wish to conceive (conditional recommendation based on very low certainty in the evidence ⊕◯◯◯).

Remarks:

- This recommendation does not imply that the interventions considered can be prescribed only as monotherapy. In some cases, multiple options can be combined, especially if control of heavy menstrual bleeding is less than optimal with the initial therapy.
- Desmopressin is not effective in type 3 and many type 2 VWD patients and is contraindicated in type 2B VWD.
- Women may require additional treatment directed at bleeding symptoms for the first several menstrual cycles after placement of a levonorgestrel-releasing intrauterine system.

Good practice statements: When feasible, the panel encourages the development of multidisciplinary clinics in which gynecologists and hematologists see patients jointly to facilitate the management of heavy menstrual bleeding for patients with bleeding disorders.

Decisions regarding the use of a levonorgestrel-releasing intrauterine system should be made in the setting of shared decision making with multidisciplinary input (eg, gynecology professionals, hematology professionals, and patients).

For some patients, there may be other benefits with use of hormonal therapy, such as treatment of menstrual pain and management of endometriosis- and polycystic ovary syndrome–related symptoms.

Both iron deficiency and anemia resulting from iron deficiency are associated with adverse outcomes, including diminished health-related quality of life. Patients with heavy menstrual bleeding should be regularly assessed and treated for iron deficiency and/or anemia.

Women with known bleeding disorders and heavy menstrual bleeding should undergo a standard gynecologic assessment that is recommended for women with heavy menstrual bleeding in the general population to rule out common pelvic pathologies, such as fibroids and polyps, especially those not responding to first-line treatment.

Special consideration is required in terms of adverse effects of therapy for those who are at high risk of endometrial hyperplasia/malignancies, such as women age >35 years and those with polycystic ovaries, high body mass index, and comorbidities, such as diabetes and hypertension.

Summary of the evidence. We found 2 comparative studies: 1 randomized clinical trial comparing tranexamic acid with desmopressin[107] and 1 observational study comparing hormonal therapy with desmopressin.[74] In addition, we found 5 case series about a levonorgestrel-releasing intrauterine system.[108-112] We also surveyed panel members to gather data on their experience. The EtD framework for this recommendation is available online at https://guidelines.ash.gradepro.org/profile/2xCXJKkZZBI. This discussion centers on first-line treatment of heavy menstrual bleeding.

Benefits, harms, and burden. There were no comparative data for evaluating tranexamic acid vs hormonal therapy. A comparison of tranexamic acid and desmopressin showed that the mean difference in menstrual blood loss as measured by PBAC was 41.6 points higher with desmopressin than with tranexamic acid (19.6 vs 63.6).[107] Quality of life, as assessed through several instruments, was not explicitly compared between the groups. Although both quality-of-life domain and instrument scores went up with both interventions, this was not statistically significant. Comparative adverse effects were not estimable between tranexamic acid and desmopressin.

There was no difference between desmopressin and hormonal therapy as assessed by alleviation of symptoms (RR, 0.90; 95% CI, 0.66-1.23).[74] Menstrual flow as assessed by PBAC was 0.9 points higher in the desmopressin group than in the hormonal therapy group (95% CI, 9.89 lower to 11.69 higher). There were no adverse events reported.

Noncomparative data regarding a levonorgestrel-releasing intrauterine system suggested control of heavy menstrual bleeding as assessed by PBAC score, improved health-related quality of life, improvement in hemoglobin values, and shortened duration of menstruation.[110,111] The expulsion rate for a levonorgestrel-releasing intrauterine system was 15%, and the malposition rate was 10%.

Overall, the certainty of these estimated effects is very low because of risk of bias and indirect comparisons in the studies and imprecision of the estimates (evidence profile provided in supplemental Data 5).

Other EtD criteria and considerations. In a survey of panel members before the meeting, responses varied as to whether women with heavy menstrual bleeding would find all treatment options acceptable. Personal values and beliefs regarding hormonal therapy may make these more or less acceptable to some women. Adverse effects of desmopressin would lower its acceptability. The panel also discussed how early experiences with and potential adverse effects of hormonal contraception may affect acceptability. Quality of life may be most improved with hormonal contraception or a levonorgestrel-releasing intrauterine system. Many physicians are familiar with oral contraceptive pills and tranexamic acid but may be less familiar with a levonorgestrel-releasing intrauterine system. The panel discussed the possibility that the acceptability of tranexamic acid would be the greatest because it has the fewest adverse effects among the treatment options. However, in patients who bleed for a prolonged number of days or who have irregular bleeding, tranexamic acid may not be as desirable. In transgender patients, specific hormonal therapies may be less acceptable or contraindicated as part of their gender-affirming therapy plan. The potential for spotting with the etonogestrel implant, particularly in the setting of an underlying bleeding disorder, limited enthusiasm for this option. Specific recommendations regarding use of VWF concentrate for prophylaxis are addressed in "Prophylaxis."

Conclusions and research needs for these recommendations. The guideline panel determined that there is very low certainty in the evidence for a net health benefit of using either hormonal therapy (CHCs or levonorgestrel-releasing intrauterine system) or tranexamic acid to reduce heavy menstrual bleeding in women with VWD. Based on the body of available evidence, it is likely that either hormonal therapy (CHC or levonorgestrel-releasing intrauterine system) or tranexamic acid improves health-related quality of life, hemoglobin levels, menstruation duration, and absence from school, work, or other required activities. However, because of