

# Devilish Definitions: Bleeding, Procedural Outcomes and Other Key Endpoints/Variables

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# Key Issues

- Differences in bleeding definitions
  - can skew safety results and alter study conclusions
  - complicate collection of optimal event narratives
  - make cross study comparisons problematic
- Bleeding definitions do not adequately capture clinical context/gravity
  - E.g., Hct drop of 2 units has very different implications when it occurs in frail elderly patient compared to young otherwise healthy pt
  - peri-procedural bleeds vs those associated w anti-thrombotic therapy
- How best to weigh and quantify bleeding “cost” versus efficacy “benefit”
  - Varying clinical significance of bleed complicates weighting
  - In SPAF, efficacy and safety outcomes both include bleeding events
- How to best predict risk
  - Risk of mortality – bleeding?
  - Risk of ischemic events – non-compliance?
  - Risk of bleeding – vulnerable subgroups...

# What currently works well

- Aspects of current standardized bleeding definitions (e.g. ISTH)
  - Simple, user-friendly
  - Cover clinically important events, both hospital-based, as well as more subjective events
  - Acknowledge differences in populations, such as surgical and non-surgical patients
  - Standardized collection and reporting of bleeding-related data

# Highest priority problems

- Need to universalize and optimize bleeding definitions and guidance
  - Compare agents with a common metric
  - Criteria defined a priori facilitate collection of best info during study to make most accurate classification
  - EMEA has guidance on bleeding but FDA does not
  - Refined bleeding definitions ideally would increase sensitivity without introducing excess noise
  - Incorporate best current understanding of prognostic significance in weighting of bleeding events
  - Challenging to capture nuance while preserving practicality and simplicity of use
- Better understanding of bleeding or mortality risk, esp. in vulnerable subgroups
  - One size does not fit all with anti-thrombotics