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

**Measure Title**: Adherence to Antiplatelet Therapy after Stent Implantation

**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**: 12/20/2013

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| **Instructions**  *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.*   * Respond to all questions as instructed with answers immediately following the question. 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. * Maximum of 10 pages (*includes questions/instructions*; minimum font size 11 pt; do not change margins). ***Contact NQF staff if more pages are needed.*** * 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 Steering Committee and other stakeholders in understanding to what degree the evidence for this measure meets NQF’s evaluation criteria.**  **Subcriterion 1a.** **Evidence to Support the Measure Focus**  The measure focus is a health outcome or is evidence-based, demonstrated as follows:   * Health outcome:**[3](#Note3)** a rationale supports the relationship of the health outcome to processes or structures of care. * Intermediate clinical outcome, Process,**[4](#Note4)** or Structure: a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence[**5**](#Note5)that the measure focus leads to a desired health outcome. * Patient experience with care: evidence that the measured aspects of care are those valued by patients and for which the patient is the best and/or only source of information OR that patient experience with care is correlated with desired outcomes. * Efficiency:**[6](#Note6)** evidence for the quality component as noted above.   **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.** 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.  **5.** The preferred systems for grading the evidence are the U.S. Preventive Services Task Force (USPSTF) [grading definitions](http://www.uspreventiveservicestaskforce.org/uspstf/grades.htm) and [methods](http://www.uspreventiveservicestaskforce.org/methods.htm), or Grading of Recommendations, Assessment, Development and Evaluation [(GRADE) guidelines](http://www.gradeworkinggroup.org/publications/index.htm).  **6.** Measures of efficiency combine the concepts of resource use and quality (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**:

Outcome

☐ Health outcome: Click here to name the health outcome

*Health outcome includes patient-reported outcomes (PRO, i.e., HRQoL/functional status, symptom/burden, experience with care, health-related behaviors)*

☐ Intermediate clinical outcome: Click here to name the process

X Process: Adherence to Antiplatelet Therapy

☐ Structure: Click here to name the structure

☐ Other: Click here to name what is being measured

**HEALTH OUTCOME PERFORMANCE MEASURE**  *If not a health outcome, skip to* [*1a.3*](#Section1a3)

**1a.2.** **Briefly state or diagram the linkage between the health outcome (or PRO) and the healthcare structures, processes, interventions, or services that influence it.**

**1a.2.1.** **State the rationale supporting the relationship between the health outcome (or PRO) and at least one healthcare structure, process, intervention, or service**.

*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.*

**intermediate outcome, PROCESS, or STRUCTURE PERFORMANCE measure**

**1a.3.****Briefly state or diagram the linkages between structure, process, intermediate outcome, and health outcomes**. Include all the steps between the measure focus and the health outcome.

The measure focus is on adherence to antiplatelet in patients following the implantation of a coronary artery drug eluting stent (DES) or a bare-metal stent (BMS). The desired outcome for this measure is better adherence to antiplatelet therapy, defined as proportion of days covered of 0.8 or higher, following the implantation of a stent. Better adherence should result in fewer stent thrombosis events and other adverse cardiovascular events and thus, fewer hospitalizations, lower costs, and fewer deaths.

Links of Process 🡪 Health Outcomes

Improved communication with and education of patient about the benefits of adherence to antiplatelet therapy 🡪

Higher rates of good adherence to antiplatelet therapy following stent implantation 🡪

Fewer stent thrombosis events and other adverse cardiovascular events 🡪

Lower hospitalization rates, lower healthcare costs, and lower mortality rates

**1a.3.1.** **What is the source of the systematic review of the body of evidence that supports the performance measure?**

X Clinical Practice Guideline recommendation – ***complete sections*** [***1a.4***](#Section1a4)***, and*** [***1a.7***](#Section1a7)

☐ US Preventive Services Task Force Recommendation – ***complete sections*** [***1a.5***](#Section1a5) ***and*** [***1a.7***](#Section1a7)

X Other systematic review and grading of the body of evidence (*e.g., Cochrane Collaboration, AHRQ Evidence Practice Center*) – ***complete sections*** [***1a.6***](#Section1a6) ***and*** [***1a.7***](#Section1a7)

X Other – ***complete section*** [***1a.8***](#Section1a8)

*Please complete the sections indicated above for the source of evidence. You may skip the sections that do not apply.*

**1a.4. CLINICAL PRACTICE GUIDELINE RECOMMENDATION**

**1a.4.1.** **Guideline citation** (*including date*) and **URL for guideline** (*if available online*):

Jneid, H., Anderson, J. L., Wright, R. S., Adams, C. D., Bridges, C. R., Casey, Jr, D. E., . . . Zidar, J. P. (2012). 2012 ACCF/AHA focused update of the guideline for the management of patients with unstable angina/non–ST-elevation myocardial infarction (updating the 2007 guideline and replacing the 2011 focused update): A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation, 126*, 875-910. Retrieved September 9, 2013, from <http://circ.ahajournals.org/content/126/7/875>

Levine, G. N., Bates, E. R., Blankenship, J. C., Bailey, S. R., Bittl, J. A., Cercek, B., . . . Ting, H. H. (2011). 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. *Circulation, 124*, e574–e651. Retrieved September 9, 2013, from <http://circ.ahajournals.org/content/124/23/e574>

O'Gara, P., Kushner, F., Ascheim, D., Casey, D., Chung, M., de Lemos, J., . . . Zhao, D. (2013). 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation, 127*, e362-e425. Retrieved September 9, 2013, from <http://circ.ahajournals.org/content/127/4/e362.full>

**1a.4.2.** **Identify guideline recommendation number and/or page number** and **quote verbatim, the specific guideline recommendation**.

Although these guidelines do not address the topic of medication adherence directly, recommendations regarding the use of a medication imply that the patient should take the medication regularly. The need for strict adherence is further documented by two studies described under 1a.8.

The measure is supported primarily by the following recommendation:

* From Levine et al. (2011, p. e605) under *Oral Antiplatelet Therapy: Recommendations, Class I,* it states in relevant part:

The duration of P2Y12 inhibitor therapy after stent implantation should generally be as follows:

a. In patients receiving a stent (BMS or DES) during PCI for ACS, P2Y12 inhibitor therapy should be given for at least 12 months. Options include clopidogrel 75 mg daily, prasugrel 10 mg daily, and ticagrelor 90 mg twice daily. *(Level of Evidence: B)*

b. In patients receiving DES for a non-ACS indication, clopidogrel 75 mg daily should be given for at least 12 months if patients are not at high risk of bleeding. *(Level of Evidence: B)*

c. In patients receiving BMS for a non-ACS indication, clopidogrel should be given for a minimum of 1 month and ideally up to 12 months (unless the patient is at increased risk of bleeding; then it should be given for a minimum of 2 weeks). *(Level of Evidence: B)*

The measure is also supported by the following recommendations:

* From O'Gara et al. (2013, p. e377) under *Antiplatelet Therapy to Support Primary PCI for STEMI: Recommendations, Class I,* it states in relevant part:

P2Y12 inhibitor therapy should be given for 1 year to patients with STEMI who receive a stent (BMS or DES) during primary PCI using the following maintenance doses:

a. Clopidogrel 75 mg daily (*Level of Evidence: B*); or

b. Prasugrel 10 mg daily (*Level of Evidence: B*); or

c. Ticagrelor 90 mg twice a day. (*Level of Evidence: B)*

* From Jneid et al. (2012, p. 891) under *Recommendations for Convalescent and Long-Term Antiplatelet Therapy, Class I,* it states in relevant part:

For UA/NSTEMI patients treated with a stent (BMS or DES), aspirin should be continued indefinitely. *(Level of Evidence: A)* The duration and maintenance dose of P2Y12 receptor inhibitor therapy should be as follows:

a. Clopidogrel 75 mg daily, prasugrel 10 mg daily, or ticagrelor 90 mg twice daily should be given for at least 12 months in patients receiving DES and up to 12 months for patients receiving BMS. *(Level of Evidence: B)*

**1a.4.3.** **Grade assigned to the quoted recommendation with definition of the grade:**

The following definitions apply to the graded recommendations from all three guidelines shown in Section 1a.4.2., above:

Size of Treatment Effect:

Class I = Benefit>>>Risk; Procedure/Treatment SHOULD be performed/administered.

Certainty (Precision) of Treatment Effect:

Level A = Multiple populations evaluated. Data derived from multiple randomized clinical trials or meta-analyses.

Level B = Limited populations evaluated; data derived from a single randomized trial or nonrandomized studies

**1a.4.4. Provide all other grades and associated definitions for recommendations in the grading system.** (*Note: If separate grades for the strength of the evidence, report them in section 1a.7.*)

The following is a complete set of definitions of the "Size of Treatment Effect" and the "Certainty (Precision) of Treatment Effect" that apply to all three guidelines listed in Section 1a.4.2., above:

Size of Treatment Effect:

Class I = Benefit >>> Risk. Procedure/Treatment SHOULD be performed/administered.

Class IIa = Benefit >> Risk. Additional studies with focused objectives needed. IT IS REASONABLE to perform procedure/administer treatment.

Class IIb = Benefit ≥ Risk. Additional studies with broad objectives needed; additional registry data would be helpful. Procedure/Treatment MAY BE CONSIDERED.

Class III No Benefit = Procedure/Test is not helpful. Treatment has no proven benefit.

Class III Harm = Procedure/Test entails excess cost without benefit or is harmful. Treatment is harmful to patients.

Certainty (Precision) of Treatment Effect:

Level A = Multiple populations evaluated. Data derived from multiple randomized clinical trials or meta-analyses.

Level B = Limited populations evaluated. Data derived from a single randomized trial or nonrandomized studies.

Level C = Very limited populations evaluated. Only consensus opinion of experts, case studies, or standard of care.

**1a.4.5. Citation and URL for methodology for grading recommendations** (*if different from 1a.4.1*)**:**

The citations and URLs for the methodologies used to conduct the literature reviews and grade the recommendations are the same as those for the three guidelines listed in Section 1a.4.1.

**1a.4.6. If guideline is evidence-based (rather than expert opinion), are the details of the quantity, quality, and consistency of the body of evidence available (e.g., evidence tables)?**

X Yes **→ *complete section*** [***1a.7***](#Section1a7)

☐No **→ *report on another systematic review of the evidence in sections*** [***1a.6***](#Section1a6) ***and*** [***1a.7***](#Section1a7)***; if another review does not exist, provide what is known from the guideline review of evidence in*** [***1a.7***](#Section1a7)

**1a.5.** **UNITED STATES PREVENTIVE SERVICES TASK FORCE RECOMMENDATION**

**1a.5.1.** **Recommendation citation** (*including date*) and **URL for recommendation** (*if available online*):

**1a.5.2.** **Identify recommendation number and/or page number** and **quote verbatim, the specific recommendation**.

**1a.5.3.** **Grade assigned to the quoted recommendation with definition of the grade**:

**1a.5.4. Provide all other grades and associated definitions for recommendations in the grading system.** (*Note: the* *grading system for the evidence should be reported in section 1a.7.*)

**1a.5.5. Citation and URL for methodology for grading recommendations** (*if different from 1a.5.1*)**:**

***Complete section*** [***1a.7***](#Section1a7)

**1a.6. OTHER SYSTEMATIC REVIEW OF THE BODY OF EVIDENCE**

**1a.6.1.** **Citation** (*including date*) and **URL** (*if available online*):

Gaglia, M. A., & Waksman, R. (2011). Systematic review of thienopyridine discontinuation and its impact upon clinical outcomes. *European Heart Journal 32,* 2358–2364.

URL: http://eurheartj.oxfordjournals.org/content/32/19/2358.full.pdf+html

**1a.6.2.** **Citation and** **URL for methodology for evidence review and grading** (*if different from 1a.6.1*)**:**

The citation and URL for the methodology used in the evidence review (Gaglia & Waksman, 2011) are the same as those provided in 1a.6.1.

***Complete section*** [***1a.7***](#Section1a7)

**1a.7. FINDINGS FROM SYSTEMATIC REVIEW OF BODY OF THE EVIDENCE supporting the measure**

**1a.7.1.** **What was the specific structure, treatment, intervention, service, or intermediate outcome addressed in the evidence review?**

Although the guideline recommendations listed in Section 1a.4.2 are evidence-based, the recommendations and the evidence reviewed to support the recommendations do not address the topic of medication adherence directly. Therefore, a separate systematic review by Gaglia and Waksman (2011) is cited for Section 1a.7. The topic addressed in this systematic review is thienopyridine discontinuation at different points in time following stent implantation and the impact on the incidence of adverse cardiac events. In addition, the need for strict adherence is further documented by two studies described under 1a.8.

**1a.7.2.** **Grade assigned for the quality of the quoted evidence with definition of the grade**:

A grade was not assigned to the overall body of evidence or individual studies in the systematic review by Gaglia and Waksman (2011).

**1a.7.3. Provide all other grades and associated definitions for strength of the evidence in the grading system.**

There are no grades or definitions for strength of the evidence in the systematic review by Gaglia and Waksman (2011).

**1a.7.4.** **What is the time period covered by the body of evidence? (*provide the date range, e.g., 1990-2010*). Date range**: June 2002 through September 2010

In the systematic review by Gaglia and Waksman (2011), the results of 19 studies of clopidogrel discontinuation and adverse cardiac events are summarized. According to Gaglia and Waksman (2011), 12 of the 19 studies used rigorous multivariate methods in their analyses. These 12 studies are listed here:

1. Airoldi et al. (2007)
2. Briguori et al. (2005)
3. Daemen et al. (2007)
4. Eisenstein et al. (2007)
5. Ho et al. (2007)
6. Ho et al. (2008)
7. Kimura et al. (2009)
8. Park et al. (2010)
9. Schulz et al. (2009)
10. Spertus et al. (2006)
11. Urban et al. (2006)
12. van Werkum et al. (2009)

Sections 1a.7.5. - 1a.7.7. contain information about these 12 studies.

**QUANTITY AND QUALITY OF BODY OF EVIDENCE**

**1a.7.5.****How many and what type of study designs are included in the body of evidence**? (*e.g., 3 randomized controlled trials and 1 observational study*)

Of the 12 studies, 7 are cohort studies (Airoldi et al., 2007; Briguori et al., 2005; Eisenstein et al., 2007; Ho et al., 2007; Ho et al., 2008; Schulz et al., 2009; Spertus et al., 2006), three are *ad hoc* analyses of clinical trial or registry data (Daemen et al., 2007; Kimura et al., 2009; Urban et al., 2006), one is a case-control study (van Werkum et al., 2009), and one is an analysis of two randomized trials (Park et al., 2010).

**1a.7.6.** **What is the overall quality of evidence across studies in the body of evidence**? (*discuss the certainty or confidence in the estimates of effect particularly in relation to study factors such as design flaws, imprecision due to small numbers, indirectness of studies to the measure focus or target population*)

The focus of the review by Gaglia and Waksman (2011) is adverse clinical outcomes after discontinuation of P2Y12 inhibitors in patients following stent implantation. The focus of the measure is adherence to P2Y12 inhibitors in patients after stent implantation. Therefore, the studies in the review are directly relevant to the focus of the measure.

Regarding the quality of evidence across studies, Gaglia and Waksman (2011) state, "Numerous non-randomized studies have attempted to examine the hazard associated with ‘premature’ discontinuation of therapy (Table 2). What qualifies as premature, however, is of course variable and debatable. In addition, these studies focus upon patients who have undergone PCI and vary in their proportion of BMSs vs. DESs." (p. 2361)

Of the 12 studies, three studies (Briguori et al., 2005; Spertus et al., 2006; van Werkum et al., 2009) include less than 1,000 patients in the study population, indicating that in these studies, the rate of adverse events may be less precise than other studies with larger study samples.

**ESTIMATES OF BENEFIT AND CONSISTENCY ACROSS STUDIES IN BODY OF EVIDENCE**

**1a.7.7.** **What are the estimates of benefit—magnitude and direction of effect on outcome(s) across studies in the body of evidence**? (*e.g., ranges of percentages or odds ratios for improvement/ decline across studies, results of meta-analysis, and statistical significance*)

Meta-analysis of the results of these studies was not possible due to study heterogeneity.

Comparison of Clinical Outcomes in Patients No Longer on Clopidogrel (clopidogrel cessation) to Patients on Clopidogrel (clopidogrel continuation)

**Outcome: Stent Thrombosis**

There are two studies with consistent direction in favor of clopidogrel continuation but differences in magnitude of effect. Adjusted hazard ratios:

* At 30 days: 36.5 (van Werkum et al., 2009) n=1,303
* At 6 months: 4.6 (van Werkum et al., 2009), 13.7 (Airoldi et al., 2007) n=3,021
* At more than 6 months: 5.9 (van Werkum et al., 2009)

There are three studies that show no effect of clopidogrel cessation on stent thrombosis:

* At 30 days, 6 months, and 1 year (Urban et al., 2006) n=15,157
* In the intervals of 31 to 180 days, 181 to 365 days, and 366 to 548 days (Kimura et al., 2009) n=10,778
* Up to 2 years (Park et al., 2010) n=2,701
* Early (0–30 days) and late (>30 days) (Daemen et al., 2007) n=8,146

**Outcome: Composite Events**

There are four studies with consistent direction in favor of clopidogrel continuation but differences in magnitude of effect comparing clopidogrel cessation to clopidogrel continuation for composite events. Adjusted hazard ratios:

* Patient-dependent cessation (i.e., variable timing): 1.82 for all-cause mortality or acute myocardial infarction (Ho et al., 2008) n=3,137, 2.4 for all-cause mortality (Ho et al., 2007) n=1,455, and 20.6 for major adverse cardiac events (Brigouri et al, 2005) n=100
* Clopidogrel status at 6 months: Adjusted 2-year rates of death or acute myocardial infarction of 3.1% (clopidogrel continuation) vs. 7.2% (clopidogrel cessation) (Eisenstein et al., 2007) n=1,216

There are three studies that show no effect of clopidogrel cessation on composite outcomes:

* At 30 days, 6 months, and 1 year: Major adverse cardiac event (MACEs) or target lesion revascularizations (TLRs) (Urban et al., 2006) n=15,157
* In the intervals of 31 to 180 days, 181 to 365 days, and 366 to 548 days: Cardiac death or myocardial infarction (Kimura et al., 2009) n=10,778
* Up to two years: Cardiac death/myocardial infarction, MI/stroke/all-cause death, MI/stroke/cardiac death (Park et al., 2010) n=2,701

Citations for 1a.7.5. - 1a.7.7.

Airoldi, F., Colombo, A., Morici, N., Latib, A., Cosgrave, J., Buellesfeld, L., . . . Godino, C. (2007). Incidence and predictors of drug-eluting stent thrombosis during and after discontinuation of thienopyridine treatment. *Circulation, 116*(7), 745-754.

Briguori, C., Colombo, A., Airoldi, F., Focaccio, A., Iakovou, I., Chieffo, A., . . . Ricciardelli, B. (2005). Sirolimus-eluting stent implantation in diabetic patients with multivessel coronary artery disease. *American Heart Journal, 150*(4), 807-813.

Daemen, J., Wenaweser, P., Tsuchida, K., Abrecht, L., Vaina, S., Morger, C., . . . Hellige, G. (2007). Early and late coronary stent thrombosis of sirolimus-eluting and paclitaxel-eluting stents in routine clinical practice: Data from a large two-institutional cohort study. *The Lancet, 369*(9562), 667-678.

Eisenstein, E. L., Anstrom, K. J., Kong, D. F., Shaw, L. K., Tuttle, R. H., Mark, D. B. . . . Kandzari, D. E. (2007). Clopidogrel use and long-term clinical outcomes after drug-eluting stent implantation. *The Journal of the American Medical Association, 297*(2), 159-168.

Gaglia, M. A., & Waksman, R. (2011). Systematic review of thienopyridine discontinuation and its impact upon clinical outcomes. *European Heart Journal, 32,* 2358–2364.

Ho, P. M., Fihn, S. D., Wang, L., Bryson, C. L., Lowy, E., Maynard, C., . . . Rumsfeld, J. S. (2007). Clopidogrel and long-term outcomes after stent implantation for acute coronary syndrome. *American Heart Journal, 154*(5), 846-851.

Ho, P. M., Peterson, E. D, Wang, L., Magid, D. J., Fihn, S. D., Larsen, G. C., . . . Rumsfeld, J. S. (2008). Incidence of death and acute myocardial infarction associated with stopping clopidogrel after acute coronary syndrome. *The Journal of the American Medical Association, 299*(5), 532-539.

Kimura, T., Morimoto, T., Nakagawa, Y., Tamura, T., Kadota, K., Yasumoto, H., . . . Meguro, T. (2009). Antiplatelet therapy and stent thrombosis after sirolimus-eluting stent implantation. *Circulation, 119*(7), 987-995.

Park, S. J., Park, D. W., Kim, Y. H., Kang, S. J., Lee, S. W., Lee, C. W., . . . Lee, S. G. (2010). Duration of dual antiplatelet therapy after implantation of drug-eluting stents. *New England Journal of Medicine, 362*(15), 1374-1382.

Schulz, S., Schuster, T., Mehilli, J., Byrne, R. A., Ellert, J., Massberg, S., . . . Schömig, A. (2009). Stent thrombosis after drug-eluting stent implantation: Incidence, timing, and relation to discontinuation of clopidogrel therapy over a 4-year period. *European Heart Journal, 30*(22), 2714-2721.

Spertus, J. A., Kettelkamp, R., Vance, C., Decker, C., Jones, P. G., Rumsfeld, J. S. . . . Bach, R. G. (2006). Prevalence, predictors, and outcomes of premature discontinuation of thienopyridine therapy after drug-eluting stent placement: Results from the PREMIER registry. *Circulation, 113*(24), 2803-2809.

Urban, P., Gershlick, A. H., Guagliumi, G., Guyon, P., Lotan, C., Schofer, J., . . . Berge, C. (2006). Safety of coronary sirolimus-eluting stents in daily clinical practice one-year follow-up of the e-Cypher registry. *Circulation, 113*(11), 1434-1441.

Van Werkum, J. W., Heestermans, A. A , Zomer, A. C., Kelder, J. C., Suttorp, M. J., Rensing, B. J., . . . Hautvast, R. W. (2009). Predictors of coronary stent thrombosis: The Dutch Stent Thrombosis Registry. *Journal of the American College of Cardiology, 53*(16), 1399-1409.

**1a.7.8.** **What harms were studied and how do they affect the net benefit (benefits over harms)?**

The review by Gaglia and Waksman (2011) acknowledges the occurrence of harms associated with antiplatelet therapy ("...because indefinite thienopyridine therapy exposes patients to an undue risk of bleeding...), but does not provide detailed information related to the frequency or nature of such harms. However, another recent review describes the most common complications of antiplatelet therapy after PCI as follows: bleeding (2-3%), hypersensitivity reactions (1.5-6%), and non-hemorrhagic adverse effects (thrombocytopenia 0.1-0.3%, and neutropenia ≤ 0.1%) (Brilakis et al., 2013). These potential harms are based on data from randomized controlled trials and selected other studies. The authors of the ACC guidelines have interpreted the body of evidence to suggest that the benefit of 12 months of antiplatelet therapy greatly outweighs the risk of potential harm.

Citation for 1a.7.8.

Brilakis, E. S., Patel, V. G., Banerjee, S. (2013). Medical Management After Coronary Stent Implantation: A Review. *JAMA, 310*(2), 189-198.

**UPDATE TO THE SYSTEMATIC REVIEW(S) OF THE BODY OF EVIDENCE**

**1a.7.9.** **If new studies have been conducted since the systematic review of the body of evidence, provide for each new study: 1) citation, 2) description, 3) results, 4) impact on conclusions of systematic review**.

**1a.8 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.*

In this section, we summarize the findings of two recent studies on the relationship between adherence to P2Y12 inhibitor therapy following the implantation of a coronary artery DES or BMS and patient outcomes.

**1a.8.1** **What process was used to identify the evidence?**

These two studies were identified using hand searches of reference lists of relevant clinical practice guidelines and other relevant articles and Web of Science citation searches of key articles. The abstracts and/or full-text articles from both types of searches were reviewed to identify those studies that addressed the relationship between adherence to P2Y12 inhibitor therapy treatment following the implantation of a coronary artery DES or BMS and patient outcomes. The two selected studies met the following criteria: the study measured adherence to P2Y12 inhibitor therapy treatment following the implantation of a coronary artery DES or BMS; the study reported patient outcomes in subgroups defined by P2Y12 inhibitor therapy adherence levels; and, the study was published in the last five years.

**1a.8.2.** **Provide the citation and summary for each piece of evidence.**

Citation: Ko, D. T., Chiu, M., Guo, H., Austin, P. C., Marquis, J. F., & Tu, J. V. (2009). Patterns of use of thienopyridine therapy after percutaneous coronary interventions with drug-eluting stents and bare-metal stents. *American Heart Journal, 158*(4), 592-598.

Summary: This retrospective cohort study focused on patients ≥65 years old in Ontario, Canada, who had a drug-eluting stent (DES) (n=5,263) or a bare-metal stent (BMS) (n=6,081) implanted between December 1, 2003, and March 31, 2006. All patients were prescribed thienopyridine therapy at the time of stent implantation. Pharmacy claims data were used to classify patients as having primary non-adherence (i.e., no prescription filled after hospital discharge), being adherent (i.e., having a proportion of days covered (PDC) ≥80%), or being suboptimally adherent (i.e., having a PDC <80%). Increased risk of mortality was observed among DES patients with PDC<80% over 12 months (hazard ratio [HR] 2.39, 95% CI 1.67-3.43) and among BMS patients with PDC<80% over 12 months (HR 1.46, 95% CI 1.10-1.93).

Citation: Din, J., Janssen, C., Robinson, S. D., Smith, R., Carere, R., Klinke, W. P., . . . Cruden, N. (2013). Non-Adherence with clopidogrel after coronary stenting is associated with increased mortality and myocardial infarction [Abstract]. *Journal of the American College of Cardiology, 61*(10\_S).

Summary: This retrospective cohort study determined the use of clopidogrel and outcomes from registry data in patients who had a drug-eluting stent (n=3,599) or bare-metal stent (n=12,030) implanted during 2004-2006 in British Columbia, Canada. Non-adherence was defined as not filling a clopidogrel prescription for 5 or more days during the 12 months after DES, or during 1 month after BMS. Clopidogrel non-adherence within 12 months after DES was associated with increased all-cause mortality (HR 1.95, 95% CI 1.47-2.58), myocardial infarction (MI) (HR 1.4, 95% CI 1.1-1.81), and death or MI (HR 1.58, 95% CI 1.29-1.92). Clopidogrel non-adherence within one month post-BMS was associated with increased all-cause mortality (HR 1.66, 95% CI 1.24-2.21), and death or MI (HR 1.43, 95% CI 1.11-1.85).