1 or 2) and (18 or 19) [PICO 4]
21. (heavy menstrual bleeding or hypermenorrhea or menorrhagia).mp.
22. (1 or 2 or 3) and 21 [PICO 5]
23. exp epidural analgesia/ or exp epidural anesthesia/
24. ((epidural or peridural or extradural) and (anesthesia or analgesia or block*)).mp.
25. (1 or 2 or 3) and (23 or 24) [PICO 6]
26. exp puerperium/
27. (puerperium or postpartum period).mp.28. (1 or 2 or 3) and (26 or 27) [PICO 7]
29. exp minor surgery/
30. (minor adj4 surg*).mp.
31. exp dental procedure/
32. (dental treatment or dental procedure* or dental surg* or t??th extraction or dental clean* or oral surg*).mp.
33. exp skin surgery/ or dermatological surgical procedure.mp.
34. exp biopsy/ or biopsy.mp.
35. joint aspiration.mp. or exp joint aspiration/
36. circumcision.mp. or exp circumcision/
37. exp eye surgery/
38. (cataract extraction or lens implantation).mp.
39. colposcopy.mp. or exp colposcopy/
40. exp intrauterine contraceptive device/
41. intrauterine device plac*.mp.
42. endoscopy.mp. or exp endoscopy/
43. or/29-42
44. (1 or 2) and 43 [PICO 8]
45. 9 or 13 or 17 or 20 or 22 or 25 or 28 or 44

46. random*.ab. or random*.ti. or (clinical adj trial*).hw,ab,ti. or exp 'health care quality'/ [RCT filter]
47. exp disease course/ or risk:.mp. or diagnos:.mp. or follow-up.mp. or ep.fs. or outcome.tw. [OS filter]
48. 46 or 47
49. 45 and 48
50. limit 49 to human
2. Values and preferences

OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to September 2019

1. exp "Patient Acceptance of Health Care"/
2. exp Patient Preference/
3. exp Patient Satisfaction/
4. exp Physician-Patient Relations/
5. exp Health Knowledge, Attitudes, Practice/6. "Attitude of Health Personnel"/
7. exp Practice Patterns, Physicians'/ or clinical practice/
8. accept*.mp.
9. prefer*.mp.
10. attitude*.mp.
11. feeling*.mp.
12. thought*.mp.
13. perception*.mp.
14. perspective*.mp.
15. valu*.mp.
16. knowledge*.mp.
17. view*.mp.
18. deci*.mp.
19. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20. exp Health Behavior/
21. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 19 or 20
22. exp von Willebrand Diseases/ or (von willebrand or VWD).mp.
23. 21 and 22

EMBASE (OVID) 1974 to 2019 September 19

1. preference.mp. or exp patient preference/
2. choice*.ti.
3. value*.ti.
4. health state value*.mp.
5. valuation*.ti.
6. expectation*.mp.

7. attitude*.mp. or exp patient attitude/ or exp attitude to health/
8. acceptab*.mp.
9. knowledge.mp.
10. point of view.mp.
11. user* participation.mp.
12. patient* participation.mp. or exp patient participation/ or exp patient satisfaction/13. patient* perspective.mp.
14. patient* perce*.mp.
15. health perception*.mp.
16. user* view*.mp.
17. patient* view*.mp.
18. (decision* and mak*).ti.
19. decision* mak*.mp.
20. (patient* or user* or men or women or man or woman).mp. and (18 or 19)
21. (discrete-choice* or discrete choice*).mp.
22. decision board*.mp.
23. decision analy*.mp.
24. (decision-support* or decision support*).mp.
25. exp decision support system/
26. decision tool*.mp. or exp medical decision making/ or exp patient decision making/
27. decision aid*.mp.
28. prospect theory.mp.
29. ("preference score " or "preference elicitation").mp.
30. health utilit*.mp.
31. ("utility value*" or "Utility score*" or "Utility estimate*").mp.
32. health state utilit*.mp. or exp health status indicator/
33. (health and utilit*).ti.
34. health state*.mp.
35. feeling thermometer*.mp. or exp visual analog scale/
36. best-worst scaling.mp.
37. standard gamble.mp.
38. time trade-off.mp.
39. TTO.mp.
40. probability trade-off.mp.
41. utility score*.mp.
42. preference based.mp.
43. preference score*.mp.
44. multiattribute.mp.
45. multi attribute.mp.46. EuroQol.mp.
47. EQ5D.mp.
48. EQ 5D.mp.
49. (SF-36 or SF 36).mp.
50. SF 6D.mp.
51. SF6D.mp.

52. SF 12.mp.
53. SF12.mp.
54. 15 D.mp.
55. HUI.mp.
56. Health Utilit* Index.mp.
57. HRQoL.mp.
58. health related quality of life.mp.
59. quality of life.mp. or exp "quality of life"/
60. or/1-17
61. or/20-27
62. or/28-41
63. (or/42-56) or 29
64. (or/49-54) or (or/57-59)
65. or/60-64
66. exp von Willebrand Disease/ or VWD.mp. or (von willebrand adj4 (disease or disorder)).mp.
67. 65 and 66

APA PsycInfo 1806 to September Week 3 2019

1. preference.mp. or exp Preferences/
2. choice*.ti.
3. value*.ti.
4. health state value*.mp.
5. valuation*.ti.
6. expectation*.mp.
7. attitude*.mp. or attitudes/ or exp consumer attitudes/ or exp health attitudes/ or exp "physical illness (attitudes toward)"/ or exp attitude measurement/ or exp attitude measures/ or exp Client Attitudes/
8. acceptab*.mp.9. knowledge.mp.
10. point of view.mp.
11. user* participation.mp.
12. patient* participation.mp. or exp Client Participation/ or exp Client Satisfaction/
13. patient* perspective.mp.
14. patient* perce*.mp.
15. health perception*.mp.
16. user* view*.mp.
17. patient* view*.mp.
18. (decision* and mak*).ti.
19. decision* mak*.mp.
20. (patient* or user* or men or women or man or woman).mp. and (18 or 19)
21. (discrete-choice* or discrete choice*).mp.
22. decision board*.mp.
23. decision analy*.mp.
24. decision-support.mp.

25. decision support*.mp. or exp Decision Support Systems/
 26. decision tool*.mp. or exp Decision Making/
 27. decision aid*.mp.
 28. prospect theory.mp.
 29. ("preference score " or "preference elicitation").mp.
 30. health utilit*.mp.
 31. ("utility value*" or "Utility score*" or "Utility estimate*").mp.
 32. health state utilit*.mp. or exp psychometrics/ or exp Utility Theory/
 33. (health and utilit*).ti.
 34. health state*.mp.
 35. feeling thermometer*.mp. or exp Rating Scales/
 36. best-worst scaling.mp.
 37. standard gamble.mp.
 38. time trade-off.mp.
 39. TTO.mp.
 40. probability trade-off.mp.
 41. utility score*.mp.
 42. preference based.mp.
 43. preference score*.mp.
 44. multiattribute.mp.
 45. multi attribute.mp.
 46. EuroQol.mp.
 47. EQ5D.mp.
 48. EQ 5D.mp.
 49. (SF-36 or SF 36).mp.
 50. SF 6D.mp.
 51. SF6D.mp.
 52. SF 12.mp.
 53. SF12.mp.
 54. 15 D.mp.
 55. HUI.mp.
 56. Health Utilit* Index.mp.
 57. HRQoL.mp.
 58. health related quality of life.mp.
 59. quality of life.mp. or exp "quality of life"/
 60. or/1-17
 61. or/20-27
 62. or/28-41
 63. (or/42-56) or 29
 64. (or/49-54) or (or/57-59)
 65. or/60-64
 66. (VWD or "von willebrand" or "vonwillebrand").mp.
 67. 65 and 66
3. Other Evidence to Decision factors

**OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid
MEDLINE(R) Daily and Ovid
MEDLINE(R) 1946 to November 2019**

1. exp "Patient Acceptance of Health Care"/2. exp Patient Preference/
3. exp Patient Satisfaction/
4. exp Physician-Patient Relations/
5. exp Health Knowledge, Attitudes, Practice/
6. "Attitude of Health Personnel"/
7. exp Practice Patterns, Physicians'/ or clinical practice/
8. accept*.mp.
9. prefer*.mp.
10. attitude*.mp.
11. feeling*.mp.
12. thought*.mp.
13. perception*.mp.
14. perspective*.mp.
15. valu*.mp.
16. knowledge*.mp.
17. view*.mp.
18. deci*.mp.
19. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20. exp Health Behavior/
21. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 19 or 20
22. feasib*.tw.
23. sustain*.tw.
24. access*.tw.
25. viab*.tw.
26. constrain*.tw.
27. barrier*.tw.
28. facilitat*.tw.
29. exp Health Knowledge, Attitudes, Practice/
30. Interprofessional Relations/ or public relations/
31. implement*.mp.
32. (program* and evaluat*).mp.
33. 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32
34. (exp Gender Identity/ or exp Gender/) and Sex/35. (gender-based or gender related or gender factors).tw.
36. ((sex or gender) adj3 (analysis or factor\$ or inequit\$ or disparit\$ or inequalit\$ or difference\$ or interact\$)).tw.
37. exp Sex Factors/
38. exp Geriatrics/
39. ((ethnic\$ or race or racial or religio\$ or cultur\$ or minorit\$ or refugee or indigenous or aboriginal or African american) adj3 (analysis or

- disparit\$ or inequalit\$ or inequit\$ or difference\$ or predict\$ or interact\$)).tw.
40. exp Homosexuality/ or exp Sexual Orientation/
41. exp Disabled Persons/
42. ((poverty or low-income or "lower income" or socioeconomic\$ or socio-economic\$ or social) adj3 (analysis or disadvantage\$ or factor\$ or inequalit\$ or depriv\$ or inequit\$ or disparit\$ or difference\$ or predict\$ or interact\$)).tw.
43. exp Educational Status/
44. exp Socioeconomic Factors/
45. ((discriminat\$ or social exclu\$ or social inclu\$) adj3 (religion or culture or race or racial or aboriginal or indigenous or ethnic\$)).tw.
46. ((urban or rural or inner-city or remote or slum) adj3 (analysis or inequit\$ or disparit\$ or inequalit\$ or difference\$ or predict\$ or interact\$)).tw.
47. ((resource-poor or ("low income" adj countr\$) or ("middle income" adj countr\$) or africa or developing countr\$ or "south america" or china or asia or "latin america") adj3 (relevance or analysis or applicab\$ or inequit\$ or disparit\$ or inequalit\$ or difference\$ or predict\$ or interact\$)).tw.
48. (inequalit\$ or in-equalit\$ or equit\$ or inequit\$ or in-equit\$ or disparit\$ or underserved or marginali\$ed).tw.
49. exp Population Groups/
50. ((native* or Indian or aborigin*) adj3 (American* or Canadian* or Alaska*)).tw.
51. (first adj2 nation*).tw.
52. (aborigin\$ or metis or inuit\$ or eskimo\$ or native or esquimaux or aleut or yuit or inughuit or unanga* or alutiiq or inup#ia* or kalaallit or Inuktitut or Nunavut or nunavik or cree or dene or haida or salish or Mohawk or ojibway or yupik or tribal or arctic).tw.
53. exp american native continental ancestry group/ or oceanic ancestry group/
54. exp Rural Health/
55. 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54
56. 21 or 33 or 55
57. exp von Willebrand Diseases/ or (von willebrand or VWD).mp.
58. 56 and 57

Appendix 2: Characteristics of studies included in the systematic reviews of first line therapy for heavy menstrual bleeding

Comparative studies

Study	Comparison	Study Design	Recruitment	Country	Setting	HMB diagnoses	Others	Bleeding disorder distribution	Interventions	N baseline	Age distribution	PBAC
Kouides, 2009	DDAVP (In) vs TxA	RCT (cross-over)	2001-2006	USA	Hemophilia treatment center, bleeding disorders clinic, gynecology care center	PBAC>100	Patients chose not to use OC because they had not responded well in the past	VWD, 7% Platelet aggregation/ release, 75% Prolonged closure time, 7% Subnormal coagulation factor level, 11%	DDAVP IN, 300ug on day 2 and 3 of MB TxA 1g 4x per day during first 5 days of MB	116	Mean, 36	Median, 224
Amesse, 2005	DDAP (IN) vs OC	Retrospective cohort	1998-2002	USA	Hematology clinic, pediatric-adolescent gynecology clinic	PBAC >100	Explicitly acknowledges that treatment was determined by physician together with patient	VWD, 100% Type 1, 98% Type 2b, 2%	DDAVP IN, 1.5 mg/mL or 150 ug per puff, based on body weight at onset and 2 more days OC, 0.15 mg desogestrel and 30 ug ethinyl estradiol daily	36	Median (range), 16 (9-18)	Mean (SD), 263.2 (171.4)

Case series

Author	Setting	Country	N	Bleeding Disorder	Dx HMB	Length of use	Age	Outcomes	Comments
Lukes, 2008	Tertiary medical center	USA	7	4 with confirmed VWD	Focused history taking	9-28 months	Median (range), 38 (28 to 48)	Duration of MB reduced 6 days (from 9 to 3) Proportion with decrease in duration, 71% Failure of therapy, 29% Anemia, 0 before or after	
Kingman, 2004	Hemophilia center	England	16	13 with VWD, 2 with FXI deficiency, 1 with platelet disorder	Subjective menorrhagia	Up to 9 months	Median (range), 38 (28 to 48)	PBAC range before, 98 to 386; after, 0 to 75, reporting that periods were much better, 100% Hemoglobin < 11 g/dL, 2 before, 0 after Periods affecting life, 0 Side effects, 0	Does not meet eligibility because they failed previous treatment
Chi, 2011	Hemophilia Center and thrombosis unit	England	26	50% with VWD, 23% platelet disorder, 23% carrier of hemophilia, 4% FVII deficiency	NR	<12 months	Median (range) 41 (18 to 53)	PBAC score range (median) decreased from 255 (134 to 683) to 35 (0-89) Hb median (range), 11.2 g/dL (9.7 to 13) before and 13.2 (11.2-14.3) after QoL outcomes reported too	Does not meet eligibility, 85% had received previous tmt that did not work
Rimmer, 2013	Bleeding disorder clinic	Canada	20	60% with VWD, 20% hemophilia carriers, 15% platelet function defect, 5% combined VWD and HC	NR	NR	Median (range), 10 (9-13)	3 expulsions and 2 malpositions 6 women for Hgb change	Inserted because of preference or failure of other therapies
Adeyemi-Fowode, 2017	NR	USA	13	VWD and low VWF	NR	NR	Median (range) 10 (9-13)	Mean (SD) time to improvement 94 (69) days Amenorrhea or occasional spotting, 61% Increase in Hgb	May not meet eligibility criteria owing to population, also 100% tried other treatments with no success

Appendix 3: Effects of levonorgestrel-releasing intrauterine system

Hormonal therapy with Mirena compared to other options for women with VWD with HMB

Patient or population: women with VWD with HMB

Intervention: hormonal therapy with Mirena

Comparison: other options

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)
Control of heavy menstrual bleeding assessed with: PBAC score	In one study with 16 women, the PBAC score changed from a range of 98 to 386 before the intervention, to 0 to 75 after the intervention. A second study with 26 women reported that the median (range) PBAC changed from 255 (134 to 683) before the intervention to 35 (0 to 89) after the intervention.	42 (2 observational studies) ^{1 2}	⊕○○○ VERY LOW ^{a,b}
Health-related quality of life assessed with: Kadir questionnaire	In one study with 26 women, the median (range) QOL scores increased from 26 (13 to 48) to 52 (39 to 59)	26 (1 observational study) ¹	⊕○○○ VERY LOW ^a
Anemia assessed with: number of women	in 1 study with 7 women, the proportion with anemia before or after the intervention was 0	7 (1 observational study) ³	⊕○○○ VERY LOW ^{a,b}
Hemoglobin assessed with: g/dL	There were 4 studies that reported this outcome, but the results were presented in a way that did not allow pooling. Overall Mirena resulted in an improvement of hemoglobin. - In 1 study with 16 patients, 12.5% had hemoglobin <11g/dL before the intervention, and 0 after - In 1 study with 26 patients, Hb median (range) was 11.2 g/dL (9.7 to 13) before the intervention and 13.2g/dL (11.2- 14.3) after the intervention - In 1 study with 6 women, mean Hb was 12.2 g/dL before the intervention and 13 g/dL after the intervention - In 1 study with 13 women, mean (range) Hb level was 11.1 g/dL (3 to 15.9) before the intervention and 13.4 g/dL (12 to 14.8) after the intervention	61 (4 observational studies) ^{1 2 4 5}	⊕○○○ VERY LOW ^a
Menstruation duration assessed with: several definitions	- Duration of menstrual bleeding reduced from 9 to 3 days (1 study, 7 patients) - Proportion of women in whom duration decreased, 71% (1 study, 7 women) - Reporting of periods "much better", 100% (1 study, 16 patients)	23 (2 observational studies) ^{2 3}	⊕○○○ VERY LOW ^{a,b}
Complications assessed with: Expulsions and malpositions	The proportion of women with expulsions was 15 % (3/20), and the proportion of women with malposition was 10% (2/10)	20 (1 observational study) ⁵	⊕○○○ VERY LOW ^{a,b}
Absence from school, work, or other required activities assessed with: periods affecting life	In one study with 16 women, the proportion whose life was affected by the periods was 0. There was no data about the proportion before the intervention was administered	16 (1 observational study) ²	⊕○○○ VERY LOW ^{a,b,c}
Adverse effects assessed with: not defined	In 1 study with 16 women, the proportion who experienced side effects was 0	16 (1 observational study) ²	⊕○○○ VERY LOW ^{a,b}
Major bleeding - not reported	-	-	-
Need for surgery - not reported	-	-	-

Hormonal therapy with Mirena compared to other options for women with VWD with HMB

Patient or population: women with VWD with HMB

Intervention: hormonal therapy with Mirena

Comparison: other options

Outcomes	Impact	No of participants (studies)	Certainty of the evidence (GRADE)
Need for multiple treatments - not reported		-	-
Transfusions - not reported		-	-

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

- a. These are case series, there is no comparison with the other options
- b. Overall sample size is small
- c. There is no comparison with a period without the intervention

Appendix 4: Characteristics of case series included in SR on von Willebrand factor levels in women with von Willebrand disease receiving neuraxial anesthesia

Study	Design	Country	Recruitment period	N	Bleeding disorder distribution
Duggan 2017	Retrospective case series	NR	2006-2016	10	Haemophilia carriers
Kadir 1997	Case series	England	1985-1995	6	Haemophilia carriers
Kadir 1998	Retrospective case series	England	1980-1996	10 (8 with VWD and 2 With FXI deficiency)	VWD and factor XI deficiency)
Chi 2008	Retrospective case series	England	1995-2005	25	Haemophilia carriers
Chi 2009	Retrospective case series	England	2000-2005	37 women, 41 pregnancies	Not reported for epidural, but of total sample 24% VWD, 25% hamophilia carriers, 30% factor XI deficiency

Appendix 5: Characteristics of studies comparing tranexamic acid to no treatment in women with VWD in the postpartum period.

Study	Design	Country	Recruitment period	N	Bleeding disorder distribution	TxA Regimen
Govorov 2016	Retrospective cohort	Sweden	1995-2012	34 women, 59 deliveries	Type 1, 62%; type 2, 26%; type 3, 9%; unknown rest	Median (range) duration, 10 days (2 days to 14 days)
Hawke 2016	Retrospective cohort	Canada	2002-2015	33 women, 62 pregnancies	Type 1 VWD, 39 (63%); type 2 VWD, 7 (11.5%); type 3 VWD, 1 (1.5%); hemophilia A carriers, 11 (18%); based on deliveries	Median (range) duration, 3 weeks (5 days to 6 weeks)

1. Chi C, Huq FY, Kadir RA. Levonorgestrel-releasing intrauterine system for the management of heavy menstrual bleeding in women with inherited bleeding disorders: long-term follow-up. *Contraception* 2011;83(3):242-7. doi: 10.1016/j.contraception.2010.07.010 [published Online First: 2011/02/12]
2. Kingman CE, Kadir RA, Lee CA, et al. The use of levonorgestrel-releasing intrauterine system for treatment of menorrhagia in women with inherited bleeding disorders. *BJOG* 2004;111(12):1425-8. doi: 10.1111/j.1471-0528.2004.00305.x [published Online First: 2005/01/25]
3. Lukes AS, Reardon B, Arepally G. Use of the levonorgestrel-releasing intrauterine system in women with hemostatic disorders. *Fertil Steril* 2008;90(3):673-7. doi: 10.1016/j.fertnstert.2007.07.1315 [published Online First: 2007/11/16]
4. Adeyemi-Fowode OA, Santos XM, Dietrich JE, et al. Levonorgestrel-Releasing Intrauterine Device Use in Female Adolescents with Heavy Menstrual Bleeding and Bleeding Disorders: Single Institution Review. *J Pediatr Adolesc Gynecol* 2017;30(4):479-83. doi: 10.1016/j.jpag.2016.04.001 [published Online First: 2016/04/25]
5. Rimmer E, Jamieson MA, James P. Malposition and expulsion of the levonorgestrel intrauterine system among women with inherited bleeding disorders. *Haemophilia* 2013;19(6):933-8. doi: 10.1111/hae.12184 [published Online First: 2013/05/29]