local availability. With the exception of venous vasodilators (such as nitrates), no safety concerns have been noted for these antihypertensives.[85] The calcium channel antagonist clevidipine, with a half-life of 1.5 min, may be particularly effective in BP control.[86] A novel strategy for BP lowering will address multiple factors by integrating analgesia, sedation and anti-sympathetic effects.[87]

For blood pressure reduction as part of care bundle treatment, please refer to Section 'Care bundles.'

Given the uncertainties about the effects of blood pressure reduction on our chosen clinical outcomes overall and in sub-groups, and in patients with haematomas >30 mL, further research is warranted. The ICH ADAPT II trial was published after the completion of this guideline.[88] The ongoing CLUTCH (NCT06402968) is comparing the effect of the short-acting clevidipine vs. standard antihypertensive therapy on SBP target with stability, which is defined as achieving a SBP of less than 150 mm Hg, but greater than 130 mm Hg, plus two subsequent consecutive recordings, taken at least 15 minutes apart, remaining within that 130-150 mm Hg range. Other ongoing trials are TIME-ICH (NCT06760078), looking at the efficacy of TXA vs. placebo both groups including plus intensive blood pressure. and the observational study of Efficacy and Safety Study of Urapidil Alone or With Esmolol in Treating Acute Hypertensive Intracerebral Hemorrhage (NCT06635707).

Haemostatic therapies

Haematoma expansion is associated with worse functional outcome and death.[89–94] Haemostatic therapies aim to reduce the risk of haematoma expansion after acute ICH. The type and effects of haemostatic therapy may vary in studies that include ICH not associated with antithrombotic therapy, ICH associated with antiplatelet therapy, and ICH associated with anticoagulation.[72] Clotting factors and antifibrinolytics have been used to treat acute spontaneous ICH. Platelet concentrates, and desmopressin have been used for ICH associated with antiplatelet therapy. For ICH associated with vitamin K-antagonists (VKAs), prothrombin complex concentrate (PCC) or fresh frozen plasma (FFP) have been used. Andexanet alfa has been used for ICH associated with factor Xa inhibitors, while idarucizumab has been used for ICH associated with the direct thrombin inhibitor dabigatran.

Analysis of current evidence

The literature search was based on the Cochrane systematic review, which included a literature search from 1949 to September 2022.[95] The literature search for this guideline was updated from September 2022 to 31 May 2024 and identified four additional RCTs,[96–99] resulting in the inclusion of 23 RCTs with 5495 participants (Supplement for PICO 3: description of single studies). The systematic search included RCTs of any haemostatic intervention (i.e. procoagulant treatments such as clotting factor concentrates, antifibrinolytic drugs, platelet transfusion or agents to reverse the action of antithrombotic drugs) compared with placebo, open control or an active comparator for acute spontaneous ICH. A description of the RCTs is provided in the Supplement. The guideline group graded the following outcomes to be critical or important for haemostatic therapies: death, death or dependence (modified Rankin Scale (mRS) 4–6) by day 90, haematoma expansion at 24 h, and thromboembolic adverse events. Most of our recommendations differ from those in the ESO Guideline on Reversal of Oral Anticoagulants in Acute Intracerebral Haemorrhage published in 2019.[94] This is mainly due to a shift in the evaluation of the benefits versus risks of treatments, with thromboembolic adverse events specifically identified as a critical outcome.

Spontaneous ICH not associated with antithrombotic drug use

rFVIIa

PICO 3.1.1 **In adults with spontaneous ICH not associated with antithrombotic drug use, does haemostatic therapy using rFVIIa versus placebo or open control reduce death or dependence, death or haematoma expansion and not increase thromboembolic adverse events?**

Evidence-based Recommendation
For adults with spontaneous ICH not associated with antithrombotic drug use, there is uncertainty about the balance of beneficial and adverse effects of rFVIIa, so we suggest against its routine use and suggest recruitment to ongoing randomised controlled trials.
Quality of evidence: Very Low ⊕
Strength of recommendation: Weak against intervention ↓?

Analysis of current evidence

Nine RCTs (1549 participants) compared rFVIIa versus placebo or open control,[90,100–106] which are described in the Supplement (Supplement for PICO 3: description of single studies). The quality of evidence is low due to heterogeneity and risk of bias (Supplement for PICO 3 GRADE evidence profile rFVIIa).

For the efficacy outcomes of death, death or dependence at 90 days and haematoma expansion, there are no statistically significant differences between rFVIIa and placebo/open control, but the direction of the effect favours rFVIIa on **death or dependence by day 90** (OR 0.71, 95% CI 0.46–1.11; 8 RCTs, 1454 participants; I^2 = 46%; Figure 8), on **death from any cause by day 90** (OR 0.69, 95% CI 0.43–1.11; 9 RCTs, 1544 participants; I^2 = 39%; Figure 9) and on **haematoma expansion at 24 h** (OR 0.65, 95% CI 0.27–1.56; 5 RCTs, 220 participants; very low-quality evidence; Figure 10).