Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

Circ Cardiovasc Qual Outcomes. Author manuscript; available in PMC 2019 January 11.

Published in final edited form as:

Circ Cardiovasc Qual Outcomes. 2018 December ; 11(12): e004981. doi:10.1161/CIRCOUTCOMES.118.004981.

A Decade of Improvement in Door-to-Needle Time Among Acute Ischemic Stroke Patients, 2008 to 2017

Xin Tong, MPH,
Division for Heart Disease and Stroke Prevention, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA

Jennifer L. Wiltz, MD, MPH,
Division for Heart Disease and Stroke Prevention, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA

United States Public Health Service, Atlanta, GA

Mary G. George, MD, MSPH,
Division for Heart Disease and Stroke Prevention, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA

Erika C. Odom, PhD, MS,
Division for Heart Disease and Stroke Prevention, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA

United States Public Health Service, Atlanta, GA

Sallyann M. Coleman King, MD, MSc,
Division for Heart Disease and Stroke Prevention, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA

United States Public Health Service, Atlanta, GA

Tiffany Chang, MPH,
Division for Heart Disease and Stroke Prevention, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA

IHRC, Inc., Atlanta, GA

Xiaoping Yin, MS,
Division for Heart Disease and Stroke Prevention, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA

IHRC, Inc., Atlanta, GA

Paul Coverdell National Acute Stroke Program team, and **Robert K. Merritt, MS**
Division for Heart Disease and Stroke Prevention, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA

Correspondence Xin Tong, MPH, Division for Heart Disease and Stroke Prevention, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, 4770 Buford Hwy, MS–F77, Atlanta, GA 30341. xtong@cdc.gov.

Disclosures
None.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Abstract

BACKGROUND: The clinical benefit of intravenous (IV) alteplase in acute ischemic stroke is time dependent. We assessed the overall temporal changes in door-to-needle (DTN) time and examine the factors associated with DTN time ≤60 and ≤45 minutes.

METHODS AND RESULTS: A total of 496 336 acute ischemic stroke admissions were identified in the Paul Coverdell National Acute Stroke Program from 2008 to 2017. We used generalized estimating equations models to examine the factors associated with DTN time ≤60 and ≤45 minutes, and calculated adjusted odds ratios and 95% CI. Between 2008 and 2017, the percentage of acute ischemic stroke patients who received IV alteplase including those transferred, increased from 6.4% to 15.3%. After excluding those who received IV alteplase at an outside hospital, a total of 39 737 (8%) acute ischemic stroke patients received IV alteplase within 4.5 hours of the time the patient last known to be well. Significant increases were seen in DTN time ≤60 minutes (26.4% in 2008 to 66.2% in 2017, $P<0.001$), as well as DTN time ≤45 minutes (10.7% in 2008 to 40.5% in 2017, $P<0.001$). Patients aged 55 to 84 years were more likely to receive IV alteplase within 60 minutes, while those aged 55 to 74 years were more likely to receive IV alteplase within 45 minutes, as compared with those aged 18 to 54 years. Arrival by emergency medical service, and patients with severe stroke were more likely to receive IV alteplase within 60 and 45 minutes. Conversely, women, black patients as compared with white, and patients with a medical history of diseases associated with stroke were less likely to receive DTN time ≤60 or 45 minutes.

CONCLUSIONS: Rapid improvements in DTN time were observed in the Paul Coverdell National Acute Stroke Program; however, opportunities to reduce disparities remain.

Keywords

brain ischemia; cerebral infarction; plasminogen; stroke; tissue plasminogen activator

Each year, nearly 800 000 people in the United States experience a new or recurrent stroke, of which nearly 90% are ischemic strokes.[1] Intravenous (IV) tissue plasminogen activator therapy (IV alteplase) is the only Food and Drug Administration approved medication for acute ischemic stroke (AIS) thrombolysis, and national guidelines recommend an arrival to treatment initiation (door-to-needle [DTN]) time of ≤60 minutes.[2] In 2013, the National Quality Forum endorsed this as a performance metric. Among clinically eligible patients, IV alteplase is recommended within 4.5 hours of the time the patient was last known to be well.[3]

In 2010, the American Heart Association/American Stroke Association launched its Target Stroke initiative with a phase I goal of ≤60 minutes for the DTN time for at least 50% of AIS patients treated with IV alteplase. Subsequently in 2014, Target Stroke phase II goals were established: to achieve a DTN time within 60 minutes in at least 75% of patients, and DTN time within 45 minutes in at least 50% of patients.[4,5] These initiatives have demonstrated the ability to improve the timeliness of IV alteplase administration in US hospitals.

Since 2001, the Centers for Disease Control and Prevention (CDC) has funded the development and implementation of the Paul Coverdell National Acute Stroke Program

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

(PCNASP), an acute stroke quality of care registry, which is state-centric and hospital based. In 2004, PCNASP was implemented in 4 state health departments (Georgia, Illinois, Massachusetts, and North Carolina), in 2007 funding to 6 health departments (Georgia, Massachusetts, Michigan, Minnesota, North Carolina, and Ohio), in 2012 funding extended to 11 states (Arkansas, California, Georgia, Iowa, Massachusetts, Michigan, Minnesota, New York, North Carolina, Ohio, and Wisconsin), and in 2015 funding to 9 states (California, Georgia, Massachusetts, Michigan, Minnesota, New York, Ohio, Washington, and Wisconsin). This public health program not only provides surveillance on stroke care quality, but implements targeted interventions to improve prehospital and in-hospital quality of acute stroke care, and improve transitions from hospital to home. Funded state health department staff provide regular and ongoing technical assistance to participating hospitals and convene hospitals as a group to promote cross-pollination of successful strategies to improve stroke quality of care on a variety of established stroke care performance measures, including improving DTN times.[6]

In this study, we conducted analyses to assess improvements in DTN times among AIS patients treated with IV alteplase in the CDC PCNASP between January 2008 and December 2017, and explored potential patient and hospital factors associated with achieving the time targets of 60 minutes or less and 45 minutes or less.

METHODS

Data collected by PCNASP is not currently publically available to other researchers for purposes of reproducing the results or replicating the procedure. However, PCNASP has established protocols where researchers can submit project proposals in which CDC analysts will provide generated result tables to fulfill research or analytic requests.

PCNASP includes patients aged ≥18 years with a physician's clinical diagnosis in the medical record of AIS, intracerebral hemorrhage (ICH), subarachnoid hemorrhage, or transient ischemic attack (TIA). The details of the PCNASP program design have been published previously.[7] This analysis included all cases collected in the PCNASP from January 2008 to December 2017, with a clinically assigned diagnosis of AIS and treated with IV alteplase within 4.5 hours of the time last known to be well. Because we used the clinical diagnosis for case identification, *International Classification of Diseases, Ninth Revision, Clinical Modification* codes were not used in this analysis.

During 2008 to 2017, there were 496 336 patients from 573 participating hospitals with a clinical diagnosis of AIS in the PCNASP. Among them, 57 712 (12%) received IV alteplase, but 16 629 (3%) of patients without DTN times were excluded because they received IV alteplase at outside hospitals and were subsequently transferred to stroke centers. Among the remaining 41 083 (8%) receiving IV atleplase, we further excluded 371 (1%) patients with missing DTN times, and 975 (2%) patients who arrived at the hospital >4.5 hours after symptom onset. The final study sample was 39 737 patients from 419 participating hospitals.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Statistical Methods

Demographic and clinical factors included: age (18–54, 55–64, 65–74, 75–84, 85+ years), sex, race (white, black, and other race), arrival by emergency medical services (EMS), National Institutes of Health Stroke Scale (NIHSS) score at admission, smoking status, history of hypertension, dyslipidemia, myocardial infarction, or coronary artery disease, heart failure, diabetes mellitus, nonvalvular atrial fibrillation (AF), and prior stroke. The hospital characteristics included: bed size (<100, 100–199, 200–399, 400+ beds), annual stroke admissions (<100, 100–299, 300+), presence of a stroke unit, teaching hospital, and certified stroke center (certified as a Joint Commission Primary Stroke Center or Joint Commission Comprehensive Stroke Center, or other similar organization). To account for the clustering of patients within hospitals, generalized estimating equations (GEE) were used to assess the association between the outcomes (DTN time ≤60, or ≤45 minutes, in-hospital all-cause mortality, and symptomatic ICH within 36 hours) and the prognostic factors. In GEE multivariable modeling using unstructured correlation structure, we included the selected variables of interest along with the year of event (2008 through 2017). Because of the collinearity between teaching hospitals, hospital bed size, and certified stroke centers, we chose to include only the hospital bed size in the final multivariate model. Because patients were clustered within hospitals, to provide appropriate estimates of the standard errors, the hospital was treated as a cluster variable in the model. Adjusted odds ratios (AORs) were obtained, along with 95% CI, and a $P<0.05$ was considered statistically significant. All analyses were done using SAS software (version 9.3; SAS Institute, Cary, North Carolina). The CDC Institutional Review Board approved this study.

RESULTS

Among 496 336 acute ischemic patients identified in PCNASP between 2008 and 2017, 57 712 (12%) patients received IV alteplase (including patients who received IV alteplase at an outside hospital and were then transferred to a Coverdell participating hospital). The percentage of patients receiving IV alteplase increased significantly from 6.4% in 2008 to 15.3% in 2017 (Figure 1, $P<0.0001$). There were 39 737 patients from 419 participating hospitals who received IV alteplase (excluding transfers) within 4.5 hours symptom onset. The median DTN time decreased significantly from 79 minutes in 2008 to 51 minutes in 2017 (Figure 2, $P<0.0001$). By 2017, 51% of patients arrived the hospital within 2 hours and treated with IV alteplase within 3 hours of last known to be well, 12% of patients arrived between 2 to 3.5 hours and were treated within 4.5 hours of last known to be well, as compared with 21% and 4%, respectively in 2008 (Figure 2, $P<0.0001$).

Of the 419 participating hospitals, 12% had <100 beds, 18% had 100–199 beds, 37% had 200–399 beds, and 33% had 400+ beds (Figure 3). Sixteen percent of the hospitals had annual stroke admissions <100, 41% had 100–299, and 43% had 300+. Forty-seven percent of hospitals had a stroke unit, 52% were teaching hospitals, and 59% were certified stroke centers (Figure 3). Among hospitals with >200 beds, 90% were teaching hospitals and 80% were stroke certified center versus only 49% and 59% among hospitals with <200 beds, respectively (Data not shown).

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

The median age of patients receiving IV alteplase within 4.5 hours of time last known to be well was 71 years (interquartile range, 59–82) and 41.4% of patients were 75 years or older (Table 1). Overall, 50.3% of patients were men and 74.7% were white. Seventy-seven percent of patients arrived by EMS and the median NIHSS score was 8 (interquartile range, 5–15). The majority of patients (70.6%) had hypertension, 43.5% had dyslipidemia, 25.6% had diabetes mellitus, 19.9% had AF, and 17.6% had a prior stroke (Table 1).

Door-to-Needle Time Within 60 Minutes

Overall, 21 217 (53.4%) patients received IV alteplase within 60 minutes and there was a significant increase in the proportion of patients treated within 60 minutes from 2008 to 2017 (26.4% in 2008 to 66.2% in 2017, $P<0.001$, Figure 1). Unadjusted analyses showed statistically significant differences in the proportion of patients treated within 60 minutes by age group, sex, race, arrival by EMS, NIHSS recorded, NIHSS score, and medical history of prior stroke, hypertension, myocardial infarction/coronary artery disease, heart failure, diabetes mellitus, and AF (Table 1). Dyslipidemia and being a smoker were not associated with IV alteplase within 60 minutes ($P=0.08$ and $P=0.94$, respectively). Hospital characteristics varied by DTN time. Hospitals who reported annual stroke admissions ≥300, having a stroke unit, being a teaching hospital, or being a certified stroke center were associated with a DTN time ≤60 minutes ($P<0.001$ for all). Patients receiving IV alteplase within 60 minutes were more likely to be discharged to home, and less likely to develop symptomatic ICH within 36 hours after IV alteplase as compared with those treated beyond 60 minutes. The percent of patients who died in-hospital was lower among those who were treated within 60 minutes than those treated beyond 60 minutes, but this was not statistically significant (6.0% versus 6.4%, $P=0.06$; Table 1).

GEE multivariate model results showed those aged 55 to 84 years were more likely to be treated within 60 minutes. The AOR for patients aged 55 to 64 years was 1.16 (95% CI, 1.07–1.25), 1.16 (95% CI, 1.08–1.25) for ages 65–74 years, and 1.15 (95% CI, 1.07–1.25) for ages 75 to 84 years compared with those aged 18 to 54 years old. Women and blacks were less likely to be treated within 60 minutes as compared with their counterparts (AOR of 0.83, 95% CI, 0.79–0.87; and 0.86, 95% CI, 0.81–0.92, respectively). Patient arrival by EMS and those with a higher NIHSS score were more likely to receive IV alteplase within 60 minutes. As compared with mild stroke (NIHSS score of 0–4), the AOR was 1.55 (95% CI, 1.46–1.65) for NIHSS scores of 5 to 9, 1.90 (95% CI, 1.76–2.04) for NIHSS scores of 10 to 14, 1.94 (95% CI, 1.80–2.10) for NIHSS scores of 15 to 20, and 1.69 (95% CI, 1.55–1.83) for NIHSS scores >20, respectively ($P<0.001$ for all). Importantly, a medical history of stroke, hypertension, myocardial infarction/coronary artery disease, heart failure, diabetes mellitus, or AF were inversely associated with DTN time ≤60 minutes. Hospital characteristics associated with greater odds of DTN time ≤60 minutes were bed size of ≥200, annual stroke admissions ≥300, or having a stroke unit. After controlling for demographic and clinical characteristics, compared with 2008, there was a significant improvement in achieving DTN time within 60 minutes in the subsequent years ($P\leq0.001$ for all, Table 2). In 2017, the AOR for achieving a DTN time ≤60 minutes was 7.32 (95% CI, 6.15–8.72) as compared with 2008.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Door-to-Needle Within 45 Minutes

There was a significant increase in the percent of patients treated within 45 minutes from 2008 to 2017 (10.7% in 2008 and 40.5% in 2017, $P<0.001$, Figure 1). Similar to achieving a DTN time ≤60 minutes, unadjusted analyses showed there were differences between patients treated within 45 minutes and those treat beyond 45 minutes by sociodemographic and clinical factors (Table 1). Patients from hospitals with annual stroke admissions ≥300, ≥400 beds, having a stroke unit, being teaching hospitals, or being a certified stroke center were more likely to be treated within 45 minutes. Significantly more patients (45%) treated within 45 minutes were discharged to home compared with those treated beyond 45 minutes. Symptomatic ICH within 36 hours were significantly less prevalent among patients treated within 45 minutes compared with those treated beyond 45 minutes (Table 1).

In GEE adjusted analyses, patients aged 55 to 74 years old were more likely to receive IV alteplase in <45 minutes compared with those aged 18 to 54 years old (Table 2). Women, blacks, patients with a medical history of stroke, hypertension, heart failure, diabetes mellitus, or AF were less likely to be treated within 45 minutes. Patients arriving by EMS, patients with higher NIHSS scores, from hospitals with ≥400 beds, or ≥300 annual stroke admissions, or from hospitals having a stroke unit were more likely to be treated within 45 minutes. After adjusting for demographic and clinical characteristics, significant improvements in achieving DTN time ≤45 minutes were identified between 2009 and 2017 compared with 2008 except for in 2010 (Table 2).

Clinical Outcomes Associated With DTN

Overall, the in-hospital all-cause mortality among those receiving IV alteplase within 4.5 hours of time last known to be well was 6.2%, and it significantly decreased from 7.2% in 2008 to 5.1% in 2017 ($P<0.001$, Figure 4). There were 1 471 (3.7%) patients who experienced symptomatic ICH within 36 hours, and 276 (0.7%) had life threatening or serious systemic hemorrhage within 36 hours (Table 1). The percentage of symptomatic ICH within 36 hours decreased significantly from 6.3% in 2008 to 3.4% in 2017 ($P<0.001$). Overall 44% patients were discharged to home, significantly increased from 23.6% in 2008 to 50.9% in 2017, respectively ($P<0.001$).

GEE adjusted analyses showed both DTN time ≤60 and DTN time ≤45 were significantly associated with the lower in-hospital all-cause mortality, symptomatic ICH within 36 hours, and higher odds of discharge to home compared with longer DTN time (Table 3).

DISCUSSION

Our results showed a substantial increase in achieving DTN time ≤60 minutes and DTN time ≤45 minutes over a decade in PCNASP. By 2013, PCNASP reached the goal of at least 50% of patients receiving IV alteplase within 60 minutes of hospital arrival. Revised goals for DTN time targets are now ≤60 minutes for at least 75% of patients and DTN time ≤45 minutes for at least 50% of patients. Based on the most recent trends demonstrated in this analysis, if current trends continue, there is potential to achieve these goals in the PCNASP in 2020. About the safety of decreasing DTN times, we observed that these reductions in

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

DTN time were associated with decreases in adverse events from thrombolysis or in-hospital all-cause mortality, and were associated with an increase in discharges to home.

Consistent with results from other studies,[8,9] we found that arrival by EMS, increasing age (except 85+), and greater stroke severity as measured by NIHSS were associated with shorter DTN times. Patients aged 55 to 74 years were more likely to meet both DTN time targets as compared with those aged 18 to 54 years. Women, blacks, and patients with stroke risk factors and other cardiovascular diseases were less likely to receive IV alteplase within DTN goals. A meta-analysis of 18 studies found that women were consistently less likely to receive IV alteplase, and another study showed blacks were significantly less likely to receive IV alteplase.[10,11] Previous studies only identified that a medical history of AF, diabetes mellitus, and prior stroke were associated with not meeting the DTN time ≤60 minutes time target.[8] In our study, in addition to the factors reported by others, we found patients with medical history of hypertension, or heart failure were also less likely to receive IV alteplase within DTN target goals, which might indicate clinically significant challenges in the care of patients with comorbidities. Our finding that achievement of the time targets were less likely among those aged 18 to 54 years could indicate challenges in diagnosing a stroke versus a stroke mimic in younger patients.

Although the best practices have been developed, recent time target initiatives have necessitated implementation of numerous strategies within hospitals and among EMS providers to achieve DTN goals.[4,5,12] The study from the Get With The Guidelines—Stroke initiative showed significant improvement in DTN ≤60 minutes after the postintervention (initiative).[13] In PCNASP, we observed similar trends in improvements but with a more steady increase. This might reflect the ongoing efforts of quality improvement from the state health department making improvement before the Get With The Guidelines Target Stroke initiative. In a recent narrative review of DTN quality improvement strategies among single centers and across multiple hospitals, successful activities in reducing DTN time included prenotification of arrival by EMS and single-call activation of the stroke team.[14]

We found that the rates of achieving DTN time targets were different among the participating PCNASP hospitals, likely reflecting varying levels of infrastructure and resources required for acute stroke care, but also reflecting variances in patients' comorbidities, stroke severity, and age. In the SITS-ISTR study (Safe Implementation of Thrombolysis in Stroke International Stroke Thrombolysis Registry), adjusted analyses showed that stroke centers with stroke case volumes ≥100 per year had greater annual decreases in DTN time.[15] One study used the failure mode, effects and criticality analysis approach to identify the common critical failures in an academic hospital and a community hospital in achieving low DTN times. Their findings included delays in the emergency department; incorrect triage diagnosis among walk-in patients; delays in IV alteplase treatment; and delays in obtaining brain imagining.[16] Another study from 10 European stroke centers found delays in DNT times for those arriving within 30 minutes of symptom onset, but DTN time was shorter among those arriving near the end of treatment windows, among men, and, similar to our findings those over age 50 versus younger, and among those <80 years versus over 80 years.[17]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Our study has several limitations. PCNASP is a quality improvement program, focused on improving care across the continuum, including in-hospital and prehospital care, as well as the posthospital transition from hospital to home; therefore, the results may not be generalizable. The hospitals that participated in the PCNASP, as well as the program requirements for participation changed over time. However, we controlled for hospital characteristics through the GEE models to minimize this bias. The PCNASP does not collect information on glucose level at the time of admission, CT scan results, or whether antihypertensive medications were required in the ED before giving IV alteplase, which might affect treatment decisions. Finally, about the concern for case selection bias with registry data, CDC requires that funded states track the extent of case abstraction of participating hospitals within the state registries; however, we do not conduct a formal national audit of the data using a sole source abstractor. While the potential for case selection bias exists, the majority of hospitals are making every effort to abstract all stroke cases. As noted above, we are unable to account for selection bias in the decision to treat with IV alteplase, but we can provide information on the real-world experience in the use of IV alteplase and DTN time targets. The strength of this study is that it included a large cohort of patients treated in a variety of academic and nonacademic hospitals with greatly varying stroke case volumes.

In conclusion, significant improvements in DTN time were observed in PCNASP over a decade, with steady increases that began in 2010. We found that patients aged 55 to 74 years, arrival by EMS, and patients with more severe stroke were more likely to receive IV alteplase within either DTN targets. Women, blacks, and patients with stroke risk factors or other cardiovascular disease were less likely to be treated according to DTN goals. Focusing on shortening DTN times through dedicated quality improvement activities has been successful, and has not been associated with an increase in serious adverse events related to thrombolysis. However, opportunities exist to reduce the disparities in treatment, especially among women and blacks, and further improve acute stroke care and systems of care.

Acknowledgments

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

REFERENCES

1. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, de Ferranti SD, Floyd J, Fornage M, Gillespie C, Isasi CR, Jiménez MC, Jordan LC, Judd SE, Lackland D, Lichtman JH, Lisabeth L, Liu S, Longenecker CT, Mackey RH, Matsushita K, Mozaffarian D, Mussolino ME, Nasir K, Neumar RW, Palaniappan L, Pandey DK, Thiagarajan RR, Reeves MJ, Ritchey M, Rodriguez CJ, Roth GA, Rosamond WD, Sasson C, Towfighi A, Tsao CW, Turner MB, Virani SS, Voeks JH, Willey JZ, Wilkins JT, Wu JH, Alger HM, Wong SS, Muntner P; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics-2017 update: a report from the American Heart Association. Circulation. 2017;135:e146–e603. doi: 10.1161/CIR.0000000000000485 [PubMed: 28122885]

2. Jauch EC, Saver JL, Adams HP, Jr, Bruno A, Connors JJ, Demaerschalk BM, Khatri P, McMullan PW, Jr, Qureshi AI, Rosenfield K, Scott PA, Summers DR, Wang DZ, Wintermark M, Yonas H; American Heart Association Stroke Council; Council on Cardiovascular Nursing; Council on Peripheral Vascular Disease; Council on Clinical Cardiology. Guidelines for the early management

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2013;44:870–947. doi: 10.1161/STR.0b013e318284056a [PubMed: 23370205]

3. Powers WJ, Rabinstei AA, Ackerso T, Adeoy OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, Jauc EC, Kidwel CS, Leslie-Mazw TM, Ovbiagel B, Scot PA, Sheth KN, Southerland AM, Summers DV, Tirschwell DL; 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:e46–e110. doi: 10.1161/STR.0000000000000158 [PubMed: 29367334]
4. Fonarow GC, Smith EE, Saver JL, Reeves MJ, Hernandez AF, Peterson ED, Sacco RL, Schwamm LH. Improving door-to-needle times in acute ischemic stroke: the design and rationale for the American Heart Association/American Stroke Association's Target: Stroke initiative. Stroke. 2011;42:2983–2989. [PubMed: 21885841]
5. Xian Y, Xu H, Lytle B, Blevins J, Peterson ED, Hernandez AF, Smith EE, Saver JL, Messe SR, Paulsen M, Suter RE, Reeves MJ, Jauch EC, Schwamm LH, Fonarow GC. Use of strategies to improve door-to-needle times with tissue-type plasminogen activator in acute ischemic stroke in clinical practice: findings from target: stroke. Circ Cardiovasc Qual Outcomes. 2017;10:e003227. doi: 10.1161/CIRCOUTCOMES.116.003227. [PubMed: 28096207]
6. Centers for Disease Control and Prevention (CDC). Paul Coverdell Acute Stroke Program 2012–2015 Evaluation Summary. https://wwwcdcgov/dhdsp/evaluation_resources/pcnasp-evaluation-summary.htm. Accessed May 1, 2018.
7. George MG, Tong X, McGruder H, Yoon P, Rosamond W, Winquist A, Hinchey J, Wall HK, Pandey DK; Centers for Disease Control and Prevention (CDC). Paul Coverdell National Acute Stroke Registry Surveillance—four states, 2005–2007. MMWR Surveill Summ. 2009;58:1–23.
8. Fonarow GC, Smith EE, Saver JL, Reeves MJ, Bhatt DL, Grau-Sepulveda MV, Olson DM, Hernandez AF, Peterson ED, Schwamm LH. Timeliness of tissue-type plasminogen activator therapy in acute ischemic stroke: patient characteristics, hospital factors, and outcomes associated with door-to-needle times within 60 minutes. Circulation. 2011;123:750–758. [PubMed: 21311083]
9. Khor MX, Bown A, Barrett A, Counsell CE, MacLeod MJ, Reid JM. Pre-hospital notification is associated with improved stroke thrombolysis timing. J R Coll Physicians Edinb. 2015;45:190–195. doi: 10.4997/JRCPE.2015.303 [PubMed: 26517096]
10. Reeves M, Bhatt A, Jajou P, Brown M, Lisabeth L. Sex differences in the use of intravenous rt-PA thrombolysis treatment for acute ischemic stroke: a meta-analysis. Stroke. 2009;40:1743–1749. doi: 10.1161/STROKEAHA.108.543181 [PubMed: 19228855]
11. Johnston SC, Fung LH, Gillum LA, Smith WS, Brass LM, Lichtman JH, Brown AN. Utilization of intravenous tissue-type plasminogen activator for ischemic stroke at academic medical centers: the influence of ethnicity. Stroke. 2001;32:1061–1068. [PubMed: 11340210]
12. Xian Y, Smith EE, Zhao X, Peterson ED, Olson DM, Hernandez AF, Bhatt DL, Saver JL, Schwamm LH, Fonarow GC. Strategies used by hospitals to improve speed of tissue-type plasminogen activator treatment in acute ischemic stroke. Stroke. 2014;45:1387–1395. doi: 10.1161/STROKEAHA.113.003898 [PubMed: 24713527]
13. Fonarow GC, Zhao X, Smith EE, Saver JL, Reeves MJ, Bhatt DL, Xian Y, Hernandez AF, Peterson ED, Schwamm LH. 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;311:1632–1640. doi: 10.1001/jama.2014.3203 [PubMed: 24756513]
14. Kamal N, Smith EE, Jeerakathil T, Hill MD. Thrombolysis: improving door-to-needle times for ischemic stroke treatment - a narrative review. Int J Stroke. 2018;13:268–276. doi: 10.1177/1747493017743060 [PubMed: 29140185]
15. Strbian D, Ahmed N, Wahlgren N, Lees KR, Toni D, Roffe C, Surakka IL, Tatlisumak T; SITS Investigators. Trends in door-to-thrombolysis time in the safe implementation of stroke thrombolysis registry: effect of center volume and duration of registry membership. Stroke. 2015;46:1275–1280. doi: 10.1161/STROKEAHA.114.007170 [PubMed: 25828238]
16. Prabhakaran S, Khorzad R, Brown A, Nannicelli AP, Khare R, Holl JL. Academic-community hospital comparison of vulnerabilities in door-to-needle process for acute ischemic stroke. Circ

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Cardiovasc Qual Outcomes. 2015;8(6 suppl 3):S148–S154. doi: 10.1161/CIRCOUTCOMES.115.002085 [PubMed: 26515203]

17. Strbian D, Michel P, Ringleb P, Numminen H, Breuer L, Bodenant M, Seiffge DJ, Jung S, Obach V, Weder B, Tiainen M, Eskandari A, Gumbinger C, Gensicke H, Chamorro A, Mattle HP, Engelter ST, Leys D, Köhrmann M, Parkkila AK, Hacke W, Tatlisumak T. Relationship between onset-to-door time and door-to-thrombolysis time: a pooled analysis of 10 dedicated stroke centers. Stroke. 2013;44:2808–2813. doi: 10.1161/STROKEAHA.113.000995 [PubMed: 23887834]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

WHAT IS KNOWN

- Intravenous alteplase is an effective treatment for acute ischemic stroke, but time to treatment is critical.
- Fewer than one-third of patients treated with intravenous alteplase had door-to-needle (DTN) ≤60 minutes between 2003 and 2009 in hospitals participating in the Get With The Guidelines-Stroke Program.
- DTN time improved significantly during the postintervention period (Target: Stroke initiative) compared with the preintervention period as well as the clinical outcomes (discharge to home, in-hospital all-cause mortality, complications).

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

WHAT THE STUDY ADDS

- The latest trends in DTN time during a 10-year span (2008–2017) based on the Paul Coverdell National Acute Stroke Program.
- Significant and steady improvements in DTN ≤60 minutes and DTN ≤45 minutes were observed among the Paul Coverdell National Acute Stroke Program participating hospitals over 10 years, demonstrating the success of the quality improvement program.
- We identified the factors associated with DTN ≤60 minutes and DTN ≤45 minutes, highlighting the opportunities to further improve the stroke care.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

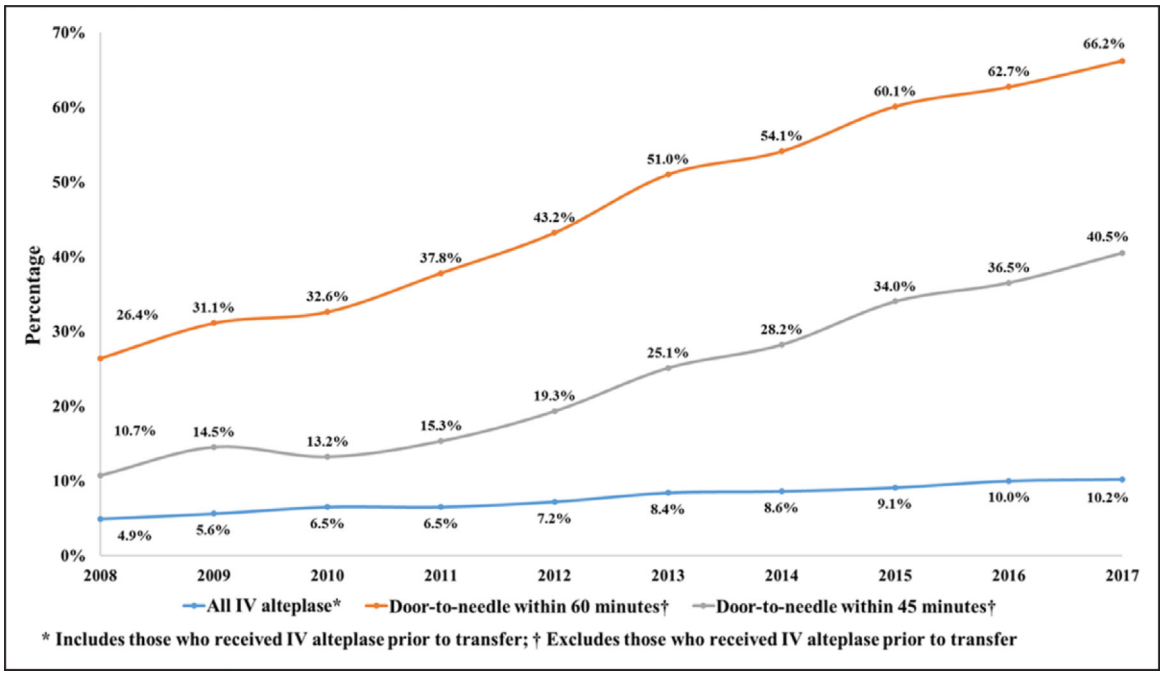

Figure 1.

Percentage of acute ischemic stroke patients given intravenous (IV) alteplase, door-to-needle time within 60 min, and door-to-needle time within 45 min among IV alteplase given within 4.5 h of symptom onset by year.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

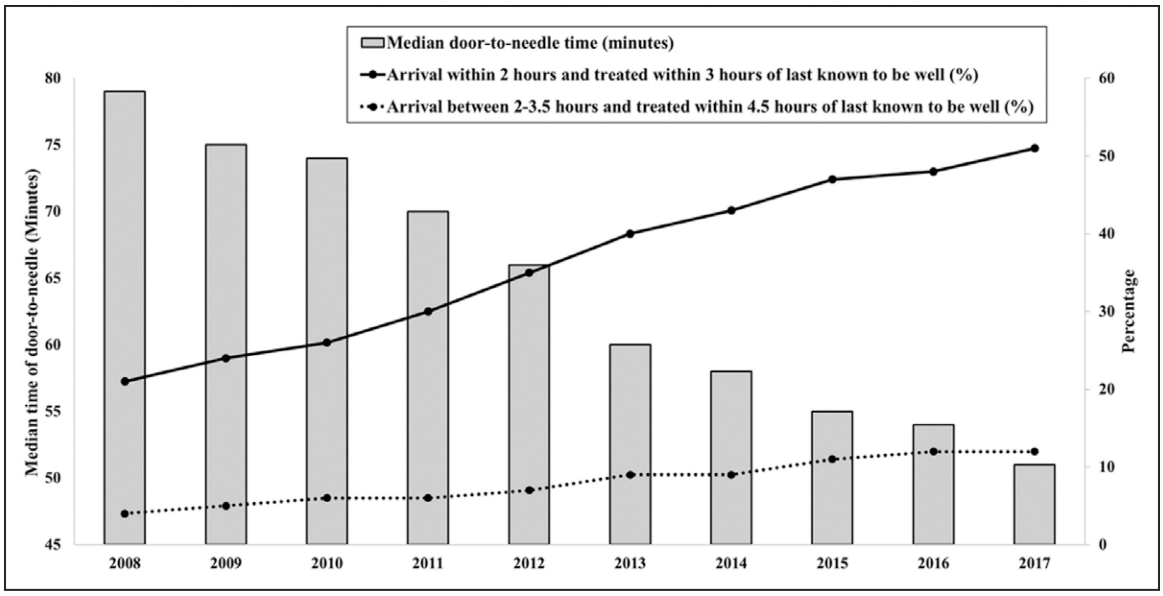

Figure 2.

Trends in median door-to-needle time and arrival and treated with intravenous (IV) alteplase times from last known to be well among patients receiving IV alteplase within 4.5 h of symptom onset, Paul Coverdell National Acute Stroke Program 2008–2017.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

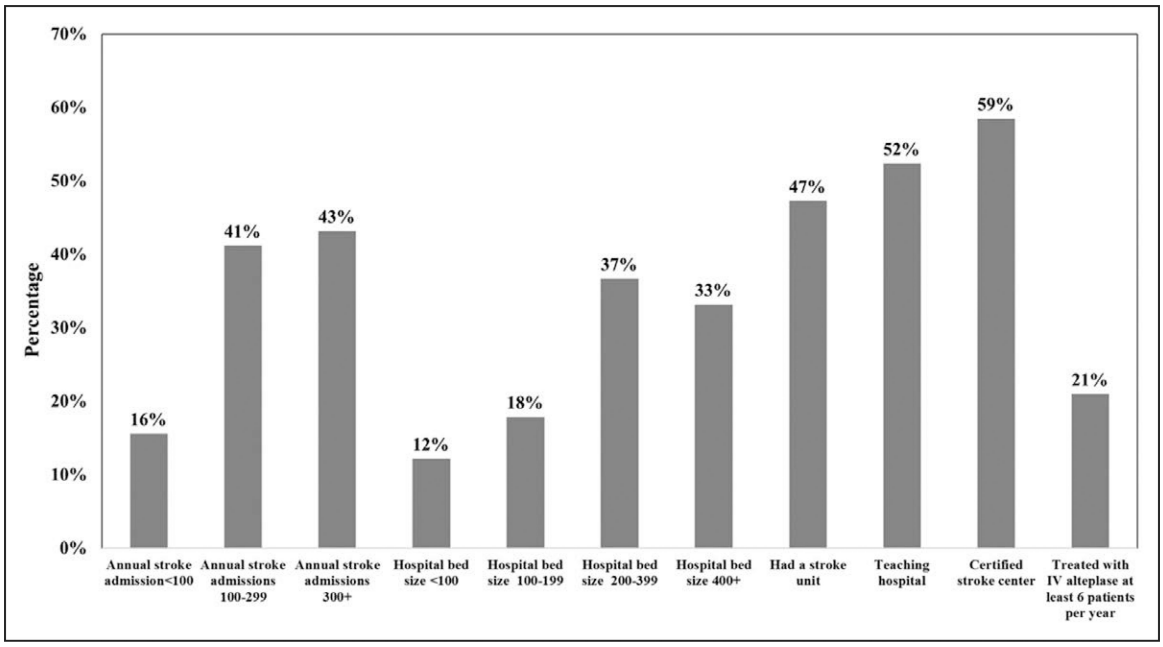

Figure 3.

Hospital characteristics among patients receiving intravenous (IV) alteplase within 4.5 h of symptom onset.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

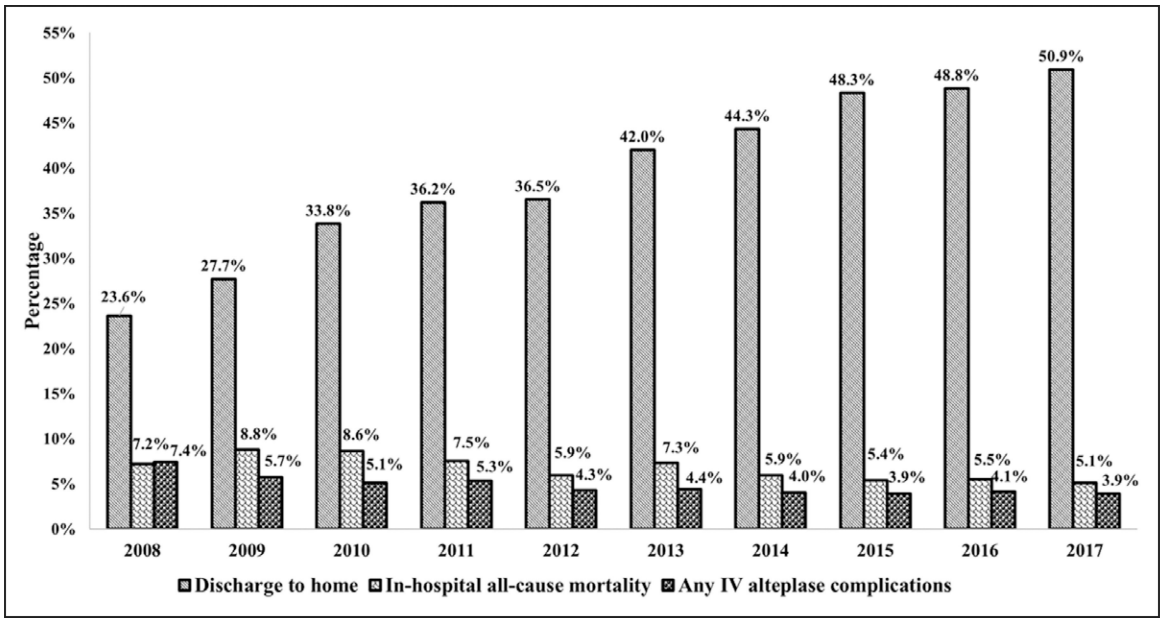

Figure 4.

Trends in percentage of in-hospital all-cause mortality, discharge to home, and symptomatic intracerebral hemorrhage (ICH) within 36 h among patients receiving intravenous (IV) alteplase within 4.5 h of symptom onset, Paul Coverdell National Acute Stroke Program 2008–2017.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Circ Cardiovasc Qual Outcomes. Author manuscript; available in PMC 2019 January 11.

Table 1.

Characteristics Among Acute Ischemic Patients Receiving IV Alteplase Within 4.5 Hours of Symptom Onset by Door-to-Needle Time Within 60 or 45 Minutes, PCNASP 2008–2017

Variables	Overall N (%) or Statistics	Door-to-Needle Time ≤60 Min			Door-to-Needle Time ≤45 Min		
		Yes	No	*P* Value*	Yes	No	*P* Value*
Total	39 737	21 217 (53.4)	18 520 (46.6)		11 445 (28.8)	28 292 (71.2)	
Demographics							
Age, y							
Median (IQR)	71 (59–82)	71 (59–82)	70 (58–82)		70 (59–81)	71 (59–82)	
Mean (SE)	69.5 (0.1)	69.8 (0.1)	69.2 (0.1)	<0.001	69.6 (0.1)	69.5 (0.1)	0.86
Age in groups							
18–54	6902 (17.4)	3471 (16.4)	3431 (18.5)		1890 (16.5)	5012 (17.7)	
55–64	7600 (19.1)	4102 (19.3)	3498 (18.9)		2260 (19.7)	5340 (18.9)	
65–74	8765 (22.1)	4822 (22.7)	3943 (21.3)		2676 (23.4)	6089 (21.5)	
75–84	9192 (23.1)	4945 (23.3)	4247 (22.9)		2613 (22.8)	6579 (23.3)	
85+	7278 (18.3)	3877 (18.3)	3401 (18.4)	<0.001	2006 (17.5)	5272 (18.6)	<0.001
Men	19 992 (50.3)	11 075 (52.2)	8917 (48.1)	<0.001	6203 (54.2)	13 789 (48.7)	<0.001
Race							
White	29 690 (74.7)	15 992 (75.4)	13 698 (74.0)		8673 (75.8)	21 017 (74.3)	
Black	7015 (17.7)	3501 (16.5)	3514 (19.0)		1799 (15.7)	5216 (18.4)	
Other race	3032 (7.6)	1724 (8.1)	1308 (7.1)	<0.001	973 (8.5)	2059 (7.3)	<0.001
Arrival by EMS	30 752 (77.4)	17 150 (80.8)	13 602 (73.4)	<0.001	9443 (82.5)	21 309 (75.3)	<0.001
NIHSS recorded	38 013 (95.7)	20 637 (97.3)	17 376 (93.8)	<0.001	11 209 (97.9)	26 804 (94.7)	<0.001
NIHSS score							
Median (IQR†)	8 (5–15)	9 (5–16)	8 (4–15)		10 (5–16)	8 (4–15)	
Mean (SE)	10.5 (0.04)	10.9 (0.1)	10.1 (0.1)	<0.001	11.1 (0.1)	10.3 (0.0)	<0.001
NIHSS in groups							
Missing	1724 (4.3)	580 (2.7)	1144 (6.2)		236 (2.1)	1488 (5.3)	
0–4	9301 (23.4)	4412 (20.8)	4889 (26.4)		2241 (19.6)	7060 (25.0)	

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Variables	Overall N (%) or Statistics	Door-to-Needle Time ≤60 Min			Door-to-Needle Time ≤45 Min		
		Yes	No	*P* Value*	Yes	No	*P* Value*
5–9	11 512 (29.0)	6320 (29.8)	5192 (28.0)		3356 (29.3)	8156 (28.8)	
10–14	6555 (16.5)	3810 (18.0)	2745 (14.8)		2152 (18.8)	4403 (15.6)	
15–20	6132 (15.4)	3587 (16.9)	2545 (13.7)		2077 (18.1)	4055 (14.3)	
>20	4513 (11.4)	2508 (11.8)	2005 (10.8)	<0.001	1383 (12.1)	3130 (11.1)	<0.001
Hospital characteristics							
No. of stroke admissions per year							
Missing	3485 (8.8)	1929 (9.1)	1556 (8.4)		1005 (8.8)	2480 (8.8)	
<100	707 (1.8)	231 (1.1)	476 (2.6)		96 (0.8)	611 (2.2)	
100–299	7901 (19.9)	3546 (16.7)	4355 (23.5)		1570 (13.7)	6331 (22.4)	
300+	27 644 (69.6)	15 511 (73.1)	12 133 (65.5)	<0.001	8 774 (76.7)	18 870 (66.7)	<0.001
Hospital size (by number of hospital beds)							
Missing	2893 (7.3)	1644 (7.7)	1249 (6.7)		871 (7.6)	2022 (7.1)	
<100	606 (1.5)	200 (0.9)	406 (2.2)		81 (0.7)	525 (1.9)	
100–199	2276 (5.7)	1008 (4.8)	1268 (6.8)		485 (4.2)	1791 (6.3)	
200–399	11 139 (28.0)	5294 (25.0)	5845 (31.6)		2527 (22.1)	8612 (30.4)	
400+	22 823 (57.4)	13 071 (61.6)	9752 (52.7)	<0.001	7481 (65.4)	15 342 (54.2)	<0.001
Stroke unit							
Missing	3047 (7.7)	1717 (8.1)	1330 (7.2)		901 (7.9)	2146 (7.6)	
Yes	24 052 (60.5)	13 415 (63.2)	10 637 (57.4)		7548 (66.0)	16 504 (58.3)	
No	12 638 (31.8)	6085 (28.7)	6553 (35.4)	<0.001	2996 (26.2)	9642 (34.1)	<0.001
Teaching hospital							
Missing	3662 (9.2)	1966 (9.3)	1696 (9.2)		995 (8.7)	2667 (9.4)	
Yes	26 956 (67.8)	15 024 (70.8)	11 932 (64.4)		8336 (72.8)	18 620 (65.8)	
No	9119 (22.9)	4227 (19.9)	4892 (26.4)	<0.001	2114 (18.5)	7005 (24.8)	<0.001
Certified stroke center							
Missing	3237 (8.1)	1730 (8.2)	1507 (8.1)		901 (7.9)	2336 (8.3)	
Yes	26 472 (66.6)	14 817 (69.8)	11 655 (62.9)		8335 (72.8)	18 137 (64.1)	
No	10 028 (25.2)	4670 (22.0)	5358 (28.9)	<0.001	2209 (19.3)	7819 (27.6)	<0.001

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Variables	Overall N (%) or Statistics	Door-to-Needle Time ≤60 Min			Door-to-Needle Time ≤45 Min		
		Yes	No	*P* Value*	Yes	No	*P* Value*
Medical history							
Prior stroke	7008 (17.6)	3469 (16.4)	3539 (19.1)	<0.001	1307 (14.9)	4486 (18.4)	<0.001
Hypertension	28 055 (70.6)	14 668 (69.1)	13 387 (72.3)	<0.001	5970 (67.9)	17 580 (71.9)	<0.001
Dyslipidemia	17 269 (43.5)	9135 (43.1)	8134 (43.9)	0.08	3659 (41.6)	10 669 (43.7)	0.001
MI/CAD	9249 (23.3)	4672 (22.0)	4577 (24.7)	<0.001	1901 (21.6)	5942 (24.3)	<0.001
Heart failure	3915 (9.9)	1949 (9.2)	1966 (10.6)	<0.001	789 (9.0)	2532 (10.4)	<0.001
Diabetes mellitus	10 174 (25.6)	5216 (24.6)	4958 (26.8)	<0.001	2033 (23.1)	6409 (26.2)	<0.001
Atrial fibrillation	7927 (19.9)	4106 (19.4)	3821 (20.6)	0.002	1704 (19.4)	5125 (21.0)	0.001
Current smoker	7660 (19.3)	4087 (19.3)	3573 (19.3)	0.94	1736 (19.8)	4764 (19.5)	0.98
Outcomes							
Discharge to home	17 322 (43.6)	9415 (44.4)	7907 (42.7)	0.0008	5154 (45.0)	12 168 (43.0)	<0.001
In-hospital death	2460 (6.2)	1269 (6.0)	119 187 (6.4)	0.06	671 (5.9)	1789 (6.3)	0.08
Symptomatic ICH within 36 h	1471 (3.7)	708 (3.3)	763 (4.1)	<0.001	341 (3.0)	1130 (4.0)	<0.001
Life threatening or serious systemic hemorrhage within 36 h	276 (0.7)	134 (0.6)	142 (0.8)	0.11	80 (0.7)	196 (0.7)	0.95

EMS indicates emergency medical service; ICH, intracranial hemorrhage; IQR, interquartile range; IV, intravenous; MI/CAD, myocardial infarction/coronary artery disease; NIHSS, National Institutes of Health Stroke Scale score; and PCNASP, Paul Coverdell National Acute Stroke Program.

*The *P* value obtained from type 3 analysis in unadjusted GEE models.

Circ Cardiovasc Qual Outcomes. Author manuscript; available in PMC 2019 January 11.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 2.

Adjusted Odds Ratios (AORs) of Predictors of Door-to-Needle Time Within 60 or 45 Minutes, PCNASP 2008–2017

	Door-to-Needle ≤60 min		Door-to-Needle ≤45 min	
Variables	**AOR (95% CI)**	***P* Value**	**AOR (95% CI)**	***P* Value**
Age in groups				
18–54	Reference		Reference	
55–64	1.16 (1.07–1.25)	<0.001	1.11 (1.02–1.21)	0.01
65–74	1.16 (1.08–1.25)	<0.001	1.12 (1.04–1.22)	0.005
75–84	1.15 (1.07–1.25)	0.003	1.06 (0.97–1.15)	0.19
85+	1.04 (0.95–1.13)	0.42	0.92 (0.84–1.01)	0.09
Sex				
Men	Reference		Reference	
Women	0.83 (0.79–0.87)	<0.001	0.80 (0.76–0.85)	<0.001
Race				
White	Reference		Reference	
Black	0.86 (0.81–0.92)	<0.001	0.82 (0.77–0.88)	<0.001
Other race	1.05 (0.96–1.15)	0.25	1.06 (0.96–1.16)	0.23
Arrival by EMS				
Yes	1.49 (1.41–1.58)	<0.001	1.46 (1.37–1.56)	<0.001
No	Reference		Reference	
NIHSS score				
0–4	Reference		Reference	
5–9	1.55 (1.46–1.65)	<0.001	1.47 (1.37–1.58)	<0.001
10–14	1.90 (1.76–2.04)	<0.001	1.89 (1.75–2.05)	<0.001
15–20	1.94 (1.80–2.10)	<0.001	2.02 (1.86–2.19)	<0.001
>20	1.69 (1.55–1.83)	<0.001	1.71 (1.56–1.87)	<0.001
Prior stroke				
Yes	0.78 (0.74–0.83)	<0.001	0.78 (0.73–0.83)	<0.001
No	Reference		Reference	
Hypertension				
Yes	0.89 (0.84–0.94)	<0.001	0.90 (0.85–0.95)	<0.001
No	Reference		Reference	
Dyslipidemia				
Yes	1.03 (0.98–1.08)	0.24	0.99 (0.94–1.05)	0.81
No	Reference		Reference	
MI/CAD				
Yes	0.90 (0.85–0.95)	0.001	0.93 (0.87–0.99)	0.02
No	Reference		Reference	
Heart failure				

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Variables	Door-to-Needle ≤60 min		Door-to-Needle ≤45 min	
	AOR (95% CI)	***P* Value**	**AOR (95% CI)**	***P* Value**
Yes	0.90 (0.83–0.97)	0.01	0.88 (0.81–0.96)	0.005
No	Reference		Reference	
Diabetes mellitus				
Yes	0.93 (0.88–0.98)	0.005	0.87 (0.82–0.93)	<0.001
No	Reference		Reference	
Atrial fibrillation				
Yes	0.86 (0.81–0.91)	<0.001	0.87 (0.81–0.93)	<0.001
No	Reference		Reference	
Current smoker				
Yes	1.00 (0.94–1.06)	0.95	0.97 (0.91–1.04)	0.41
No	Reference		Reference	
Hospital size (by no. of hospital beds)				
<200	Reference		Reference	
200–399	1.14 (1.03–1.25)	0.01	1.05 (0.93–1.17)	0.44
400+	1.43 (1.29–1.57)	<0.001	1.37 (1.22–1.53)	<0.001
Annual stroke admissions				
<300	Reference		Reference	
300+	1.29 (1.21–1.38)	<0.001	1.50 (1.39–1.62)	<0.001
Stroke unit				
Yes	1.19 (1.12–1.25)	<0.001	1.21 (1.14–1.28)	<0.001
No	Reference		Reference	
Year				
2008	Reference		Reference	
2009	1.43 (1.16–1.76)	0.001	1.49 (1.12–1.97)	0.006
2010	1.48 (1.22–1.79)	<0.001	1.27 (0.98–1.65)	0.07
2011	1.89 (1.56–2.27)	<0.001	1.56 (1.21–2.00)	<0.001
2012	2.32 (1.94–2.79)	<0.001	2.06 (1.62–2.64)	<0.001
2013	3.37 (2.83–4.02)	<0.001	2.94 (2.32–3.72)	<0.001
2014	3.88 (3.26–4.62)	<0.001	3.59 (2.84–4.53)	<0.001
2015	5.41 (4.55–6.44)	<0.001	4.96 (3.93–6.25)	<0.001
2016	6.18 (5.19–7.35)	<0.001	5.70 (4.52–7.18)	<0.001
2017	7.32 (6.15–8.72)	<0.001	6.98 (5.54–8.80)	<0.001

EMS indicates emergency medical service; MI/CAD, myocardial infarction/ coronary artery disease; NIHSS, National Institutes of Health Stroke Scale score; and PCNASP, Paul Coverdell National Acute Stroke Program.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 3.

Adjusted Odds Ratios (AORs)* for Clinical Outcomes Among Patients With Door-to-Needle Time Within 60 or 45 Minutes Among Patients Receiving IV Alteplase Within 4.5 Hours of Symptom Onset, PCNASP 2008–2017

	Door-to-Needle ≤60 min		Door-to-Needle ≤45 min	
Outcome	**AOR (95% CI)**	***P* Value**	**AOR (95% CI)**	***P* Value**
Discharge home	1.16 (1.10–1.22)	<0.001	1.15 (1.09–1.22)	<0.001
In-hospital death	0.88 (0.80–0.97)	0.01	0.87 (0.78–0.97)	0.01
Symptomatic ICH ≤36 h	0.77 (0.68–0.87)	<0.001	0.69 (0.61–0.80)	<0.001

*Variables included in multivariable models were age, sex, race, arrival by EMS, NIHSS score, smoking status, history of hypertension, dyslipidemia, myocardial infarction or coronary artery disease, heart failure, diabetes mellitus, nonvalvular atrial fibrillation, stroke, hospital size, annual stroke admissions, stroke unit, and year of admission. ICH indicates intracerebral hemorrhage; IV, intravenous; and PCNASP, Paul Coverdell National Acute Stroke Program.

Circ Cardiovasc Qual Outcomes. Author manuscript; available in PMC 2019 January 11.