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

**Measure Number** (*if previously endorsed*)**:** 1952

**Measure Title**: Time to Intravenous Thrombolytic Therapy

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

**Date of Submission**: 11/1/2019

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

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

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

Outcome

Outcome: 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.* (*A PRO-based performance measure is not a survey instrument. Data may be collected using a survey instrument to construct a PRO measure.)*

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

Process: Time from hospital arrival to initiation of intravenous alteplase, among ischemic stroke patients

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

Structure: Click here to name the structure

Composite: Click here to name what is being measured

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

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

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

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

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

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

Clinical Practice Guideline recommendation (with evidence review)

☐ US Preventive Services Task Force Recommendation

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

☐ Other

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| **Source of Systematic Review:**   * **Title** * **Author** * **Date** * **Citation, including page number** * **URL** | AHA/ASA 2013 Guideline:  Jauch EC, Saver JL, Adams HP, Bruno A, Connors JJ, Demaerschalk BM, et al; American Heart Association Stroke Council; Council on Cardiovascular Nursing; Council on Peripheral Vascular Disease; Council on Clinical Cardiology. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2013;44(3):870-947.  *Note that while the American Heart Association / American Stroke Association (AHA/ASA) has made minor updates to this evidence attachment since the last NQF submission, the underlying evidence and intent of the measure have not changed. Updates were made to capture the current language in the most recent guideline, in support of the measure.*  AHA/ASA 2018 Guidelines:  **Title:** 2018 Guidelines for the Early Management of Patients with Acute Ischemic Stroke  **Author:** William J. Powers, MD, FAHA, Chair; Alejandro A. Rabinstein, MD, FAHA, Vice Chair; Teri Ackerson, BSN, RN; Opeolu M. Adeoye, MD, MS, FAHA; Nicholas C. Bambakidis, MD, FAHA; Kyra Becker, MD, FAHA; José Biller, MD, FAHA; Michael Brown, MD, MSc; Bart M. Demaerschalk, MD, MSc, FAHA; Brian Hoh, MD, FAHA; Edward C. Jauch, MD, MS, FAHA; Chelsea S. Kidwell, MD, FAHA; Thabele M. Leslie-Mazwi, MD; Bruce Ovbiagele, MD, MSc, MAS, MBA, FAHA; Phillip A. Scott, MD, MBA, FAHA; Kevin N. Sheth, MD, FAHA; Andrew M. Southerland, MD, MSc; Deborah V. Summers, MSN, RN, FAHA; David L. Tirschwell, MD, MSc, FAHA; on behalf of the American Heart Association Stroke Council  **Date:** December 11, 2017  **Citation, including page number:** Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, Jauch EC, Kidwell CS, Leslie-Mazwi TM, Ovbiagele B, Scott PA, Sheth KN, Southerland AM, Summers DV, Tirschwell DL; on behalf of the American Heart Association Stroke Council. 2018 Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2018;49:e53 and e65. doi: 10.1161/STR.0000000000000158.  **URL:** https://www.ahajournals.org/doi/full/10.1161/  STR.0000000000000158 |
| Quote the guideline or recommendation verbatim about the process, structure or intermediate outcome being measured. If not a guideline, summarize the conclusions from the SR. | AHA/ASA 2013 Guideline:  In patients eligible for intravenous rtPA, benefit of therapy is time dependent, and treatment should be initiated as quickly as possible. The door-to-needle time (time of bolus administration) should be within 60 minutes from hospital arrival. (Class I; Level of Evidence A) p. 898  *The AHA/ASA 2018 Guidelines note that the above recommendation from the 2013 Guideline remains unchanged and is reiterated, but re-worded for clarity.*  AHA/ASA 2018 Guidelines:  Recommendation 1: In patients eligible for IV alteplase, benefit of therapy is time dependent, and treatment should be initiated as quickly as possible. (Class I; Level A)  Recommendation 2: It is recommended that DTN time goals be established. A primary goal of achieving DTN times within 60 minutes in ≥50% of AIS patients treated with IV alteplase should be established. (Class I; Level B-NR) |
| Grade assigned to the **evidence** associated with the recommendation with the definition of the grade | AHA/ASA 2013 Guidelines:  The weight of the evidence in support of the listed AHA/ASA recommendations included in section 1a.4.2 is rated as Level A, as noted parenthetically. Level A evidence refers to “Data derived from multiple randomized clinical trials or meta-analyses.”  AHA/ASA 2018 Guidelines:  Recommendation 1 - Level A:   * High-quality evidence from more than 1 RCT * Meta-analyses of high-quality RCTs * One or more RCTs corroborated by high-quality registry studies   Recommendation 2 - Level B-NR (Nonrandomized)   * Moderate-quality evidence from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies * Meta-analyses of such studies |
| Provide all other grades and definitions from the evidence grading system | AHA/ASA 2013 Guidelines:  Levels A evidence is described in 1a.7.2. Level B evidence refers to “Data derived from a single randomized trial, or nonrandomized studies.” Level C evidence refers to “Only consensus opinion of experts, case studies, or standard-of-care.” Additional details and information about the evidence rating scheme can also be seen in 1a.4.2. and 1a.4.3.  AHA/ASA 2018 Guidelines:  These classifications apply the American College of Cardiology (ACC)/ AHA 2015 Levels of Evidence (LOE) to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care\*. The LOE denotes the confidence in or certainty of the evidence supporting the recommendation, based on the type, size, quality, and consistency of pertinent research findings.   |  |  | | --- | --- | | **Level (Quality) of Evidence\*\*** | | | Level A | -High-quality evidence\*\* from more than 1 randomized controlled trials (RCT) | | -Meta-analyses of high-quality RCTs | | -One or more RCTs corroborated by high-quality registry studies | | Level B-R (Randomized) | -Moderate-quality evidence\*\* from 1 or more RCTs | | -Meta-analyses of moderate-quality RCTs | | Level B-NR (Nonrandomized) | -Moderate-quality evidence\*\* from one or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies | | -Meta-analyses of such studies | | Level C-LD (Limited Data) | -Randomized or nonrandomized observational or registry studies with limitations of design or execution | | -Meta-analyses of such studies | | -Physiological or mechanistic studies in human subjects | | Level C-EO (Expert Opinion) | -Consensus of expert opinion based on clinical experience | | Class of Recommendation (COR) and LOE are determined independently (any COR may be paired with any LOE). | | | A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test of therapy is useful or effective. | | | \*The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information). | | | \*\*The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee. | |   (adapted from AHA/ASA 2018 Guidelines on the Early Management of Patients with Acute Ischemic Stroke) |
| Grade assigned to the **recommendation** with definition of the grade | AHA/ASA 2013 Guideline:  The AHA/ASA recommendation included in section 1a.4.2. has been assigned a Class I. Class I recommendations refer to “Conditions for which there is evidence for and/or general agreement that the procedure or treatment is useful and effective.”  AHA/ASA 2018 Guidelines:  Both recommendations supporting this measure received a Class I (Strong) strength of recommendation. Class I recommendations indicate that the “Benefit >>> Risk” and are recommended and indicated/useful/effective/beneficial. |
| Provide all other grades and definitions from the recommendation grading system | AHA/ASA 2013 Guidelines:  The standard AHA algorithm for classifying recommendations and levels of evidence focuses on therapeutic questions and, consequently, emphasizes evidence from randomized clinical trials. As such, AHA/ASA 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:  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 e 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.    Additional detail regarding AHA/ASA’s gradation recommendations is provided in the following table.    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](http://my.americanheart.org/idc/groups/ahamah%20%20public/@wcm/@sop/documents/downloadable/ucm_319826.pdf).  AHA/ASA 2018 Guidelines:  These classifications apply the ACC/AHA 2015 Class of Recommendations (COR) to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care\*. The COR reflects the magnitude of benefit over risk and corresponds to the strength of the recommendation. Class I recommendations are strong and indicate that the treatment, procedure, or intervention is useful and effective and should be performed or administered for most patients under most circumstances (Halperin et al., 2016).   |  |  | | --- | --- | | Class (Strength) of Recommendation | | | Class I (Strong) Benefit >>>Risk | Suggested phrases for writing recommendations: -Is recommended -Is indicated / useful / effective / beneficial -Should 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 | | Class IIa (Moderate) Benefit >>Risk | Suggested phrases for writing recommendations: -Is reasonable -Can be useful / effective / beneficial -Comparative-Effectiveness Phrases\*\*: --Treatment / strategy A is probably recommended / indicated in preference to treatment B --It is reasonable to choose treatment A over treatment B | | Class IIb (Weak) Benefit ≥Risk | Suggested phrases for writing recommendations: -May / might be reasonable -May / might be considered -Userfulness / effectiveness is unknown / unclear / uncertain or not well established | | Class III: No Benefit (Moderate) Benefit = Risk | Suggested phrases for writing recommendations: -Is not recommended -Is not indicated / useful / effective / beneficial -Should not be performed / administered / other | | Class III: Harm (Strong) Risk>Benefit | Suggested phrases for writing recommendations: -Potentially harmful -Causes harm -Associated with excess morbidity / mortality -Should not be performed / administered / other | | COR and LOE are determined independently (any COR may be paired with any LOE). | | | \*The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information). | | | \*\*For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated. | |   (adapted from AHA/ASA 2018 Guidelines on the Early Management of Patients with Acute Ischemic Stroke) |
| Body of evidence:   * Quantity – how many studies? * Quality – what type of studies? | AHA/ASA 2013 Guidelines:  Information regarding the total number of studies and type of study designs included in the body of evidence is not available.  However, the guidelines cite that 16 randomized control trials, 1 open trial, 32 observational studies, and 4 meta-analyses were reviewed to develop the recommendations provided in 1a4.2 and most relevant to the patient populations addressed in the measure.  AHA/ASA 2013 Guidelines:  Information regarding the overall quality of evidence across studies is not available.  AHA/ASA 2018 Guidelines:  Recommendation 1: The Guideline notes that there is no new pertinent evidence for this unchanged recommendation and refers to the 2013 Guideline. The 2013 Guideline cited that 16 randomized control trials, 1 open trial, 32 observational studies, and 4 meta-analyses were reviewed to develop the recommendation.  Recommendation 2: There are 3 retrospective observational (analytic) studies supporting this recommendation between 2014 and 2017. Combined, these studies looked at 1,943 hospitals. |
| Estimates of benefit and consistency across studies | AHA/ASA 2013 Guidelines:  The guideline does not include an overall estimate of benefit from the body of evidence. However, they do include the following summary information regarding the benefits of timely rtPA treatment, “Intravenous administration of rtPA remains the only FDA-approved pharmacological therapy for treatment of patients with acute ischemic stroke. Its use is associated with improved outcomes for a broad spectrum of patients who can be treated within 3 hours of the last known well time before symptom onset and a mildly more selective spectrum of patients who can be treated between 3 and 4.5 hours of the last known well time. Most importantly, earlier treatment is more likely to result in a favorable outcome.”  (*e.g., ranges of percentages or odds ratios for improvement/ decline across studies, results of meta-analysis, and statistical significance*)  AHA/ASA 2018 Guidelines:  Recommendation 1: The 2018 Guideline notes that there is no new pertinent evidence for this unchanged recommendation and refers to the 2013 AHA/ASA Guideline. The 2013 Guideline did not include an overall estimate of benefit and consistency from the body of evidence supporting the recommendation. As noted in the previous submission, the 2013 Guidelines included the following summary regarding the benefits of timely alteplase administration: “Intravenous administration of rtPA remains the only FDA-approved pharmacological therapy for treatment of patients with acute ischemic stroke. Its use is associated with improved outcomes for a broad spectrum of patients who can be treated within 3 hours of the last known well time before symptom onset and a mildly more selective spectrum of patients who can be treated between 3 and 4.5 hours of the last known well time. Most importantly, earlier treatment is more likely to result in a favorable outcome.”  Recommendation 2:  Per the data supplement to the AHA/ASA 2018 guidelines, the conclusions of the studies supporting the second recommendation are as follows:   * The 2017 retrospective observational study looked at 888 hospitals and 16,901 patients with acute ischemic stroke treated with alteplase within 4.5 hours of symptom onset, between June 2014 and April 2015. The study found that the median door-to-needle (DTN) time for alteplase administration was 56 minutes (IQR 42-75) and concluded that a median DTN time of less than 60 minutes were achievable in a majority of patients. * The 2014 retrospective observational study evaluated the pre- and post- Target:Stroke intervention results among 71,169 stroke patients treated with alteplase across 1,030 hospitals between April 2003 and September 2013. This study found that the median DTN time for alteplase administration declined from 77 minutes (IQR 60-98 minutes) during the pre-intervention period to 67 minutes (IQR 51-87 minutes) during the post-intervention period (P<.001). The study concluded that the implementation of the Target:Stroke quality improvement initiative was associated with improved timeliness of tPA delivery, and that a median hospital DTN target times of less than 60 minutes was achievable in over 50% of cases. * The second 2014 retrospective observational study looked at 1,193 acute ischemic stroke patients treated within 4.5 hours of symptom onset, across 25 hospitals between January 2009 and December 2012. The mean DTN time for alteplase administration was 82.9 minutes and the median time was 76 minutes. The study concluded that approximately one-quarter of patients were treated within 60 minutes.   In addition, both recommendations supporting this measure received a Class I (Strong) strength of recommendation, which reflects a high magnitude of benefit over risk. Class I recommendations are strong and indicate that the treatment, procedure, or intervention is useful and effective and should be performed or administered for most patients under most circumstances (Halperin et al., 2016). |
| What harms were identified? | AHA/ASA 2013 Guidelines:  Harms studied focused on the harms of treatment rather than the harms of time-initiated therapy.  As noted in the AHA/ASA guidelines, intracranial hemorrhages were reported in community based-settings prior to the approval of rtPA as a treatment option. However, the guidelines state it is now clear that the risk of hemorrhage is proportional to the degree to which the NINDS protocol is not followed. Other adverse events studied include systemic bleeding, myocardial rupture if fibroinolytics are given within a few days of acute myocardial infarction and reactions such as anaphylaxis or angioedema also has occurred, but these events are rare. Orolingual angioedema reactions have occurred in 1.3%-5.1% of patients, however, reactions are typically mild. Despite the harms listed, it is ultimately determined that the benefits of timely treatment outweigh all harms studied.  Although faster door-to-needle times could lead to rushed assessments and increased complications, the literature demonstrates that as more patients have door-to-needle times ≤ 60 minutes, there is a corresponding improvement in variables such as in-hospital mortality, symptomatic intracranial hemorrhage rates, and discharge to the home. Tong et al. found among patients who received IV alteplase within 4.5 hours of time last known to be well, and as a greater percent of these patients had door-to-needle times ≤ 60 minutes throughout the last decade, in-hospital all-cause mortality decreased from 7.2% in 2008 to 5.1% in 2017 (P<0.001), symptomatic intracranial hemorrhage rates within 36 hours decreased from 6.3% in 2008 to 3.4% in 2017 (P<0.001), and discharge to the home increased from 23.6% 2008 to 50.9% in 2017 (P<0.001) (2018). In addition, a 2016 Scientific Statement put forth by the AHA/ASA addresses the risk of symptomatic intracranial hemorrhages and makes the following recommendation: For severe stroke symptoms, intravenous alteplase is indicated within 3 hours from symptom onset of ischemic stroke. Despite increased risk of hemorrhagic transformation, there is still proven clinical benefit for patients with severe stroke symptoms (Demaerschalk et al., 2016). (Class I; Level A) |
| Identify any new studies conducted since the SR. Do the new studies change the conclusions from the SR? | 1. Citation: Fonarow GC, Zhao X, Smith EE, Saver JL, Reeves MJ, Bhatt DL, et al. Door-to-needle times for tissue plasminogen activator administration and clinical outcomes in acute ischemic stroke before and after a quality improvement initiative. JAMA. 2014;311(16):1632-1640. DOI:10.1001/jama.2014.3203.   Description: Observational study as a part of Target Stroke Initiative that looked to evaluate door-to-needle times for tPA administration. Additionally the study evaluated the proportion of patients with door-to-needle times of ≤ 60 minutes before and after a quality improvement initiative to determine if improvements in door-to-needle times were associated with improved clinical outcomes.  Results: “Importantly, the improvement in timeliness in tPA administration following the start of the program was associated with improved clinical outcomes including lower in-hospital mortality, more frequent discharge to a more independently functioning environment, and lower rates of tPA complications, including symptomatic intracranial hemorrhage. These findings further reinforce the importance and clinical benefits of more rapid administration of intravenous tPA.”  Conclusion: This study further highlights the importance of a door-to-needle time of ≤ 60 minutes for the administration of tPA following an ischemic stroke. While timely administration leads to improved clinical outcomes, the study highlights that less than 30% of patients are receiving treatment within the recommended timeline and further emphasizes the opportunity for improvement for facilities.   1. Citation: Emberson J, Lees KR, Lyden P, Blackwell L, Albers G, Bluhmki E, et al. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomized trials. Lancet. 2014;384(9958):1929-1935.   Description: Meta-analysis of individual patient data from 6756 patients in nine randomized trials comparing alteplase with placebo or open control. The primary goal of the analysis was to explore the extent to which treatment delay affected the effect of the alteplase and to establish if age or stroke severity affected treatment effects. The authors defined good stroke outcome as no significant disability at 3-6 months as defined by a modified Rankin scale of 0 or 1. Additional outcomes included symptomatic intracranial hemorrhage, fatal intracranial hemorrhage within 7 days and 90-day mortality.  Results: “Alteplase significantly increased the odds of a good outcome, with earlier treatment resulting in significantly greater proportional benefit increasing proportional benefit with earlier treatment.” The study also states, “The effect of alteplase on a good outcome was chiefly driven by treatment delay; after controlling for treatment delay, neither age nor severity of stroke contributed significant additional predictive value.”  The tables below demonstrate the importance of early treatment for improved outcomes.      Conclusion: The results of the meta-analysis indicate that the early administration of tPA from symptom onset is effective in improving good outcomes for stroke patients. The meta-analysis further emphasizes the importance of timely administration of tPA and shows a proportional benefit with earlier treatment.  Provided below are the citations of new studies in support of this measure, since the publication of the 2018 AHA/ASA Guidelines. There are no significant updates to the body of evidence since the 2018 guideline supporting this measure, that would contradict or impact the intent of this measure, namely that the benefit of alteplase is time dependent, amongst ischemic stroke patients.   1. Ringleb, P., Bendszus, M., Bluhmki, E., Donnan, G., Eschenfelder, C., Fatar, M., … ECASS-4 study group (2019). Extending the time window for intravenous thrombolysis in acute ischemic stroke using magnetic resonance imaging-based patient selection. International journal of stroke : official journal of the International Stroke Society, 14(5), 483–490. doi:10.1177/1747493019840938 2. Tong, X., Wiltz, J. L., George, M. G., Odom, E. C., King, S. M. C., Chang, T., …. (2018). A Decade of Improvement in Door-to-Needle Time Among Acute Ischemic Stroke Patients, 2008 to 2017. *Circulation: Cardiovascular Quality and Outcomes, 11*(12). doi: 10.1161/circoutcomes.118.004981 |

Citations (Note: when applicable, we adhered to journals’ request for a specific citation format to be followed for their study; otherwise we followed the APA format for citations):

1. Demaerschalk BM, Kleindorfer DO, Adeoye OM, Demchuk AM, Fugate JE, Grotta JC, Khalessi AA, Levy EI, Palesch YY, Prabhakaran S, Saposnik G, Saver JL, Smith EE; on behalf of the American Heart Association Stroke Council and Council on Epidemiology and Prevention. Scientific rationale for the inclusion and exclusion criteria for intravenous alteplase in acute ischemic stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2016;47:581–641.
2. Halperin JL, Levine GN, Al-Khatib SM, Birtcher KK, Bozkurt B, Brindis RG, Cigarroa JE, Curtis LH, Fleisher LA, Gentile F, Gidding S, Hlatky MA, Ikonomidis J, Joglar J, Pressler SJ, Wijeysundera DN. Further evolution of the ACC/AHA clinical practice guideline recommendation classification system: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation.* 2016;133:1426-1428. DOI: 10.1161/CIR.0000000000000312.
3. Tong, X., Wiltz, J. L., George, M. G., Odom, E. C., King, S. M. C., Chang, T., … . (2018). A Decade of Improvement in Door-to-Needle Time Among Acute Ischemic Stroke Patients, 2008 to 2017. *Circulation: Cardiovascular Quality and Outcomes, 11*(12). doi: 10.1161/circoutcomes.118.004981

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

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

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

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

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