

NATIONAL QUALITY FORUM—Evidence (subcriterion 1a)

Measure Number (if previously endorsed): Click here to enter NQF number

Measure Title: Percutaneous Coronary Intervention (PCI): Post-Procedural Aspirin Therapy

IF the measure is a component in a composite performance measure, provide the title of the

Composite Measure here: Percutaneous Coronary Intervention (PCI): Post-Procedural Optimal Medical Therapy Composite

Date of Submission: 12/23/2013

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](#).

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.

1a. Evidence to Support the Measure Focus

The measure focus is evidence-based, demonstrated as follows:

- **Health outcome:** ³ a rationale supports the relationship of the health outcome to processes or structures of care. Applies to patient-reported outcomes (PRO), including health-related quality of life/functional status, symptom/symptom burden, experience with care, health-related behavior.
- **Intermediate clinical outcome:** a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence ⁴ that the measured intermediate clinical outcome leads to a desired health outcome.
- **Process:** ⁵ a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence ⁴ 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 that the measured structure leads to a desired health outcome.
- **Efficiency:** ⁶ evidence not required for the resource use component.

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 U.S. Preventive Services Task Force (USPSTF) [grading definitions](#) and [methods](#), or Grading of Recommendations, Assessment, Development and Evaluation ([GRADE](#)) [guidelines](#).
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](#); [AQA Principles of Efficiency Measures](#)).

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

Outcome

- ☐ Health outcome: Click here to name the health outcome
- ☐ Patient-reported outcome (PRO): Click here to name the PRO
PROs include HRQoL/functional status, symptom/symptom burden, experience with care, health-related behaviors
- ☐ Intermediate clinical outcome (e.g., lab value): Click here to name the intermediate outcome
- ☒ Process: Percutaneous Coronary Intervention (PCI): Post-Procedural Aspirin Therapy
- ☐ Structure: Click here to name the structure
- ☐ Other: Click here to name what is being measured

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

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

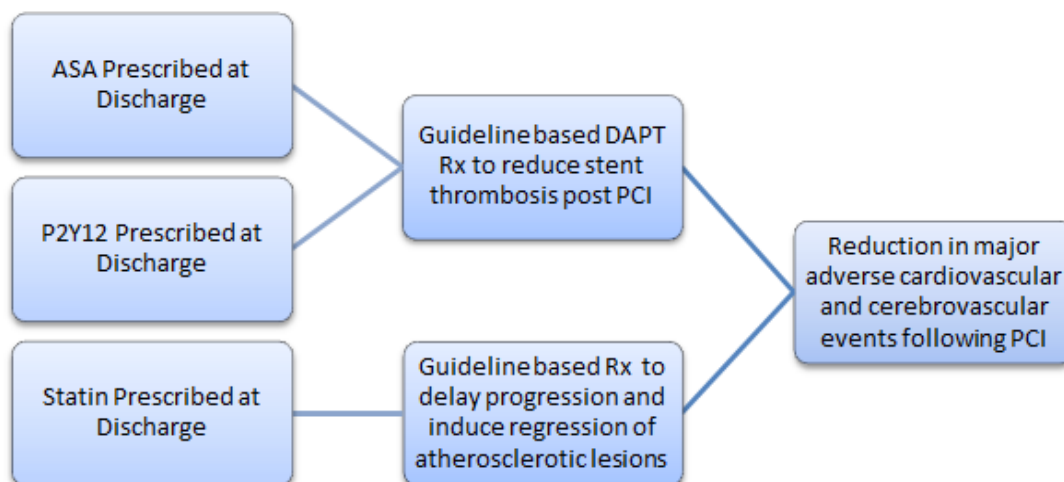
1a.2.1. State the rationale supporting the relationship between the health outcome (or PRO) to at least one healthcare structure, process, intervention, or service (i.e., influence on outcome/PRO).

Note: For health outcome/PRO 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 path between structure, process, intermediate outcome, and health outcomes. Include all the steps between the measure focus and the health outcome.

Intracoronary stents, either drug eluting or bare metal, are deployed in the majority of patients who undergo percutaneous coronary intervention (PCI) to improve symptoms related to their obstructive coronary artery disease. These stents have a dual function; to prevent abrupt closure of the treated artery soon after the procedure, as well as reducing the need for repeat revascularization compared to the prevalence of repeat PCI for patients undergoing only balloon angioplasty. However, stent restenosis and stent thrombosis are potential complications of coronary artery stenting. While stent thrombosis is an uncommon complication, it often presents as death and is almost always accompanied by MI, usually with ST-segment elevation. Recommended treatment therapy with dual antiplatelet therapy (DAPT: aspirin plus platelet P2Y₁₂ receptor inhibitors) significantly lowers the risk of stent thrombosis. Two of the three medications included in this composite medication are included for this purpose, to reduce the risk of adverse outcomes such as MI or death after stenting. The third medication included in this composite measure is the Statin class to delay progression and induce the regression of atherosclerotic lesion in this patient population. The use of these three medication classes is guideline driven and guideline supported in order to reduce the adverse events or mortality following PCI.



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

- ☒ Clinical Practice Guideline recommendation – **complete sections [1a.4](#), and [1a.7](#)**
- ☐ US Preventive Services Task Force Recommendation – **complete sections [1a.5](#) and [1a.7](#)**
- ☒ Other systematic review and grading of the body of evidence (e.g., *Cochrane Collaboration*, *AHRQ Evidence Practice Center*) – **complete sections [1a.6](#) and [1a.7](#)**
- ☐ Other – **complete section [1a.8](#)**

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):

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.

URL for guideline: <http://content.onlinejacc.org/article.aspx?articleid=1147816>

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

Page 41 of 79; e84. Section 6.1 Postprocedural Antiplatelet Therapy: Recommendations

CLASS I

#1. After PCI, use of aspirin should be continued indefinitely. (Level of Evidence: A)

CLASS IIa

#1. After PCI, it is reasonable to use aspirin 81 mg per day in preference to higher maintenance doses) .
(Level of Evidence: B)

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

ACCF/AHA/SCAI recommendations included in section 1a.4.2 have been assigned a Class I and Class IIa recommendation. Class I recommendations refer to “Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective.” Class IIa recommendations refer to “Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment. Weight of evidence/opinion is in favor of usefulness/efficacy.”

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.)

ACCF/AHA guideline methodology categorizes indications as class I,II, or III on the basis of a multifactorial assessment of risk and expected efficacy viewed in the context of current knowledge and the relative strength of this knowledge. These classes summarize the recommendations for procedures or treatments as follows and noted in the table below:

Classification Types

Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective.

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.

- IIa: Weight of evidence/opinion is in favor of usefulness/efficacy
- IIb: Usefulness/efficacy is less well established by evidence/opinion.

Class III: Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective and in some cases may be harmful.

- No Benefit- Procedure/Test not helpful or Treatment w/o established proven benefit
- Harm- Procedure/Test leads to excess cost w/o benefit or is harmful, and or Treatment is harmful

Additional detail regarding the classification of recommendation and level of evidence is provided in the following table.

ESTIMATE OF CERTAINTY (PRECISION) 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 per- form 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 or CLASS III Harm					
	Procedure/ Test		Treatment			
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Sufficient evidence from multiple randomized trials or meta-analyses 		<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from multiple randomized trials or meta-analyses 		<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Greater conflicting evidence from multiple randomized trials or meta-analyses 	
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Evidence from single randomized trial or nonrandomized studies 		<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from single randomized trial or nonrandomized studies 		<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Greater conflicting evidence from single randomized trial or nonrandomized studies 	
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Only expert opinion, case studies, or standard of care 		<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Only diverging expert opinion, case studies, or standard of care 		<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Only diverging expert opinion, case studies, or standard of care 	
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial		is reasonable can be useful/effective/beneficial is probably recommended or indicated		may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	
Comparative effectiveness phrases ¹	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B		treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		COR III: No Benefit is not recommended is not indicated should not be performed/ administered/ other is not useful/ beneficial/ effective	
					COR III: Harm potentially harmful causes harm associated with excess morbidity/mortality should not be performed/ administered/ other	

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

ACCF/AHA Task Force on Practice Guidelines. Methodology Manual and Policies From the ACCF/AHA Task Force on Practice Guidelines. American College of Cardiology Foundation and American Heart Association, Inc. Cardiosource.com. 2010.

http://assets.cardiosource.com/Methodology_Manual_for_ACC_AHA_Writing_Committees.pdf and http://my.americanheart.org/idc/groups/ahamah-public/@wcm/@sop/documents/downloadable/ucm_319826.pdf.

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)?

- ☐ Yes → **complete section 1a.7**
- ☒ No → **report on another systematic review of the evidence in sections 1a.6 and 1a.7; if another review does not exist, provide what is known from the guideline review of evidence in 1a.7**

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](#)

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

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

Brilakis ES, Patel VG, Banerjee S. Medical management after coronary stent implantation: a review. *JAMA*. 2013;310(2):189-198. doi:10.1001/jama.2013.7086
<http://jama.jamanetwork.com/article.aspx?articleid=1710463>

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

The methodology for evidence review is included in the methods section of the review cited in 1a.6.1. The authors do not provide an overall grade for the evidence.

Complete section [1a.7](#)

1a.7. FINDINGS FROM SYSTEMATIC REVIEW OF BODY OF THE EVIDENCE SUPPORTING THE MEASURE

If more than one systematic review of the evidence is identified above, you may choose to summarize the one (or more) for which the best information is available to provide a summary of the quantity, quality, and consistency of the body of evidence. Be sure to identify which review is the basis of the responses in this section and if more than one, provide a separate response for each review.

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

ACCF/AHA/SCAI 2011 Guidelines:

The section of the ACCF/AHA/SCAI guideline which includes the recommendations referenced in 1a.4.2. pertains to the post procedural considerations for medical therapy in patients undergoing PCI.

2013 JAMA Review:

The review focused on medical therapy after percutaneous coronary intervention (PCI).

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

ACCF/AHA/SCAI 2011 Guidelines:

The weight of the evidence in support of most of the ACCF/AHA/SCAI recommendations included in section 1a.4.2 is rated as Level A and Level B respectively as noted parenthetically. Level A evidence refers to "Data derived from multiple randomized clinical trials or meta-analyses." The weight of the evidence in support of the additional recommendation is rated as Level B. Level B evidence refers to "Data derived from a single randomized trial, or nonrandomized studies."

2013 JAMA Review:

The authors of the systematic review did not assign a grade to the overall quality of the evidence

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

See 1a.7.2. and 1a.4.3. and 1a.4.4.

1a.7.4. What is the time period covered by the body of evidence? (provide the date range, e.g., 1990-2010). Date range: ACCF/AHA/SCAI 2011 Guidelines: 1996- 2010; JAMA Review: 2000-2013

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)

ACCF/AHA/SCAI 2011 Guidelines:

Two meta-analyses were evaluated (one collaborative meta-analysis reviewing 287 studies involving 135,000 patients in comparisons of antiplatelet therapy versus control and 77,000 in comparisons of different antiplatelet regimens and one meta-analysis of risk of bleeding complications after different doses of aspirin in 192,036 patients enrolled in 31 randomized controlled trials); one observational analysis from a double-blind, placebo-controlled, randomized trial 15,595 patients; two scientific advisory groups were consulted (the 2008 American College of Chest Physicians Evidence-Based Clinical Practice Guidelines and the 2007 Science Advisory Statement from the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association, with representation from the American College of Physicians); and two clinical trials were included in this body of evidence.

2013 JAMA Review:

The systematic review included 91 publications, with priority given to data from large randomized-controlled trials, systematic reviews, and meta-analyses.

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)

ACCF/AHA/SCAI 2011 Guidelines:

Information regarding the overall quality of evidence across studies is not available.

2013 JAMA Review:

The authors of the review did not provide an assessment of the overall quality of evidence across studies.

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)

ACCF/AHA/SCAI 2011 Guidelines:

Quantitative estimates of benefit of Aspirin therapy across this body of evidence are not reported.

2013 JAMA Review:

Quantitative estimates of benefit of Aspirin therapy across this body of evidence are not reported.

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

ACCF/AHA/SCAI 2011 Guidelines:

The guidelines document addresses a post hoc analysis of the PLATO study, specifically that the based on the results in the U.S. patient cohort, a black box warning was developed stating that maintenance doses of aspirin above 100 mg reduce the effectiveness of ticagrelor, a P2Y12 Inhibitor, and should be avoided. After any initial dose, ticagrelor should be used with aspirin 75 mg to 100 mg per day. Ticagrelor has not been studied in elective PCI or in patients who received fibrinolytic therapy; thus, no recommendations about its use in these clinical settings can be made.

2013 JAMA Review:

The 2013 JAMA review considered issues surrounding appropriate dose and duration of anti-platelet drugs, drug allergies, method of administration, surgery following stent implantation, oral anticoagulation, and risk of bleeding. After consideration of these various issues, the authors concluded that dual antiplatelet therapy consisting of aspirin and a P2Y12 inhibitor remains the main medical therapy for optimizing outcomes following PCI

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.

The body of evidence is current through 2013, and no additional, relevant studies have been identified.

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.

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

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

NATIONAL QUALITY FORUM—Evidence (subcriterion 1a)

Measure Title: Percutaneous Coronary Intervention (PCI): Post-Procedural P2Y12 Inhibitor Therapy

IF the measure is a component in a composite performance measure, provide the title of the

Composite Measure here: Percutaneous Coronary Intervention (PCI): Post-Procedural Optimal Medical Therapy Composite

Date of Submission: 12/23/2013

Instructions

- For composite performance measures:
 - A separate evidence form is required for each component measure unless several components were studied together.
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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 a rationale supports the relationship of the health outcome to processes or structures of care.
- Intermediate clinical outcome, Process,⁴ or Structure: a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence⁵ 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 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](#) and [methods](#), or Grading of Recommendations, Assessment, Development and Evaluation ([GRADE guidelines](#)).

6. Measures of efficiency combine the concepts of resource use and quality (NQF's [Measurement Framework](#):

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 intermediate outcome
- ☒ Process: P2Y12 Inhibitors prescribed at discharge for PCI patients /Prescribing optimal medical therapy at discharge for patients undergoing PCI
- ☐ 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](#)*

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.

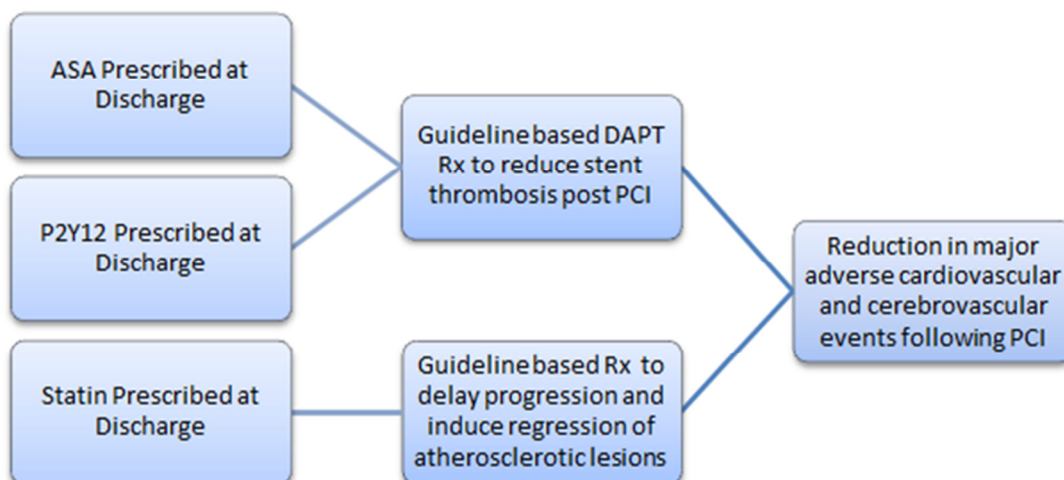
1a.2.1. State the rationale supporting the relationship between the health outcome (or PRO) and at least one healthcare structure, process, intervention, or service.

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.

Intracoronary stents, either drug eluting or bare metal, are deployed in the majority of patients who undergo percutaneous coronary intervention (PCI) to improve symptoms related to their obstructive coronary artery disease. These stents have a dual function; to prevent abrupt closure of the treated artery soon after the procedure, as well as reducing the need for repeat revascularization compared to the prevalence of repeat PCI for patients undergoing only balloon angioplasty. However, stent restenosis and stent thrombosis are potential complications of coronary artery stenting. While stent thrombosis is an uncommon complication, it often presents as death and is almost always accompanied by MI, usually with ST-segment elevation. Recommended treatment therapy with dual antiplatelet therapy (DAPT: aspirin plus platelet P2Y12 receptor inhibitors) significantly lowers the risk of stent thrombosis. Two of the three medications included in this composite medication are included for this purpose, to reduce the risk of adverse outcomes such as MI or death after stenting. The third medication included in this composite measure is the Statin class to delay progression and induce the regression of atherosclerotic lesion in this patient population. The use of these three medication classes is guideline driven and guideline supported in order to reduce the adverse events or mortality following PCI.



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

- ☒ Clinical Practice Guideline recommendation – **complete sections 1a.4, and 1a.7**
- ☐ US Preventive Services Task Force Recommendation – **complete sections 1a.5 and 1a.7**
- ☒ Other systematic review and grading of the body of evidence (e.g., *Cochrane Collaboration, AHRQ Evidence Practice Center*) – **complete sections 1a.6 and 1a.7**
- ☐ Other – **complete section 1a.8**

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):

Guideline citation:

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.

URL for guideline:

<http://content.onlinejacc.org/article.aspx?articleid=1147816>

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

Page 41 of 79; e84. Section 6.1. Postprocedural Antiplatelet Therapy: Recommendations

1) 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(570), prasugrel 10 mg daily (567), and ticagrelor 90 mg twice daily (568). (*Class I, 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 the patient is not at high risk of bleeding (208,212,571). (*Class I, 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) (572). (*Class I, Level of Evidence: B*)

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

ACCF/AHA/SCAI 2011 Guidelines:

All ACCF/AHA/SCAI recommendations included in section 1a.4.2 have been assigned a Class I recommendation. Class I recommendations refer to “Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective.”

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.*)

ACCF/AHA/SCAI 2011 Guidelines:

ACCF/AHA guideline methodology categorizes indications as class I,II, or III on the basis of a multifactorial assessment of risk and expected efficacy viewed in the context of current knowledge and the relative strength of this knowledge. These classes summarize the recommendations for procedures or treatments as follows and noted in the table below:

Classification Types

Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective.

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.

- IIa: Weight of evidence/opinion is in favor of usefulness/efficacy
- IIb: Usefulness/efficacy is less well established by evidence/opinion.

Class III: Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective and in some cases may be harmful.

No Benefit: Procedure/Test not helpful or Treatment w/o established proven benefit

Harm: Procedure/Test leads to excess cost w/o benefit or is harmful, and or Treatment is harmful

Additional detail regarding the classification of recommendation and level of evidence is provided in the following table.

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT					
	CLASS I <i>Benefit >>> Risk</i> Procedure/Treatment SHOULD be performed/ administered	CLASS IIa <i>Benefit >> Risk</i> Additional studies with focused objectives needed IT IS REASONABLE to per- form procedure/administer treatment	CLASS IIb <i>Benefit ≥ Risk</i> Additional studies with broad objectives needed; additional registry data would be helpful Procedure/Treatment MAY BE CONSIDERED	CLASS III <i>No Benefit</i> or CLASS III <i>Harm</i>	
				Procedure/ Test	Treatment
				COR III: No benefit	COR III: No Proven Benefit
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Sufficient evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Greater conflicting evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> Recommendation that procedure or treatment is not useful/effective and may be harmful Sufficient evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> Excess Cost w/o Benefit or Harmful Harmful to Patients
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Greater conflicting evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> Recommendation that procedure or treatment is not useful/effective and may be harmful Evidence from single randomized trial or nonrandomized studies 	
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Only expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Only diverging expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Only diverging expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> Recommendation that procedure or treatment is not useful/effective and may be harmful Only expert opinion, case studies, or standard of care 	
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit is not recommended is not indicated should not be performed/ administered/ other	COR III: Harm potentially harmful causes harm associated with excess morbidity/mortality should not be performed/ administered/ other
Comparative effectiveness phrases ¹	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		is not useful/ beneficial/ effective	

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

ACCF/AHA/SCAI 2011 Guidelines:

ACCF/AHA Task Force on Practice Guidelines. Methodology Manual and Policies From the ACCF/AHA Task Force on Practice Guidelines. American College of Cardiology Foundation and American Heart Association, Inc. Cardiosource.com. 2010. Available at:

http://assets.cardiosource.com/Methodology_Manual_for_ACC_AHA_Writing_Committees.pdf and

http://my.americanheart.org/idc/groups/ahamah-public/@wcm/@sop/documents/downloadable/ucm_319826.pdf.

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)?

☐ Yes → *complete section [1a.7](#)*

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

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](#)

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

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

Brilakis ES, Patel VG, Banerjee S. Medical management after coronary stent implantation: a review. *JAMA*. 2013;310(2):189-198. doi:10.1001/jama.2013.7086
<http://jama.jamanetwork.com/article.aspx?articleid=1710463>

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

The methodology for evidence review is included in the methods section of the review cited in 1a.6.1. The authors do not provide an overall grade for the evidence.

Complete section [1a.7](#)

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?

ACCF/AHA/SCAI 2011 Guidelines:

The section of the ACCF/AHA/SCAI guideline which includes the recommendations referenced in 1a.4.2. pertains to post-procedural antiplatelet therapy.

2013 JAMA Review:

The review focused on medical therapy after percutaneous coronary intervention (PCI).

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

ACCF/AHA/SCAI 2011 Guidelines:

The weight of the evidence in support of the various ACCF/AHA/SCAI recommendations included in section 1a.4.2 is rated as Level B, as noted parenthetically. Level B evidence refers to "Data derived from a single randomized trial, or nonrandomized studies."

2013 JAMA Review:

The authors of the systematic review did not assign a grade to the overall quality of the evidence

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

See 1a.7.2. and 1a.4.2., 1a.4.3 and 1.a.4.

1a.7.4. What is the time period covered by the body of evidence? (*provide the date range, e.g., 1990-2010*). Date range: ACCF/AHA/SCAI 2011 Guidelines: 2001-2009; AHA/ACC/ACS/ADA scientific advisory: 1996-1998 2013 JAMA Review: 2000-2013

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*)

ACCF/AHA/SCAI 2011 Guidelines:

4 randomized controlled trials, 1 observational study, and 1 science advisory statement are cited in support of the recommendation provided in 1a4.2. The science advisory statement cites an additional 5 randomized controlled trials.

Science advisory statement citation: Grines CL, Bonow RO, Casey DE Jr., et al. Prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents: a science advisory from the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association, with representation from the American College of Physicians. J Am Coll Cardiol. 2007;49:734 –9.

2013 JAMA Review:

The systematic review included 91 publications, with priority given to data from large randomized-controlled trials, systematic reviews, and meta-analyses.

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*)

ACCF/AHA/SCAI 2011 Guidelines:

Information regarding the overall quality of evidence across studies is not available.

2013 JAMA Review:

The authors of the review did not provide an assessment of the overall quality of evidence across studies

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*)

ACCF/AHA/SCAI 2011 Guidelines:

Quantitative estimates of benefit across studies in the body of evidence is not reported. The science advisory statement includes the following summary table which includes the percentage of reported major adverse cardiovascular events in patients treated with dual antiplatelet therapy (ie, aspirin and a P2Y12 inhibitor) compared to aspirin alone or the use of aspirin and warfarin.

TABLE 1. After Bare-Metal Stent Placement, Aspirin Plus Thienopyridine Reduces Cardiac Events Compared With Aspirin Alone or With Oral Antithrombins

Study	No. of Pts Studied	No. of Pts Treated	MACE, %*			P
			ASA Thienopyridine	ASA Warfarin	ASA Alone	
ISAR ³²	517	626	1.6	6.2	...	0.01
FANTASTIC ³³	473	485	5.7†	8.6†	...	0.37
STARS ³⁴	1653	1965	0.5	2.7	3.6	0.0001
MATTIS ³⁵	350	350	5.6	11.0	...	0.07
Hall et al ³⁶	226	358	0.8	...	3.9	0.1

MACE indicates major adverse cardiovascular events; Pts, patients; ASA, aspirin; ISAR, Intracoronary Stenting and Antithrombotic Regimen trial; FANTASTIC, Full ANTicoagulation versus ASpirin TIClopidine after stent implantation; STARS, STent Anticoagulation Regimen Study; and MATTIS, Multicenter Aspirin and Ticlopidine Trial after Intracoronary Stenting.

*Cardiac death, acute MI, or repeat target-vessel revascularization at 30 days (except for the FANTASTIC study).

†Death, MI, or stent occlusion at 6 weeks.

Adapted from ten Berg et al.¹

2013 JAMA Review:

The authors of the review did The 2013 JAMA review includes the following summary table of pivotal trials of P2Y12 inhibitors following PCI which includes the event rate, point estimate, and p-value found in each trial.

Table 2. Pivotal P2Y₁₂ Inhibitor Trials Post-Coronary Stent Implantation

	PCI Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) ²⁹	Clopidogrel for the Reduction of Events During Observation (CREDO) ³⁰	TRITON-TIMI 38 ³¹	Study of Platelet Inhibition and Patient Outcomes (PLATO) ³²
No.	2658	2116	13 608	18 624
Population	Non-STEMI ACS patients	ACS (excluding STEMI) and stable angina patients	Moderate- to high-risk ACS patients with planned PCI	ACS patients treated with early invasive or conservative approach
Follow-up, mo	8	12	14.5	12
Therapy	Clopidogrel vs placebo	Clopidogrel vs placebo	Prasugrel vs clopidogrel	Ticagrelor vs clopidogrel
Ischemic end point	CV death, MI	Death, MI, stroke	CV death, MI, stroke	Vascular death, MI, stroke
Event rate, %	4.5 vs 6.4	8.5 vs 11.5	9.9 vs 12.1	9.8 vs 11.7
Point estimate (95% CI)	RR, 0.70 (0.50-0.97)	RRR, 26.9% (3.9%-44.4%)	HR, 0.81 (0.73-0.90)	HR, 0.84 (0.77-0.92)
P value	.03	.02	.01	.001
No. needed to treat	53	33	45	53
Bleeding end point	Disabling bleeding, intraocular bleeding, bleeding requiring ≥2 units of blood	TIMI major	Non-CABG-related TIMI major	Non-CABG-related TIMI major
Event rate, %	2.7 vs 2.5	8.8 vs 6.7	2.4 vs 1.8	2.8 vs 2.2
Point estimate (95% CI)	RR, 1.12 (0.70-1.78)	NR	HR, 1.32 (1.03-1.68)	HR, 1.19 (1.02-1.38)
P value	.64	.07	.03	.03
No. needed to harm			167	167

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

The guidelines refer to the potential risk of morbidity from P2Y₁₂ inhibitor therapy after stent implantation and that this may prompt the reasonable earlier discontinuation (e.g., < 12 months) of P2Y₁₂ inhibitor therapy in some patients.

The science advisory statement includes the following regarding the risk of dual antiplatelet therapy: Dual antiplatelet therapy is not without risk. Like all antithrombotic agents, both aspirin and clopidogrel increase the risk of bleeding compared with placebo. When compared with aspirin, clopidogrel may be associated with lower risk of GI bleeding. However, when clopidogrel was combined with aspirin and administered for prolonged duration (up to 28 months), randomized trials demonstrated an absolute increase (ranging from 0.4% to 1.0%) in major bleeding, compared with aspirin alone

The 2013 JAMA review considered issues surrounding appropriate dose and duration of anti-platelet drugs, drug allergies, method of administration, surgery following stent implantation, oral anticoagulation, and risk of bleeding. After consideration of these various issues, the authors concluded that dual antiplatelet therapy consisting of aspirin and a P2Y₁₂ inhibitor remains the main medical therapy for optimizing outcomes following PCI. The authors emphasized the importance of tailoring the

P2Y12 treatment regimen to the patient's unique clinical profile to ensure that the drug, dose, and duration are appropriate for the individual patient's needs.

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.

The body of evidence is current through 2013, and no additional, relevant studies have been identified.

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.

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

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

NATIONAL QUALITY FORUM—Evidence (subcriterion 1a)

Measure Title: Percutaneous Coronary Intervention (PCI): Post-Procedural Statin Therapy

IF the measure is a component in a composite performance measure, provide the title of the

Composite Measure here: Percutaneous Coronary Intervention (PCI): Post-Procedural Optimal Medical Therapy Composite

Date of Submission: 12/23/2013

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](#).

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 a rationale supports the relationship of the health outcome to processes or structures of care.
- Intermediate clinical outcome, Process,⁴ or Structure: a systematic assessment and grading of the quantity, quality, and consistency of the body of evidence⁵ 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 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](#) and [methods](#), or Grading of Recommendations, Assessment, Development and Evaluation ([GRADE guidelines](#)).

6. Measures of efficiency combine the concepts of resource use and quality (NQF's [Measurement Framework: Evaluating Efficiency Across Episodes of Care](#); [AQA Principles of Efficiency Measures](#)).

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 intermediate outcome
- ☒ Process: Statin prescribed at discharge for PCI patients
- ☐ 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](#)*

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.

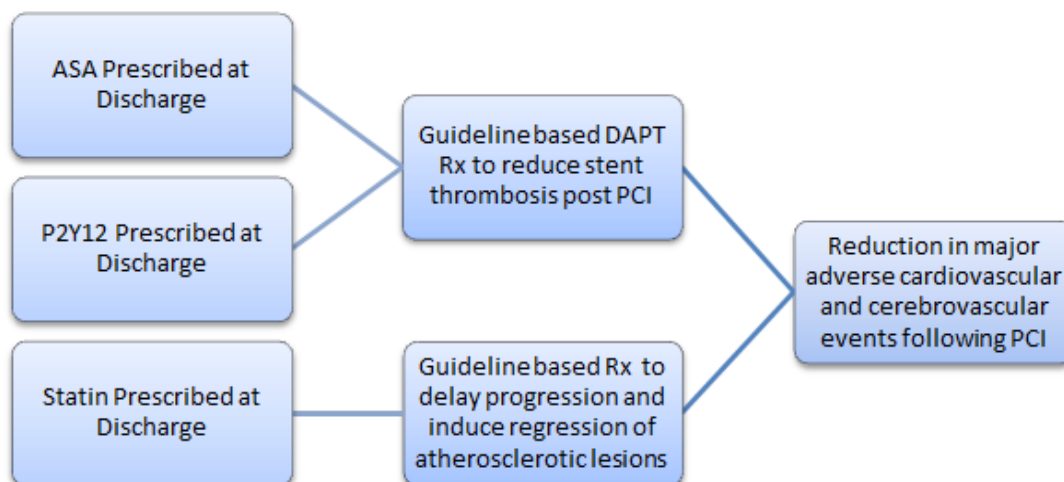
1a.2.1. State the rationale supporting the relationship between the health outcome (or PRO) and at least one healthcare structure, process, intervention, or service.

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.

Intracoronary stents, either drug eluting or bare metal, are deployed in the majority of patients who undergo percutaneous coronary intervention (PCI) to improve symptoms related to their obstructive coronary artery disease. These stents have a dual function; to prevent abrupt closure of the treated artery soon after the procedure, as well as reducing the need for repeat revascularization compared the prevalence of repeat PCI for patients undergoing only balloon angioplasty. However, stent restenosis and stent thrombosis are potential complications of coronary artery stenting. While stent thrombosis is an uncommon complication, it often presents as death and is almost always accompanied by MI, usually with ST-segment elevation. Recommended treatment therapy with dual antiplatelet therapy (DAPT: aspirin plus platelet P2Y₁₂ receptor inhibitors) significantly lowers the risk of stent thrombosis. Two of the three medications included in this composite medication are included for this purpose, to reduce the risk of adverse outcomes such as MI or death after stenting. The third medication included in this composite measure is the Statin class to delay progression and induce the regression of atherosclerotic lesion in this patient population. The use of these three medication classes is guideline driven and guideline supported in order to reduce the adverse events or mortality following PCI.



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

- ☒ Clinical Practice Guideline recommendation – **complete sections [1a.4](#), and [1a.7](#)**
- ☐ US Preventive Services Task Force Recommendation – **complete sections [1a.5](#) and [1a.7](#)**
- ☐ Other systematic review and grading of the body of evidence (e.g., *Cochrane Collaboration*, *AHRQ Evidence Practice Center*) – **complete sections [1a.6](#) and [1a.7](#)**
- ☐ Other – **complete section [1a.8](#)**

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):

Guideline citation

Stone NJ, Robinson J, Lichtenstein AH, et al. 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2013;():. doi:10.1016/j.jacc.2013.11.002.

URL for guideline:

<http://content.onlinejacc.org/article.aspx?articleid=1770217>

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

Secondary Prevention Recommendations - Page 23

Recommendation 1 - High-intensity statin therapy should be initiated or continued as first-line therapy in women and men ≤75 years of age who have clinical atherosclerotic cardiovascular disease (ASCVD*), unless contraindicated. (NHLBI Grade A, Strong; ACC/AHA Class I Level A)

Recommendation 2 - In individuals with clinical ASCVD* in whom high-intensity statin therapy would otherwise be used, when high-intensity statin therapy is contraindicated† or when characteristics predisposing to statin-associated adverse effects are present, moderate-intensity statin should be used as the second option if tolerated). (NHLBI Grade A, Strong; ACC/AHA Class I Level A)

*ASCVD (defined from the RCT inclusion criteria as acute coronary syndromes; history of MI, stable or unstable angina, coronary revascularization, stroke, or TIA presumed to be of atherosclerotic origin, and peripheral arterial disease or revascularization)

The NHLBI initiated these guidelines by sponsoring rigorous systematic evidence reviews and partnered with the ACC and AHA to complete and publish the guideline. Recommendations were derived from randomized trials, meta-analyses, and observational studies evaluated for quality, and were not formulated when sufficient evidence was not available. Each recommendation has been mapped from the NHLBI grading format to the ACC/AHA Class of Recommendation/Level of Evidence (COR/LOE) construct and is expressed in both formats.

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

Recommendations 1 and 2

- NHLBI: Grade A, Strong Recommendation (There is high certainty based on evidence that the net benefit is substantial)
- ACC/AHA Class I: Procedure/Treatment should be performed/administered

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.)

NHLBI Grading the Strength of Recommendations

- Grade B: Moderate recommendation: There is moderate certainty based on evidence that the net benefit is moderate to substantial, or there is high certainty that the net benefit is moderate.
- Grade C: Weak recommendation: There is at least moderate certainty based on evidence that there is a small net benefit.
- Grade D: Recommendation against. There is at least moderate certainty based on evidence that it has no benefit or that risks/harms outweigh benefits.
- Grade E: Expert opinion: There is insufficient evidence or evidence is unclear or conflicting, but this is what the Work Group recommends. Net benefit is unclear. Balance of benefits and harms cannot be determined because of no evidence, insufficient evidence, unclear evidence, or conflicting evidence, but the Work Group thought it was important to provide clinical guidance and make a recommendation. Further research is recommended in this area.
- Grade N: No recommendation for or against: There is insufficient evidence or evidence is unclear or conflicting. Net benefit is unclear. Balance of benefits and harms cannot be determined because of no evidence, insufficient evidence, unclear evidence, or conflicting evidence, and the Work Group thought no recommendation should be made. Further research is recommended in this area

ACC/AHA

Class of Recommendation (COR) is an estimate of the size of the treatment effect considering risks versus benefits in addition to evidence and/or agreement that a given treatment or procedure is or is not useful/effective or in some situations may cause harm.

Class IIa: It is reasonable to perform procedure/administer treatment

Class IIb: Procedure/Treatment may be considered

Class III: No benefit (Not helpful or No proven benefit)

Class III: Harm (Excess cost w/o benefit or Harmful to patients)

Specific COR definitions are included in Table 1 below.

ACC/AHA Table 1. Applying Classification of Recommendation and Level of Evidence

SIZE OF TREATMENT EFFECT					
ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	CLASS I <i>Benefit >>> Risk</i> Procedure/Treatment SHOULD be performed/ administered	CLASS IIa <i>Benefit >> Risk</i> Additional studies with focused objectives needed IT IS REASONABLE to per- form procedure/administer treatment	CLASS IIb <i>Benefit ≥ Risk</i> Additional studies with broad objectives needed; additional registry data would be helpful Procedure/Treatment MAY BE CONSIDERED	CLASS III <i>No Benefit or CLASS III Harm</i>	
				Procedure/ Test	Treatment
				COR III: No benefit	No Proven Benefit
				COR III: Harm	Excess Cost w/o Benefit or Harmful to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Sufficient evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Greater conflicting evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> Recommendation that procedure or treatment is not useful/effective and may be harmful Sufficient evidence from multiple randomized trials or meta-analyses 	
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Greater conflicting evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> Recommendation that procedure or treatment is not useful/effective and may be harmful Evidence from single randomized trial or nonrandomized studies 	
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Only expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Only diverging expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Only diverging expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> Recommendation that procedure or treatment is not useful/effective and may be harmful Only expert opinion, case studies, or standard of care 	
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit is not recommended is not indicated should not be performed/ administered/ other is not useful/ beneficial/ effective	COR III: Harm potentially harmful causes harm associated with excess morbidity/mortality should not be performed/ administered/ other
Comparative effectiveness phrases†	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B			

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

Methodology described within document cited 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)?

☒ Yes → **complete section 1a.7**

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

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](#)

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

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

1a.6.2. Citation and URL for methodology for evidence review and grading (if different from 1a.6.1):
Complete section [1a.7](#)

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?

The evidence review focused on LDL-C and non-HDL-C goals for the secondary and primary prevention of atherosclerotic cardiovascular disease (ASCVD) with cholesterol-lowering drug therapy.

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

Recommendations 1 and 2

- ACC/AHA: Level A Evidence

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

ACC/AHA

The Level of Evidence (LOE) is an estimate of the certainty or precision of the treatment effect.

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

Specific LOE definitions are included in Table 1 found in Section 1a.4.4. above.

1a.7.4. What is the time period covered by the body of evidence? (provide the date range, e.g., 1990-2010). Date range: 1996-2010.

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)

19 Randomized Control Trials (RCT)

1 Meta-analysis – 201 Cholesterol Treatment Trialsist (CTT)

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 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults does not make any qualifying statements about the overall quality of evidence across studies. The guideline states that the recommendations were derived from randomized trials, meta-analyses, and observational studies evaluated for quality, and were not formulated when sufficient evidence was not available.

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)

The guideline Expert Panel reviewed 19 RCTs to determine the LDL-C and non-HDL-C goals for the secondary and primary prevention of atherosclerotic cardiovascular disease (ASCVD) with cholesterol-lowering drug therapy. According to the guideline, the majority of studies confirmed the efficacy of cholesterol reduction in improving clinical outcomes in patients with clinical ASCVD using a single fixed-dose statin therapy to lower LDL-C levels.

The meta-analysis conducted by the Cholesterol Treatment Trialists (CTT) in 2010 includes percent reductions in LDL-C for a specific statin and dose calculated for the RCTs included in which statin therapy reduced ASCVD events. The CTT meta-analysis provided the following results:

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL-C on average, by approximately ≥50%	Daily dose lowers LDL-C on average, by approximately 30% to <50%	Daily dose lowers LDL-C on average, by <30%

The guideline defines High- Moderate- and Low-Intensity Statin Therapy in Table 5 on page 26 of the guideline.

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

The guideline states that women and men with clinical ASCVD are at increased risk for recurrent ASCVD and ASCVD death. Evidence demonstrates that high-intensity statin therapy reduces ASCVD events more than moderate-intensity statin therapy in individuals with clinical ASCVD.

Furthermore, the guideline states that in order to optimize the safety of statins, selection of the appropriate statin and dose should be based on patient characteristics, level of ASCVD risk, and potential for adverse effects. Moderate-intensity statin therapy should be used in individuals in whom high-intensity statin therapy would otherwise be recommended when characteristics predisposing them to statin associated adverse effects are present. Characteristics predisposing individuals to statin adverse effects include, but are not limited to:

- Multiple or serious comorbidities, including impaired renal or hepatic function.
- History of previous statin intolerance or muscle disorders.
- Unexplained alanine transaminase elevations >3 times Upper Limits of Normal
- Patient characteristics or concomitant use of drugs affecting statin metabolism.
- >75 years of age.

Statins modestly increase the excess risk of type-2 diabetes in individuals with risk factors for diabetes. The potential for an ASCVD risk reduction benefit outweighs the excess risk of diabetes in all but the lowest risk individuals.

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.

A recent Cochrane review was carried out to assess the effects, both harms and benefits, of statins used for primary prevention in people with no history of cardiovascular disease. Reductions in all-cause mortality, major vascular events and revascularizations were found with no excess of adverse events among people without evidence of CVD treated with statins. Although this measure focuses on secondary prevention, the Cochrane review provides further evidence that statins reduce total mortality, and adverse events.

Taylor F, Huffman MD, Macedo AF et al. Statins for the primary prevention of cardiovascular disease. The Cochrane database of systematic reviews 2013; Issue 1. Art. No.: CD004816. DOI: 10.1002/14651858.CD004816.pub5.

A recent meta-analysis included individual participant data from 22 trials of statin versus control and five trials of more versus less statin. The analysis concluded that statins reduce LDL cholesterol and prevent vascular events in individuals at low risk of vascular events.

Cholesterol Treatment Trialists Collaboration. The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. *Lancet* 2012;380:581–90.

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.

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

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