have major bleeding (2.7% vs 0%), serious adverse events in the mother (2.7% vs 0%), and postpartum hemorrhage (17% vs 5.9%) and to receive transfusion (10% vs 0%). There were no spinal hematomas, maternal deaths, or adverse events in the child reported in either group. Although the survey of guideline panelists' experience suggested better outcomes with a higher target VWF level, the panel did not feel it was substantial enough to justify recommending the higher target, given the lack of adequate published evidence available to make judgments about how the desirable effects and harms of the options compare (evidence profile provided in supplemental Data 5).

***Other EtD criteria and considerations.*** The panel judged that there is possibly important uncertainty or variability in patient values and preferences, with some individuals placing a high value on avoiding bleeding and others a higher value on avoiding thrombotic complications. The panel also discussed the fact that values may vary in patients with more significant bleeding phenotypes and certain VWD subtypes, particularly types 2 and 3. Targeting a higher level would increase costs of therapy and result in potential delays if a specific VWF level were required before the procedure.

***Conclusions and research needs for this recommendation.*** The guideline panel determined that there is very low certainty in the evidence for a net health benefit for targeting VWF levels of 0.50 to 1.50 IU/mL in women with VWD for whom neuraxial anesthesia is deemed suitable during labor. Based on the body of available evidence, there is very low certainty that there is an effect of targeting VWF levels of 0.50 to 1.50 IU/mL on outcomes, such as major bleeding and spinal hematoma. However, because of low certainty in the evidence or no published information about other outcomes, the fact that we did not find evidence of an effect on these outcomes does not imply that such an effect does not exist.

Given that there is no evidence to support a judgment on how the options compare with regard to their effects on epidural health outcomes, the recommendation for targeting VWF levels of 0.50 to 1.50 IU/mL over targeting a level of >1.50 IU/mL in women with VWD in labor who require or desire epidural treatment places a high value on increasing health equity and the lower cost of targeting levels of 0.50 to 1.50 IU/mL. Recent research suggests that targeting higher VWF levels may be beneficial in preventing PPH.[118] Moreover, although higher factor levels may reduce PPH, some indirect data suggest correlation between the presence of an epidural itself and higher risk of PPH. Women who have neuraxial anesthesia are more likely to have a longer second stage of labor, increased need for oxytocin, and higher rate of instrumental deliveries. There may be a larger potential risk of thrombosis when VWF levels are >1.50 IU/mL than when they are 0.50 to 1.50 IU/mL.

The panel identified the following additional research needs: (1) studies evaluating whether patients with type 2 or 3 VWD completely correct defects in hemostasis and whether there are differences in this correction between plasma-derived and recombinant VWF replacement therapies; (2) studies to determine the role of platelet-derived VWF in hemostasis during pregnancy, particularly in the settings of labor, delivery, and postpartum hemorrhage; (3) development and evaluation of clinical testing to ensure adequate primary hemostasis and determine whether therapy can be guided by these tests to improve outcomes; and (4) studies to directly compare delivery and neurologic outcomes in women with VWD who are treated to achieve different target VWF and FVIII levels, specifically evaluating the difference between a target level of ≥0.50 IU/mL and a target level of ≥1.50 IU/mL.

## Obstetrics: postpartum management

*In women with VWD, should tranexamic acid be prescribed (or not) during the postpartum period?*

**Recommendation 8**

The guideline panel *suggests* the use of tranexamic acid over not using it in women with type 1 VWD or low VWF levels (and this may also apply to types 2 and 3 VWD) during the postpartum period) (conditional recommendation based on low certainty in the evidence of effects ⊕⊕◯◯).

**Good practice statements:** Tranexamic acid may be given systemically via the oral or IV route. The oral dose is 25 mg/kg (typically 1000-1300 mg) 3 times per day for 10 to 14 days or longer if blood loss remains heavy.

Patients who intend to breastfeed should be provided education about the safety of tranexamic acid during breastfeeding in conjunction with its benefits in reducing bleeding.

***Summary of the evidence.*** We found 2 studies that addressed this question, both retrospective cohorts.[118,119] Outcomes evaluated included vaginal hematoma, thrombotic complications, and blood loss. No studies evaluated the risk of major bleeding, need for other medical procedures, or mortality. The EtD framework for this recommendation is available online at https://guidelines.ash.gradepro.org/profile/Z0HQ-0k8FJE.

***Benefits, harms, and burden.*** Tranexamic acid reduced the risk of secondary postpartum hemorrhage (RR, 0.42; 95% CI, 0.20-0.91). Tranexamic acid may also reduce the risk of primary postpartum hemorrhage (RR, 0.25; 95% CI, 0.04-1.75), severe primary postpartum hemorrhage (RR, 0.36; 95% CI, 0.05-2.59), need for blood transfusion (RR, 0.24; 95% CI, 0.01-4.23), and vaginal hematoma (RR, 0.34; 95% CI, 0.02-6.39), but the estimates were imprecise, and CIs did not exclude the absence of an effect. Adverse events in the mother, such as thrombosis, were not estimable; however, given the available evidence, the guideline panel considered the risk of adverse effects to be most likely small.

Overall, the certainty of these estimated effects is very low because of risk of bias and inconsistency in the studies' findings 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, all of them said they believed tranexamic acid is a treatment that patients would accept. It was judged that no important uncertainty existed around values. They noted that some women, however, may be concerned about potential adverse effects of tranexamic acid while breastfeeding as a major threat to acceptability and that patients need to be reassured that tranexamic acid is safe in this situation.[120,121]

***Conclusions and research needs for this recommendation.*** The guideline panel determined that there is low certainty in the evidence for a net health benefit from using tranexamic acid. Based on the body of available evidence, it is likely that tranexamic acid reduces the risk of developing secondary postpartum hemorrhage