### 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)
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| 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
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| 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
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| BARC | Major bleeding was defined as Type 3–5 according to the Bleeding Academic Research Consortium (BARC) definition  |