### Supporting Information 5: Primary definition of bleeding used in different studies

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| **Study/Acronym** | **Definition** |
| TIMI | Major bleeding was defined according to the Thrombolysis In Myocardial Infarction **(TIMI)** criteria:   * Any intracranial bleeding (excluding microhemorrhages <10 mm evident only on gradient-echo MRI) * Clinically overt signs of hemorrhage associated with a drop in hemoglobin of > 5 g/dL * Fatal bleeding (bleeding that directly results in death within 7 days) |
| ACUITY | The protocol definition of major bleeding was defined as :   * Intracranial or intraocular hemorrhage * Access-site hemorrhage requiring intervention * > 5-cm hematoma * Retroperitoneal * Reduction in hemoglobin concentration of > 4 g/dL without an overt source of bleeding * Reduction in hemoglobin concentration of > 3 g/dL with an overt source of bleeding * Reoperation for bleeding * Use of any blood product transfusion |
| REPLACE-2 2003 | Major bleeding was defined as:   * Intracranial, intraocular, or retroperitoneal * Overt blood loss with hemoglobin decrease > 3 g/dl * Any hemoglobin decrease > 4 g/dL * Transfusion of > 2 U blood products |
| BARC | Major bleeding was defined as Type 3–5 according to the Bleeding Academic Research Consortium (BARC) definition |