**National Quality Forum—Evidence (subcriterion 1a)**

**Measure Number** (*if previously endorsed*)**:** 2459

**Measure Title**: In-hospital Risk Standardized Bleeding Rate for Patients Undergoing PCI

**IF the measure is a component in a composite performance measure, provide the title of the Composite Measure here:** Click here to enter composite measure #/ title

**Date of Submission**: 11/1/2018

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| **Instructions**  *Complete 1a.1 and 1a.2 for all measures. If instrument-based measure, complete 1a.3.*  *Complete* ***EITHER 1a.2, 1a.3 or 1a.4*** *as applicable for the type of measure and evidence.*  *For composite performance measures:*  *A separate evidence form is required for each component measure unless several components were studied together.*  *If a component measure is submitted as an individual performance measure, attach the evidence form to the individual measure submission.*   * All information needed to demonstrate meeting the evidence subcriterion (1a) must be in this form. An appendix of *supplemental* materials may be submitted, but there is no guarantee it will be reviewed. * If you are unable to check a box, please highlight or shade the box for your response. * Contact NQF staff regarding questions. Check for resources at [Submitting Standards webpage](http://www.qualityforum.org/Measuring_Performance/Submitting_Standards.aspx). |

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| **Note: The information provided in this form is intended to aid the Standing Committee and other stakeholders in understanding to what degree the evidence for this measure meets NQF’s evaluation criteria.**   1a. Evidence to Support the Measure Focus The measure focus is evidence-based, demonstrated as follows:   * Outcome: [**3**](#Note3) Empirical data demonstrate a relationship between the outcome and at least one healthcare structure, process, intervention, or service. If not available, wide variation in performance can be used as evidence, assuming the data are from a robust number of providers and results are not subject to systematic bias. * Intermediate clinical outcome: a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [**4**](#Note4)that the measured intermediate clinical outcome leads to a desired health outcome. * Process: [**5**](#Note5) a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [**4**](#Note4) that the measured process leads to a desired health outcome. * Structure: a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence [**4**](#Note4) that the measured structure leads to a desired health outcome. * Efficiency: [**6**](#Note6) evidence not required for the resource use component. * For measures derived from patient reports, evidence should demonstrate that the target population values the measured outcome, process, or structure and finds it meaningful. * Process measures incorporating Appropriate Use Criteria: See NQF’s guidance for evidence for measures, in general; guidance for measures specifically based on clinical practice guidelines apply as well.   **Notes**  **3.** Generally, rare event outcomes do not provide adequate information for improvement or discrimination; however, serious reportable events that are compared to zero are appropriate outcomes for public reporting and quality improvement.  **4.** The preferred systems for grading the evidence are the Grading of Recommendations, Assessment, Development and Evaluation [(GRADE) guidelines](http://www.gradeworkinggroup.org) and/or modified GRADE.  **5.** Clinical care processes typically include multiple steps: assess → identify problem/potential problem → choose/plan intervention (with patient input) → provide intervention → evaluate impact on health status. If the measure focus is one step in such a multistep process, the step with the strongest evidence for the link to the desired outcome should be selected as the focus of measurement. Note: A measure focused only on collecting PROM data is not a PRO-PM.  **6.** Measures of efficiency combine the concepts of resource use and quality (see NQF’s [Measurement Framework: Evaluating Efficiency Across Episodes of Care](http://www.qualityforum.org/Publications/2010/01/Measurement_Framework__Evaluating_Efficiency_Across_Patient-Focused_Episodes_of_Care.aspx); [AQA Principles of Efficiency Measures](http://www.aqaalliance.org/files/PrinciplesofEfficiencyMeasurementApril2006.doc)). |

**1a.1.This is a measure of**: (*should be consistent with type of measure entered in De.1*)

Outcome

Outcome: Reduction in bleeding events for patients undergoing PCI

Patient-reported outcome (PRO): Click here to name the PRO

*PROs include HRQoL/functional status, symptom/symptom burden, experience with care, health-related behaviors.* (*A PRO-based performance measure is not a survey instrument. Data may be collected using a survey instrument to construct a PRO measure.)*

Intermediate clinical outcome (*e.g., lab value*): Click here to name the intermediate outcome

Process: Click here to name what is being measured

Appropriate use measure: Click here to name what is being measured

Structure: Click here to name the structure

Composite: Click here to name what is being measured

**1a.2** **LOGIC MODEL** Diagram or briefly describe the steps between the healthcare structures and processes (e.g., interventions, or services) and the patient’s health outcome(s). The relationships in the diagram should be easily understood by general, non-technical audiences. Indicate the structure, process or outcome being measured.

CLASS I: All patients should be evaluated for risk of bleeding before PCI. (Level of Evidence: C)

*“*Intra and post - procedural bleeding is recognized as a major risk factor for subsequent mortality . Bleeding may lead to mortality directly (because of the bleeding event) or through ischemic complications that occur when antiplatelet or anticoagulant agents are withdrawn in response to the bleeding. Bleeding may also be a marker of comorbidities associated with worse prognosis (e.g., occult cancer). The risk of bleeding is associated with a number of patient factors (e.g., advanced age, low body mass index, CKD, baseline anemia), as well as the degree of platelet and thrombin inhibition, vascular access site, and sheath size. The overall approach to PCI should be individualized to minimize both ischemic and bleeding risks.”

*Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. J Am Coll Cardiol. 2011;58(24):e44-e122. doi:10.1016/j.jacc.2011.08.007.*

**1a.3** **Value and Meaningfulness:**  **IF** this measure is derived from patient report, provide evidence that the target population values the measured ***outcome, process, or structure*** and finds it meaningful. (Describe how and from whom their input was obtained.)

Among patients enrolled in both randomized trials and various clinical registries, there is an approximate 3- to 10-fold increase in in-hospital and 30-day mortality for bleeding versus no bleeding. One retrospective analysis of incidence, predictors, and prognostic impact of periprocedural bleeding and transfusions involving 10,974 PCI patients from 2003 indicated patients who had major bleeding had higher in-hospital and 1-year mortality compared with patients with minor or no bleeding. Bleeding was identified as an independent predictor of in-hospital death [1].

An evaluation of the trends and factors associated with femoral bleeding after PCI was performed from 1994 – 2005 at the Mayo Clinic. A population of 17,901 patients was studied to determine factors were associated with bleeding. A multivariate analysis determined that sheath size, intensity and duration of anticoagulation with heparin, and procedure time were each independent predictors of complications. Major femoral bleeding and blood transfusion were associated with decreased long-term survival [2].

Chhatriwalla et al. recently determined the post PCI bleeding events were associated with increased risk of in-hospital mortality, with an estimated 12.1% of deaths related to bleeding complications. They retrospectively analyzed patient data from 3,386,688 PCI procedures in our CathPCI Registry performed in the US between 2004 and 2011 [3].

Data from the Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel--Thrombolysis in Myocardial Infarction 38 (TRITON-TIMI 38) was analyzed to identify baseline characteristics that independently predict bleeding and to determine how bleeding events impact the subsequent mortality. The authors determined that major predictors of serious bleeding were a combination of patient and procedural characteristics and antiplatelet therapies. They added that serious bleeding was strongly associated with mortality within the first month after the PCI [4].

Data from the National Heart, Lung, and Blood Institute Dynamic Registry from 2007, suggest that access site complications, especially hematomas requiring transfusions, are a significant predictor of adverse procedural success and patient outcome. This prospective, multi-center, cohort study of consecutive patients undergoing PCI during 3 NHLBI Dynamic Registry recruitment waves (1997-2002) identified that in-hospital mortality and 1-year death rate was 9 and 4.5 times higher respectively in patients experiencing hematomas requiring transfusions compared to those PCI patients without the complication [5].

The REPLACE-2 Trial involving 6,001 patients undergoing PCI, noted 3.2% experienced a major hemorrhage. They determined that a number of baseline and periprocedural factors independently predicted major hemorrhage, including treatment with heparin plus GPI, and in patients undergoing elective or urgent PCI, major hemorrhage was an independent predictor of 1-year mortality [6].

The ACUITY Trial involved 13,819 PCI patients with moderate- and high-risk ACS who were randomized to to heparin (unfractionated or enoxaparin) plus glycoprotein IIb/IIIa inhibition (GPI), bivalirudin plus GPI, or bivalirudin monotherapy (plus provisional GPI). Logistic regression was used to determine predictors of 30-day major bleeding and mortality. Major bleeding was determined to be a powerful independent predictor of 30-day mortality in patients with ACS managed invasively. Several factors independently predict major bleeding, including treatment with heparin plus GPI compared with bivalirudin monotherapy. Knowledge of these findings might be useful to reduce bleeding risk and improve outcomes in ACS [7].

Periprocedural bleeding is recognized to be associated with subsequent mortality and the avoidance of bleeding complications is a critical consideration in performing PCI.

**Utility of risk scores associated with bleeding**

A total of 17,421 patients with acute coronary syndomes were studied in the ACUITY (Acute Catheterization and Urgent Intervention Triage strategY) and the HORIZONS-AMI (Harmonizing Outcomes with RevasculariZatiON and Stents in Acute Myocardial Infarction) trials. In developing a risk score, the data from these two trials were combined to develop a practical risk score to predict the risk and implications of major bleeding. An integer risk score for major bleeding within 30 days was developed from a multivariable logistic regression model. This practical ACUITY/HORIZONS-AMI scoring system with 6 readily available baseline clinical and laboratory variables plus the anticoagulation regimen used, can be used as a rapid and reliable tool to predict the rate of non–CABG-related major bleeding in patients with ACS and its impact on subsequent mortality within 1 year. The tool and the knowledge derived from its use aids in the accurate prognostication of patients with ACS, facilitating appropriate personalized decision-making for the patient at high risk of bleeding and mortality [8].

Baseline clinical and procedural variables from two contemporary, multicenter, randomized PCI trials were used for risk score development (the REPLACE-2 trial, n = 6002) and validation (the REPLACE-1 trial, n = 1056) to predict the incidence of major peri-procedural bleeding after contemporary PCI using the femoral approach. Variables were identified as independent correlates of major bleeding: (age >55 years, female gender, estimated glomerular filtration rate <60 mL/min/1.73 m(2), pre-existing anemia, administration of low-molecular-weight heparin within 48 h pre-PCI, use of glycoprotein IIb/IIIa inhibitors, and intra-aortic balloon pump use). In the development set, the risk of major bleeding varied from 1.0% in patients without risk factors to 5.4% in high-risk patients. The discriminatory power of this risk model was confirmed in the validation data set, cstat = 0.62). [9]

One additional risk model was developed using a development sample of 71, 277 PCI patients and validated with a sample of 17,857. This CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA guidelines) model identifies 8 independent baseline predictors of in-hospital major bleeding among community-treated NSTEMI patients enrolled in this quality Improvement Initiative. The bleeding score quantifies risk for in-hospital major bleeding across all post admission treatments, enhancing baseline risk assessment for the care of patients with NSTEMI diagnoses [10].

[1] Incidence, predictors, and prognostic implications of bleeding and blood transfusion following percutaneous coronary interventions. Kinnaird TD, Stabile E, Mintz GS, Lee CW, Canos DA, Gevorkian N, Pinnow EE, Kent KM, Pichard AD, Satler LF, Weissman NJ, Lindsay J, Fuchs S. Am J Cardiol. 2003;92(8):930.

[2] Major femoral bleeding complications after percutaneous coronary intervention: incidence, predictors, and impact on long-term survival among 17,901 patients treated at the Mayo Clinic from 1994 to 2005. Doyle BJ, Ting HH, Bell MR, Lennon RJ, Mathew V, Singh M, Holmes DR, Rihal CS. JACC Cardiovasc Interv. 2008;1(2):202.

[3] Association between bleeding events and in-hospital mortality after percutaneous coronary intervention. Chhatriwalla AK, Amin AP, Kennedy KF, House JA, Cohen DJ, Rao SV, Messenger JC, Marso SP, National Cardiovascular Data Registry. JAMA. 2013 Mar;309(10):1022-9.

[4] Predictors of bleeding and time dependence of association of bleeding with mortality: insights from the Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel--Thrombolysis in Myocardial Infarction 38 (TRITON-TIMI 38). Hochholzer W, Wiviott SD, Antman EM, Contant CF, Guo J, Giugliano RP, Dalby AJ, Montalescot G, Braunwald E. Circulation. 2011;123(23):2681.

[5] Access site hematoma requiring blood transfusion predicts mortality in patients undergoing percutaneous coronary intervention: data from the National Heart, Lung, and Blood Institute Dynamic Registry. Yatskar L, Selzer F, Feit F, Cohen HA, Jacobs AK, Williams DO, Slater J. Catheter Cardiovasc Interv. 2007;69(7):961.

[6] Predictors and impact of major hemorrhage on mortality following percutaneous coronary intervention from the REPLACE-2 Trial. Feit F., Voeltz M.D., Attubato M.J., et al;. Am J Cardiol. 2007;100:1364-1369.

[7] Impact of major bleeding on 30-day mortality and clinical outcomes in patients with acute coronary syndromes: an analysis from the ACUITY Trial. J Am Coll Ca he purpose of this study was to determine the predictors of major bleeding and the impact of major bleeding on outcomes, including mortality, in acute coronary syndromes (ACS). Manoukian S.V., Feit F., Mehran R., et al. J Am Coll Cardiol*.* 2007; 49:1362-1368.

[8] A risk score to predict bleeding in patients with acute coronary syndromes. Mehran R., Pocock S.J., Nikolsky E., et al; J Am Coll Cardiol. 2010;55:2556-2566.

[9] Development and validation of a prognostic risk score for major bleeding in patients undergoing percutaneous coronary intervention via the femoral approach. Nikolsky E., Mehran R., Dangas G., et al; Eur Heart J. 2007;28:1936-1945.

[10] Subherwal S., Bach R.G., Chen A.Y., et al; Baseline risk of major bleeding in non-ST-segment-elevation myocardial infarction: the CRUSADE (Can Rapid risk stratification of Unstable angina patients Suppress ADverse outcomes with Early implementation of the ACC/AHA Guidelines) Bleeding Score. Circulation. 2009;119:1873-1882.

*Note: For health outcome performance measures, no further information is required; however, you may provide evidence for any of the structures, processes, interventions, or service identified above.*

**\*\*RESPOND TO ONLY ONE SECTION BELOW -EITHER 1a.2, 1a.3 or 1a.4) \*\***

**1a.2** **FOR OUTCOME MEASURES including PATIENT REPORTED OUTCOMES - Provide empirical data demonstrating the relationship between the outcome (or PRO) to at least one healthcare structure, process, intervention, or service.**

Published trials and observational studies have found that specific processes of care, including the use of radial arterial access, mechanical closure devices when femoral access is used, and bivalirudin for anticoagulation, are associated with lower risks of bleeding.

1. Vora, A. N., Peterson, E. D., McCoy, L. A., Garratt, K. N., Kutcher, M. A., Marso, S. P., Roe, M. T., Messenger, J. C.,  & Rao, S. V. (2016).  The impact of bleeding avoidance strategies on hospital-level variation in bleeding rates following percutaneous coronary intervention. Journal of the American College of Cardiology: Cardiovascular Interventions, 9(8), 771-779.
2. Jolly SS, Amlani S, Hamon M, et al. Radial versus femoral access for coronary angiography or intervention and the impact on major bleeding and ischemic events: a systematic review and meta-analysis of randomized trials. Am Heart J2009;157:132-40.

[CrossRef](https://www.bmj.com/lookup/external-ref?access_num=10.1016/j.ahj.2008.08.023&link_type=DOI)[PubMed](https://www.bmj.com/lookup/external-ref?access_num=19081409&link_type=MED&atom=%2Fbmj%2F350%2Fbmj.h1302.atom)[Web of Science](https://www.bmj.com/lookup/external-ref?access_num=000261851700021&link_type=ISI)[Google Scholar](https://www.bmj.com/lookup/google-scholar?link_type=googlescholar&gs_type=article&q_txt=Jolly+SS%2C+Amlani+S%2C+Hamon+M%2C+et+al.+Radial+versus+femoral+access+for+coronary+angiography+or+intervention+and+the+impact+on+major+bleeding+and+ischemic+events%3A+a+systematic+review+and+meta-analysis+of+randomized+trials.+Am+Heart+J2009%3B157%3A132-40.)

1. Kastrati A, Neumann FJ, Mehilli J, et al. Bivalirudin versus unfractionated heparin during percutaneous coronary intervention. N Engl J Med2008;359:688-96.

[CrossRef](https://www.bmj.com/lookup/external-ref?access_num=10.1056/NEJMoa0802944&link_type=DOI)[PubMed](https://www.bmj.com/lookup/external-ref?access_num=18703471&link_type=MED&atom=%2Fbmj%2F350%2Fbmj.h1302.atom)[Web of Science](https://www.bmj.com/lookup/external-ref?access_num=000258397900005&link_type=ISI)[Google Scholar](https://www.bmj.com/lookup/google-scholar?link_type=googlescholar&gs_type=article&q_txt=Kastrati+A%2C+Neumann+FJ%2C+Mehilli+J%2C+et+al.+Bivalirudin+versus+unfractionated+heparin+during+percutaneous+coronary+intervention.+N+Engl+J+Med2008%3B359%3A688-96.)

1. Marso SP, Amin AP, House JA, et al. Association between use of bleeding avoidance strategies and risk of periprocedural bleeding among patients undergoing percutaneous coronary intervention. JAMA2010;303:2156-64.

[CrossRef](https://www.bmj.com/lookup/external-ref?access_num=10.1001/jama.2010.708&link_type=DOI)[PubMed](https://www.bmj.com/lookup/external-ref?access_num=20516416&link_type=MED&atom=%2Fbmj%2F350%2Fbmj.h1302.atom)[Web of Science](https://www.bmj.com/lookup/external-ref?access_num=000278182100024&link_type=ISI)[Google Scholar](https://www.bmj.com/lookup/google-scholar?link_type=googlescholar&gs_type=article&q_txt=Marso+SP%2C+Amin+AP%2C+House+JA%2C+et+al.+Association+between+use+of+bleeding+avoidance+strategies+and+risk+of+periprocedural+bleeding+among+patients+undergoing+percutaneous+coronary+intervention.+JAMA2010%3B303%3A2156-64.)

1. Sanborn TA, Ebrahimi R, Manoukian SV, et al. Impact of femoral vascular closure devices and antithrombotic therapy on access site bleeding in acute coronary syndromes: the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial. Circ Cardiovasc Interv2010;3:57-62.

[Abstract/FREE Full Text](https://www.bmj.com/lookup/ijlink/YTozOntzOjQ6InBhdGgiO3M6MTQ6Ii9sb29rdXAvaWpsaW5rIjtzOjU6InF1ZXJ5IjthOjQ6e3M6ODoibGlua1R5cGUiO3M6NDoiQUJTVCI7czoxMToiam91cm5hbENvZGUiO3M6OToiY2lyY2N2aW50IjtzOjU6InJlc2lkIjtzOjY6IjMvMS81NyI7czo0OiJhdG9tIjtzOjIzOiIvYm1qLzM1MC9ibWouaDEzMDIuYXRvbSI7fXM6ODoiZnJhZ21lbnQiO3M6MDoiIjt9)[Google Scholar](https://www.bmj.com/lookup/google-scholar?link_type=googlescholar&gs_type=article&q_txt=Sanborn+TA%2C+Ebrahimi+R%2C+Manoukian+SV%2C+et+al.+Impact+of+femoral+vascular+closure+devices+and+antithrombotic+therapy+on+access+site+bleeding+in+acute+coronary+syndromes%3A+the+Acute+Catheterization+and+Urgent+Intervention+Triage+Strategy+(ACUITY)+trial.+Circ+Cardiovasc+Interv2010%3B3%3A57-62.)

1. Stone GW, McLaurin BT, Cox DA, et al. Bivalirudin for patients with acute coronary syndromes. N Engl J Med2006;355:2203-16.

[CrossRef](https://www.bmj.com/lookup/external-ref?access_num=10.1056/NEJMoa062437&link_type=DOI)[PubMed](https://www.bmj.com/lookup/external-ref?access_num=17124018&link_type=MED&atom=%2Fbmj%2F350%2Fbmj.h1302.atom)[Web of Science](https://www.bmj.com/lookup/external-ref?access_num=000242170900007&link_type=ISI)[Google Scholar](https://www.bmj.com/lookup/google-scholar?link_type=googlescholar&gs_type=article&q_txt=Stone+GW%2C+McLaurin+BT%2C+Cox+DA%2C+et+al.+Bivalirudin+for+patients+with+acute+coronary+syndromes.+N+Engl+J+Med2006%3B355%3A2203-16.)

1. Stone GW, Witzenbichler B, Guagliumi G, et al. Bivalirudin during primary PCI in acute myocardial infarction. N Engl J Med2008;358:2218-30.

[CrossRef](https://www.bmj.com/lookup/external-ref?access_num=10.1056/NEJMoa0708191&link_type=DOI)[PubMed](https://www.bmj.com/lookup/external-ref?access_num=18499566&link_type=MED&atom=%2Fbmj%2F350%2Fbmj.h1302.atom)[Web of Science](https://www.bmj.com/lookup/external-ref?access_num=000256023600004&link_type=ISI)[Google Scholar](https://www.bmj.com/lookup/google-scholar?link_type=googlescholar&gs_type=article&q_txt=Stone+GW%2C+Witzenbichler+B%2C+Guagliumi+G%2C+et+al.+Bivalirudin+during+primary+PCI+in+acute+myocardial+infarction.+N+Engl+J+Med2008%3B358%3A2218-30.)

**1a.3.****SYSTEMATIC REVIEW(SR) OF THE EVIDENCE (for intermediate outcome, PROCESS, or STRUCTURE PERFORMANCE measures, including those that are instrument-based) If the evidence is not based on a systematic review go to section 1a.4) If you wish to include more than one systematic review, add additional tables.**

**What is the source of the systematic review of the body of evidence that supports the performance measure? A systematic review is a scientific investigation that focuses on a specific question and uses explicit, prespecified scientific methods to identify, select, assess, and summarize the findings of similar but separate studies. It may include a quantitative synthesis (meta-analysis), depending on the available data. (IOM)**

☐ Clinical Practice Guideline recommendation (with evidence review)

☐ US Preventive Services Task Force Recommendation

☐ Other systematic review and grading of the body of evidence (*e.g., Cochrane Collaboration, AHRQ Evidence Practice Center*)

☐ Other

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| **Source of Systematic Review:**   * **Title** * **Author** * **Date** * **Citation, including page number** * **URL** |  |
| Quote the guideline or recommendation verbatim about the process, structure or intermediate outcome being measured. If not a guideline, summarize the conclusions from the SR. |  |
| Grade assigned to the **evidence** associated with the recommendation with the definition of the grade |  |
| Provide all other grades and definitions from the evidence grading system |  |
| Grade assigned to the **recommendation** with definition of the grade |  |
| Provide all other grades and definitions from the recommendation grading system |  |
| Body of evidence:   * Quantity – how many studies? * Quality – what type of studies? |  |
| Estimates of benefit and consistency across studies |  |
| What harms were identified? |  |
| Identify any new studies conducted since the SR. Do the new studies change the conclusions from the SR? |  |

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**1a.4 OTHER SOURCE OF EVIDENCE**

*If source of evidence is NOT from a clinical practice guideline, USPSTF, or systematic review, please describe the evidence on which you are basing the performance measure.*

**1a.4.1** **Briefly SYNTHESIZE the evidence that supports the measure.** A list of references without a summary is not acceptable.

**1a.4.2 What process was used to identify the evidence?**

**1a.4.3.** **Provide the citation(s) for the evidence.**