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Enhancing Community Delivery of tPA in Stroke through Community-Academic Collaborative Clinical Knowledge Translation

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Introduction

Improving the clinical outcomes of stroke patients depends on the adoption of proven new therapies throughout the broader medical community. Approximately 1 percent of stroke patients in community settings are receiving tPA therapy twelve years after FDA approval.¹⁻⁷ Data suggest substantial improvement in treatment rates is possible, with current treatment rates considerably below estimates of eligible patients⁸, as well as those reported in optimized stroke care systems.^{1, 9, 10}

Knowledge translation, the process by which the results of clinical investigations are adopted by clinicians and incorporated into routine practice is important, but is often overlooked. The development and implementation of educational interventions to motivate physicians and other healthcare providers, along with health care organizations, to learn the principles of acute stroke care has been declared a high-priority objective of the National Institute of Neurological Disorders and Stroke (NINDS).¹¹ Ideally, knowledge translation is a collaborative process involving physicians practicing in a community environment and academic physicians with special expertise.

Given the societal burden of stroke, the demonstrated efficacy of thrombolytic therapy, and the potential of even more aggressive stroke treatment strategies (glycoprotein 2B3A inhibitors, intra-arterial thrombolysis, mechanical clot disruption, etc.) effective and efficient methods to enhance physician delivery of acute stroke care must be realized. Failure to do so marginalizes the impact of proven and future stroke therapies.

This article reviews the history of tPA use in stroke as a case study of a breakdown of knowledge translation in emergency medicine. Furthermore, it briefly reviews knowledge translation

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concepts and theory and explores practical community-academic collaborative methods based on these tenets to enhance acute stroke care delivery in the community setting.

Knowledge Translation

Definition

Simply put, “knowledge translation”, or KT, reflects the movement of new findings from the laboratory setting, to clinical investigation, to common usage. A widely cited KT definition was published in 2004 by the Canadian Institutes for Health Research where knowledge translation was defined as “the exchange, synthesis and ethically-sound application of knowledge within a complex system of interactions among researchers and users – to accelerate the capture of the benefits of research...through improved health, more effective services and products, and a strengthened health care system.”¹²

The Institute of Medicine has subdivided the knowledge translation process based on obstacles to implementation of new science. The first subdivision (T1) represents the challenges in research moving from basic science to human investigational studies. The second subdivision (T2) represents those difficulties in moving successful therapies from clinical trials into common practice and health decision making.¹³ This second area represents the focus of this article.

With the emergency department positioned as both the portal through which many patients are admitted and where routine healthcare is often provided, the premature, late- or non-adoption of new medical science has profound implications with respect to patient and societal health and efficient use of resources.

Indeed, even for less critical injuries, the failure to adopt proven strategies carries cost. Lang et al examined the knowledge translation failure of implementation and adherence to the Ottawa Ankle Rules. Even though the rules are well-validated, extensively published, low-risk and provide estimated cost savings of (US) \$3,145,910 per 100,000 patients evaluated, utilization of the tool remains limited.¹⁴

The recognition of the importance of knowledge translation in emergency medicine was underscored in 2007 by the *Academic Emergency Medicine* consensus conference to establish a research agenda on KT and evidence uptake.¹⁵

Theories of Behavioral Change

Physicians and other health care providers have traditionally relied on persuading individuals to change through “informational power” (sharing facts about disease processes) and “expert power” (using professional credentials to impress others with the potential effectiveness of the prescribed behavioral change).¹⁶ Such approaches, however, do not fully mesh with current theories of health promotion and behavior change theories.

Knowledge appears to be necessary, but insufficient alone, for behavioral changes to take place. While differences exist among the predominant behavioral change theories (Health Belief Model, Theory of Reasoned Action, Subjective Expected Utility Theory and Social Cognitive (Learning) Theory) several core concepts are common among them: perceived *probability* of disease occurring, perceived *severity* of disease, perceived *effectiveness* of the behavioral change in decreasing the probability and severity of disease, and perceived *cost* of (or barriers to) enacting the change.¹⁷⁻¹⁹ Some component of *self-efficacy*, the perception of one’s own ability to successfully take action, has also been incorporated into most current theories of health promotion behavior. Thus, multi-level interventions may be required to change practice behavior.

Knowledge Translation of tPA use in Stroke

Bench to Bedside

In 1995, the NINDS rt-PA Stroke Study Group demonstrated the efficacy of tissue plasminogen activator (alteplase) in the treatment of acute stroke.²⁰ This study elaborated one set of clinical conditions under which use of tissue plasminogen activator resulted in a favorable outcome. These conditions included: (1) use of a lower dose than given in myocardial infarction, (2) administration within three hours of symptom onset (defined as the time the patient was last normal) and (3) excluded patients with blood pressure in excess of 185/110 at the time of treatment.

Of the 624 patients in the trial, 43% of treated patients were neurologically intact at three months as compared to 27% of placebo treated patients. These results were statistically and clinically significant and durable out to one year.²¹ Mortality was 17% in treated patients and 21% in the placebo group, a difference which was not statistically significant. Patients with intracranial hemorrhages were included in the benefit analysis and the higher rate of good outcomes occurred despite an increased risk of symptomatic hemorrhage (6.4% vs. 0.6%) within 36 hours in the treatment group.

Seven other randomized, double blind, placebo controlled clinical trials evaluating use of thrombolytic drugs in stroke have been published.²²⁻²⁷ These evaluated significantly different clinical trial conditions including different drugs and doses, time windows of treatment, and subject inclusion/exclusion criteria. These studies were unsuccessful in defining a set of conditions in which treatment was efficacious. A summary of these studies and their differences with the NINDS trial are in Table 1.

Bedside to Clinical Practice

Governmental and Professional Approval—Based on the NINDS rt-PA stroke study, the US Food and Drug Administration approved tPA for use in acute stroke in 1996. Canada's Health Products and Food Branch subsequently approved its use in 1999, and the European Agency for the Evaluation of Medicinal Products followed in 2002.²⁸

Numerous professional and community organizations have endorsed tPA use in stroke, including: the American Academy of Neurology²⁹, American College of Chest Physicians, American Heart Association/American Stroke Association³⁰, Canadian Stroke Consortium, National Stroke Association and multiple others. Additionally, the National Institutes of Health sponsored national symposia on promoting treatment of acute stroke in 1997³¹ and again in 2002.³²

Notably absent from the list of endorsing professional organizations was emergency medicine representation. In 1996 the American College of Emergency Physicians agreed "with reservations" to the new stroke guidelines.³³ In 2002, ACEP issued a policy statement indicating "intravenous t-PA may be an efficacious therapy" but that "there is insufficient evidence to endorse the use of t-PA...when systems are not in place to ensure that...NINDS guidelines...are followed." The decision to use tPA "should begin at the institutional level."³⁴ The American Academy of Emergency Medicine issued a position statement in 2002 to address issues of medical-legal liability. Their position paper stated, "Debate on the safety, efficacy and applicability of tPA has limited its widespread use. Nonetheless, an increasing number of liability suits are emerging against physicians for not administering tPA..." and stated that there was insufficient evidence to classify tPA use in stroke as a standard of care.³⁵

In an effort to address these concerns and statistical criticisms of the original study, the NIH/NINDS sponsored an independent, external re-analysis of the study data by personnel not connected with the original trial. The reviewers had access to the entire data set and reported their findings at the 2003 Society of Academic Emergency Medicine annual meeting. This presentation, and subsequent publication of the results, confirmed the original findings of benefit to tPA-treated patients in the trial.³⁶

Post-Approval Studies—Over the past decade, multiple post-approval studies and smaller case series have reported on tPA use in various settings. The following summarizes major studies geographically:

United States: The Standard Treatment with Alteplase to Reverse Stroke (STARS) study was a prospective, 57 center study involving 24 academic and 33 community hospitals in the United States. Three hundred, eighty-nine stroke patients consecutively treated with tPA between 1997 and 1998 were evaluated.

This study found a 30-day mortality of 13% and a very favorable outcome (defined as a modified Rankin Score of ≤ 1) of 35%, with 43% being functionally independent ($mRS \leq 2$). The rate of symptomatic intracranial hemorrhage within three days of treatment was 3.3% [95% CI: 1.8% to 5.6%], lower than that reported in the NINDS trial. Protocol deviations occurred in 33% of patients, with treatment beyond the three-hour window, premature use of anticoagulants (within 24 hours), and excessive pre-tPA blood pressures, identified in 13%, 9% and 7% of patients, respectively.³⁷

Canada: The Canadian federal government, as a condition of drug licensure, mandated the Canadian Alteplase for Stroke Effectiveness Study (CASES). This was a prospective treatment registry with patient follow-up 90 days after stroke to assess the safety and effectiveness of alteplase in the context of routine care.

A total of 1,135 sequentially treated stroke patients were included from 60 centers between 1999 and 2001. This represented an estimated 84% of all treated ischemic stroke patients in the country over that period. Excellent clinical outcomes occurred in 37% and symptomatic intracranial hemorrhage was identified in 4.6% [95% CI: 3.4% to 6.0%] of patients. Again, these compare favorably to the results of the NINDS data.³⁸ The median time from stroke onset to treatment was 155 minutes [interquartile range: 130-175]. Protocol violations occurred in 14%, with treatment beyond three hours, elevated INR, and inappropriate dosing of tPA (> 90 mg), accounting for 86%, 8% and 5%, of violations, respectively.

European Union: The largest post-approval study to date was the 2007 observational Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST) from the European Union.²⁸ As with CASES, this study was mandated by the EU as a condition of drug licensure to assess the safety profile of alteplase in routine clinical practice when administered within 3 hours of symptom onset.

SITS-MOST was a prospective, open, multi-center study of tPA use in the European Union (as of 2002) in addition to Norway and Iceland. Two-hundred, eighty-five centers participated. Comparisons were made between the 6,483 patients treated according to EU label eligibility criteria and pooled data from the NINDS, ECASS I and II, and ATLANTIS stroke studies. EU label eligibility limited treatment to patients between 18 and 80 years of age and NIH stroke scale scores ≤ 25 .

It is important to note participating centers were required to have a stroke unit or similar monitoring capability for tPA treated patients and that clinical responsibility for patient

management was held by a neurologist or stroke physician with experience. Furthermore, the label eligibility requirement of the study limited a complete exploration of the clinical use of tPA as there were no data on treatment eligibility violations or its effects. This profoundly limits the usefulness of these data.

In this large cohort, mortality within three months was 11.3% [95% CI 10.5 to 12.1]. The symptomatic intracranial hemorrhage rate was 7.3% [95% CI: 6.7% to 7.9%], slightly higher than that reported in the NINDS trial. In comparing new treatment centers against experienced treatment centers, there was no increase in intracranial hemorrhages. A small difference in 90-day mortality was identified, with new centers reporting 13.3% [95% CI: 14.1 to 21.1] versus 10.6% [95% CI: 9.8 to 11.6] for experienced centers, though both values were below the comparison pooled results.

Very favorable outcome (modified Rankin Score ≤ 1) occurred in 39% of patients, identical to the NINDS study. Functional independence (mRS of ≤ 2) was achieved in 54.8% [95% CI: 53.5% to 56.0%]. The authors concluded that alteplase, when used within three hours of stroke onset and according to label eligibility requirements, had a safety profile at least as good as that seen in published clinical trials.²⁸

Current Utilization—The proportion of stroke patients potentially or actually eligible for thrombolytic therapy has been reported to range from 0% to 22%.³⁹ Despite the accumulating evidence, however, intravenous tPA therapy remains unused in the vast majority of patients.

Data from Cleveland indicate 17% of ischemic stroke patients were admitted within 3 hours of symptom onset, yet only 1.8% received intravenous tPA.³ Data from the multi-state Paul Coverdell Stroke Registry indicate only 3% of patients received some form of fibrinolytic therapy (either intravenous or intra-arterial).⁴⁰ The Nationwide (US) Inpatient Sample data taken between 1999 and 2004 indicate thrombolytic use occurred in 1.1% [95% CI: 0.95 to 1.32] of ischemic stroke hospitalizations. Importantly, 70% of the approximately 1,000 hospitals reporting data *never* used thrombolysis for stroke. In those which did, the mean annual number of treatments was three.⁷ These data support previous reports of usage rates of 1 to 3 percent in the community setting.^{1-5, 7}

Contrasting these figures to the cardiac data is revealing. In the National Registry of Myocardial Infarction, of the 240,989 patients with myocardial infarction between 1990 and 1993, 35% received thrombolytic therapy.⁴¹

While stroke is typically more difficult for the layperson to recognize and often a greater diagnostic challenge for the clinician, it is reasonable to believe treatment of a larger proportion of patients with ischemic stroke is possible. A veteran stroke service in Houston, TX reported 8.7% of admitted patients with symptoms of cerebral ischemia were treated with intravenous tPA from 1996 to 2000. Impressively, during the study's final six-months, 12.9% of all patients were treated with IV tPA.⁹

Thus, based on the proportion of eligible patients, the utilization of thrombolytics in the setting of myocardial infarction and the experience of well-developed thrombolytic stroke teams, it appears possible to increase stroke treatment beyond current levels.

Emergency Medicine Acceptance of Acute Stroke Treatment—A 1999 survey reporting the perceptions of 701 PGY 1-4 emergency medicine residents regarding tPA use found 73% considered their knowledge of thrombolytic therapy very good or somewhat good and 88% indicated they would personally use tPA if they had a stroke. Only 4% indicated they would not use tPA in stroke under any circumstances.⁴²

This relative enthusiasm of emergency physicians in training contrasts with the findings of a subsequent 2005 survey from 1,105 ACEP members that found extremely limited acceptance of acute treatment of stroke with tPA. In this survey, forty-five percent [95% CI 37% to 44%] reported they were not likely to use tPA for stroke even in the ideal setting. Of those, 65% reported their reluctance was due to perceived risk of symptomatic intracranial hemorrhage, 23% due to lack of benefit, and 12% to both.⁴³

Knowledge Translation Barriers in Stroke

Understanding Barriers in Knowledge Translation

Cabana et al published a comprehensive assessment of the barriers to physician adherence to clinical practice guidelines and organized them into a theoretical framework. This framework details their interplay and their effects on physician knowledge, attitudes and behavior – the domains necessary to influence for successful knowledge translation (Figure 1).

Specific barriers that may limit successful adoption of new guidelines include those influencing: awareness, familiarity, and physician agreement with, new recommendations on treatment. Other barriers include: the belief that a given practitioner can deliver a new therapy (self-efficacy), that a particular outcome following treatment will be observed (outcome expectancy), and overcoming the inertia of previous practice. Lastly, external barriers, those issues outside the control of the clinician, may prevent new treatment guideline adoption.

The implications of this framework indicate successful knowledge translation is dependent upon addressing unique barriers at the level of both the individual physician and their practice environment. Thus, what is effective in improving treatment behavior in one hospital setting is dependent on the presence, type and intensity of barriers faced, and may not be successful in another.

Barriers to tPA Utilization

An examination of the barriers to improving the treatment of stroke patients is found within the NINDS Proceedings on the Rapid Identification and Treatment of Acute Stroke. The authors noted “Delivery systems for acute stroke hospital care are relatively primitive compared to systems for...cardiac care...and the recent approval of intravenous tPA has exposed these deficiencies and mandates changes in the hospital care system.”³¹ The lack of a systems-based approach is of major concern to emergency physicians as stated above in the ACEP policy on tPA use in stroke.

In a systematic review of barriers to tPA delivery in acute stroke, Kwan et al noted the following specific barriers within the health care system to thrombolytic delivery: EMS triage of stroke as an emergency, emergency department failure to triage stroke as an emergency, delays in neuroimaging, inefficient processes of emergency stroke care, and physician uncertainty in administering tPA. Other identified barriers included inadequate training in stroke for doctors.³⁹

Identifying Site Specific Stroke Barriers

Interventions to improve knowledge translation would therefore ideally target those barriers found in a specific hospital/emergency department environment. Since behavioral change to increase tPA use in stroke needs to occur within a complex organization (a hospital) the organization’s barriers to treatment must be identified, understood and addressed for education to succeed and behavior to change. The following techniques may prove useful in identifying site-specific barriers to stroke care.

Qualitative assessment—Qualitative research derives information from observation, interviews and/or verbal interactions to establish insights into the perceptions or experiences of a target group. Analysis is interpretative and subjective and statistical tests are not utilized. These techniques are commonly used in marketing and social science and may be beneficial in evaluating barriers to knowledge translation at the staff level. Methods used include focus groups and structured interviews and allow understanding of participant knowledge, attitudes, behavior and motivations.

Prior qualitative work found physician characteristics are related to specific barriers. In research examining adherence to national guidelines for asthma management, senior physicians mentioned lack of agreement with medication recommendations and the inertia of previous prescribing patterns as barriers, whereas younger physicians described lack of confidence in dosing or recognizing contraindications. Both groups mentioned time limitations.⁴⁴

Understanding potential group differences can enhance the effectiveness of local knowledge translation processes in acute stroke care and other disease conditions. While an extensive review of the use of qualitative techniques in identifying stroke barriers is beyond the scope of this article, additional detail on may be found in a review by Muerer et al.⁴⁵

Site resource assessment—While health care providers possess strong internal motivation to assimilate new information in order to improve the quality of care they provide, this desire must compete against numerous environmental barriers. Thus, an assessment of physical resources and tools considered necessary in the delivery of tPA in stroke is reasonable. One suggested listing of these is in Box 1.

Box 1. Suggested Elements of Acute Stroke Treatment Resource Assessment

- Clinical Policy/Procedure for acute stroke care/tPA use
- Triage screening tool (Cincinnati Prehospital Stroke Scale; LAPSS)
- Neurology on-call list
- Specialized stroke response paging system
- Stroke specific documentation templates for nursing; for physicians
- Rapid laboratory result access
- Rapid CT scanner access
- Rapid CT interpretation access
- Pre-printed nursing orders for stroke patients
- Blood pressure management guidelines for pre- and post-tPA treatment
- tPA use inclusion/exclusion checklists
- Pre-printed tPA use in stroke informed consent (with outcome expectation, mortality and intracerebral hemorrhage complication information pre-printed)
- tPA weight-based dosing worksheets
- NIH Stroke Scale Scoring forms
- Rapid drug access (pharmacy or emergency department stock)

- Pre-printed admission or transfer orders for post-tPA patients

Changing Stroke Practice: T2 KT

In general, six methods are available at the local level to influence physician behavior change: education, audit/feedback mechanisms, physician champion development, administrative intervention, and financial incentives/disincentives.⁴⁶

Education

Post-training education of physicians typically consists of “traditional” continuing medical education (CME) offered as a didactic lecture to enhance physician knowledge. While successful in increasing knowledge, the impact of traditional CME alone in changing physician behavior is extremely limited.^{47,48} Randomized controlled trials of the impact of “interactive” CME (small group, workshops, training sessions, etc.) and “mixed” CME (elements of both didactic and interactive formats) have found greater success.⁴⁹⁻⁵⁵ It appears unlikely that stroke education, offered in isolation via standard CME processes, will substantially alter stroke treatment behavior but is an important first step.

Repetition appears important in increasing the likelihood of success in educational efforts. In a review of randomized controlled trials of CME, Davis et al. found seven of ten repetitive CME interventions (the majority using 2 sessions in a series) had a positive effect compared to two of seven singular interventions.⁴⁹

The use of simulation training (e.g. “mock stroke codes”) and immediately available treatment protocols provide alternate delivery vehicles for educational content and may address other barriers to behavior change as well.

Ideally, the educational topics presented, whether addressed in CME-type forums or in other educational methods, will address major categories of barriers (lack of awareness, familiarity, agreement, self-efficacy, outcome expectancy, inertia or external barriers) previously identified. Suggestions for educational methods and content to address specific barriers follow and are summarized in Table 2.

Improving awareness—Physicians may be unaware of recommendations for the use of tPA by the NINDS and other national groups (American Heart Association, American Academy of Neurology). Conversely, they may adhere to more limited recommendations by the American Academy of Emergency Medicine or American College of Emergency Physicians. Information in a lecture format describing the various recommendations, their development process, and the data used to develop them, could address this barrier.

Increasing agreement—Within emergency medicine, considerable debate has emerged regarding agreement on the appropriateness of the use of tPA in stroke. In a BMJ article a member of the board of the American College of Emergency Physicians was quoted, “Leaders in emergency medicine are raising significant scientific, ethical and implementation issues [regarding the use of tPA in stroke].” This stance has been heatedly debated within the emergency medicine community.⁵⁶⁻⁵⁸

The essential issues voiced in these debates regard concern over lack of efficacy, concern over lack of effectiveness - that results obtained by highly motivated researchers are not replicable in the general community – and limited system support for TPA delivery.

To address efficacy issues, a discussion examining the results of the original NINDS trial and the subsequent independent re-examination of the data³⁶ is suggested. To address issues

regarding effectiveness, a review of the post-approval studies noted above and use of tPA by emergency physicians is recommended.⁵⁹⁻⁶⁴

Enhancing self-efficacy—Self-efficacy is the belief that one can actually perform a behavior. Increased self-efficacy is associated with increased likelihood that a person will perform a given behavior.⁶⁵ The delivery of tPA in stroke requires confidence in: patient evaluation skills; knowledge on indications and contra-indications of tPA use; expected risks and benefits for discussion with patients/families; and the ability to coordinate care between the emergency department, radiology and neurology. A mixed continuing education session targeting specific topics of interest could include reviewing neurological assessment skills using case-presentation formats; the use of the NIH stroke scale as an evaluation tool; and/or reviewing EP accuracy in stroke diagnosis. Other methods to address self-efficacy barriers include clinical guideline development and stroke simulation scenarios.

Stroke Treatment Protocol Development: Clinical practice guidelines, another form of physician education, have only limited effects on changing physician behavior⁶⁶⁻⁶⁸ often due to multiple barriers, both internal and external to the behavior change process as described above.⁶⁹ The advantages of these tools, however, are standardization of processes and care, low cost and ease of distribution. Such tools are readily available and can be in paper or electronic format. One popular tool includes a palm-based application for stroke assessment and treatment (HandiStroke,[®]) available for free from the Foundation for Emergency Research in Neurological Emergencies at <http://www.ferne.org>.

Simulation: Mock Stroke Codes: “Code” situations are medical or surgical emergencies requiring an immediate response for successful patient resuscitation. Patients presenting with acute stroke eligible for tPA represent a neurologic “code” situation. However, even in large hospitals, a stroke “code” represents a low-frequency event – more akin to pediatric/neonatal resuscitation codes than the more familiar cardiac or trauma.

Previous work indicates residents in medical training fail to maintain knowledge and skills learned in advanced life support courses and often return to their pre-training level within 12 months.^{70, 71} In a study of resident physician performance in pediatric codes, Cappelle et al. found a series of code simulations resulted in significant improvements in residents’ perceived need for additional knowledge, confidence in their performance and motor skills in arrest situations.⁷²

It is reasonable, therefore, to conduct mock acute stroke “codes” for training purposes. Planning of such events should incorporate both nursing and physician input using the framework advocated by Funkhouser et al in the development of multidisciplinary mock codes.⁷³ This utilizes an assessment-planning-implementation-evaluation process and designates various on-site responsibilities prior to the session. This enhances “buy-in” of the process from key personnel.

Frequency of mock code delivery should be based on baseline stroke volume, staff turnover, perceived need, performance and other factors. Codes should be interdisciplinary, conducted with advance notification to staff to enhance participation and reduce anxiety, utilize pre- and post-code sessions to review objectives and evaluate performance, use actual supplies (protocols, triage tools, communication assets), and include usual nursing and physician charting.

Code scenarios should incorporate a vignette, role-played by a staff-member, (or use a mannequin) with a directing facilitator, who provides baseline presentation information. It is recommended to test multiple scenarios over time and include patients both eligible and

ineligible for tPA. The actions of the participants determine the outcome of the vignette and the observer/reviewer should have pre-established detailed instructions for critical decision points. Codes typically last 15-30 minutes and should be followed by a 10-minute debriefing to allow participants to evaluate their success and areas for improvement.

Increasing outcome expectancy—Outcome expectancy is the belief that performing a behavior will lead to the desired outcome. High outcome expectancy is associated with an increased likelihood of performing a behavior.⁶⁵ Emergency physicians are often insulated from the ultimate outcome of treated patients. These factors potentially contribute to low outcome expectancy within the emergency department. Reviewing outcome data from the NINDS trial and the post-approval studies noted above could potentially address this issue. Promoting case reports of local treatment success is an additional method.

Removing inertia of previous practice—The inertia of previous practice due to habit, custom or previous training is also a barrier to the use of tPA in stroke. To address this element, physicians will have to be motivated to move from a pre-contemplative stage to an action stage in terms of readiness to change practice. Techniques that may help overcome the inertia of previous practice include performance feedback and opinion leader beliefs.⁷⁴ Incorporating the use of local opinion leaders and discussing performance may aid in creating a competitive performance environment between stakeholders.

Reducing external barriers—These barriers represent impediments to tPA delivery in stroke beyond the physician's immediate control. Educational interventions to address barriers of this nature should focus on planned or completed modifications to eliminate specific barriers. These may often be of an administrative or resource nature. A frequent issue of this type is real-time access to neurology/stroke-specialist consultation.

Given the low-frequency, high-morbidity, high-mortality nature of ischemic stroke - in addition to the highly variable presentations of stroke patients and stroke "mimics" - the promotion of local consultation systems to provide real-time access to stroke specialists may remove the perception of isolation to the treating emergency physician and improve physician-to-physician knowledge transfer. However, not all facilities have access to local neurologists and/or stroke experts.

The use of simple telephone consultation with tertiary stroke centers has been shown to substantially increase stroke treatment volume and be a safe, practical, and effective method of extending care to hospitals with limited resources.^{75, 76} More sophisticated telemedicine applications, combining real-time audio and video transmission with remote patient evaluation and management by stroke specialists are also available and have proven feasible and effective in expanding acute stroke treatment.^{77, 78} Limitations of these techniques include the need to establish relationships in advance with remote consultants and processes to access them in a time-critical setting.

Education Summary—In conclusion, educational efforts to enhance physician stroke education should deliver content in a learner-centered, active format; address the learner's needs; which is simultaneously engaging and reinforcing.⁴⁹ The multiple sequencing of events, both within a single day, and over multiple months offers a "learn-work-learn" opportunity in which education may be translated into practice.

Audit/Feedback

Audit and feedback interventions involve providing information to physicians regarding their practices or individual patient outcomes. Two-way communication maintained over time

allows for the convergence of ideas between teachers and learners – a central component of communication theory.⁷⁹ The addition of audit and feedback mechanisms and reminders, can help facilitate change in practice behavior.^{49, 80-82} Audit and feedback techniques encompass any summary of clinical performance over a specified period and can include reminders or recommendations for clinical action.

Conditions proposed for successful feedback strategies include 1) physician recognition of need for improvement, 2) physician ability to act upon information, 3) prospective reminders appear more successful than retrospective feedback and 4) achievable target expectations.⁸³⁻⁸⁷ Examples of such systems include targeted messaging and critical incident defusing.

Targeted Messaging—With email systems, electronic feedback is easily accomplished within time constraints. Previous work has demonstrated the use of electronic mail-based case discussions as part of a successful multi-level intervention to improve hand-washing behavior⁸⁸ among physicians. From the perspective of addressing KT barriers, an effective audit-feedback/reminder system addresses elements of outcome expectancy, lack of awareness and familiarity, lack of agreement and external barriers. Combining hospital-specific data with brief reminders or tips on acute stroke care may further enhance recall of the message. This method also allows incorporation of pertinent new stroke literature, highlighting of local stroke treatment successes, distribution of printable reminders regarding tPA use in stroke and promotion of access to other electronically available stroke treatment tools (triage and personal device assistant (PDA) stroke protocols).

Critical Incident Defusing—Healthcare professionals are regularly featured in the literature exploring critical incident stress and the results of such critical incidents may include sudden change in the daily standard operating procedures for those experiencing them. It is easy to conceive that the occurrence of an intracerebral hemorrhage, even after appropriate use of tPA in stroke, could alter future willingness to consider acute stroke treatment. Given that a small percentage of patients will experience such events, a plan to address such events should be considered.

Critical incident defusing is an abbreviated form of critical incident stress debriefing, typically lasts less than 1 hour, and is designed to resolve the emotional content of an incident.⁸⁹ The CID target should involve the treating physician, consultants and staff. These should be conducted by respected, trained colleagues and based on the three components of the critical incident defusing process: introduction, exploration, and information.

The objective is to provide professional support in a review of the process leading to the treatment decision. This should be conducted in a descriptive manner and avoid performance critique.

Champion Development

While guidelines and education by themselves may not change practice, evidence exists that providing them to local “opinion leaders” appears to hold substantial promise in altering physician behavior and maintaining the change. These “educational influentials” are opinion leaders within a community who influence the acceptance of an innovation or practice by that community.⁹⁰

Interventions that target these persons may be effective in altering local consensus or agreement regarding a guideline or treatment process.^{91, 92} In one study, cesarean delivery rates fell dramatically after opinion leaders were recruited and trained to promote compliance with a guideline for the management of women with a previous cesarean section.⁹³ In another study, significant changes in antibiotic use were found when authoritative senior staff members were

targeted for person-to-person messaging on appropriate use in conjunction with ordering reminders.⁹⁴

To increase the likelihood emergency physicians will adhere to recommendations for tPA use in stroke such opinion leaders should be identified and encouraged to champion stroke care. Searches for such leaders need not be restricted to within the emergency department itself. Local neurologists, internists, hospitalists and vascular specialists may also serve in this role.

Academic detailing

While targeting only local opinion leaders is an efficient strategy to alter physician behavior, the process known as “academic detailing” – targeting populations of individual physicians for individual contact – has proven remarkably effective in almost every study in which it has been used.⁹⁵⁻⁹⁸ Limitations of targeting individual physicians include the time and expense of contacting each physician however departmental staff meetings may allow efficient access to entire hospital populations of specific physicians.

Administrative intervention

Administrative interventions can effect behavior change by creating/removing barriers to alter practice (e.g. enhancing CT access for stroke, providing stroke treatment protocols, providing thrombolytic stroke expert access, etc.). In the area of changing physician prescribing habits, administrative interventions have proven extremely successful in reducing drug costs by altering available selections or requiring drug selection review.⁹⁹ An easily recognizable national administrative intervention has been the monitoring of the time for early antibiotic delivery in emergency patients with pneumonia.

However, as Greco et al. note, there is a risk of achieving desired changes in physician practice which may ultimately cause patient harm.⁴⁶ They cite a Medicaid program limiting reimbursement for prescription drugs which successfully reduced the number of drugs prescribed, but inadvertently increased the rate of admission to nursing homes.¹⁰⁰ Thus, caution is advised in implementing administrative interventions as important events may go unrecognized if there is no evaluation of their impact.

Potential Impact of Knowledge Translation Success in Stroke

Recent work in other fields has demonstrated the dramatic impact successful knowledge translation can have in improving health care. In 2006, Provonost et al reported that an evidence-based intervention resulted in a large and sustained reduction (up to 66%) in rates of catheter-related bloodstream infection. Their intervention incorporated local champion development and training, audit/feedback mechanisms, education and protocols (checklists) to ensure adherence to infection-control practices in 108 intensive care units.¹⁰¹

With respect to stroke and emergency medicine, previous studies have demonstrated community and academic hospitals can deliver tPA effectively.^{4, 37, 59, 60, 102-106} However, numerous barriers exist to expanding the delivery of tPA.^{31, 107} Only limited data currently exist on proven methods to overcome these barriers and increase physician and hospital utilization of tPA. One study, using a quasi-experimental design, evaluated a combination of community and professional education to increase thrombolytic use in stroke in emergency departments in rural east Texas. Treatments increased from a pre-intervention rate of 2.2% to a post-intervention rate of 11.3% ($p=0.007$), with the data suggesting the professional education component was the critical element in increasing use.^{1, 10} The change appeared durable, however, the study was limited by its single community setting.¹

Currently, a cluster-randomization, multi-center, controlled trial evaluating a standardized, multi-level, barrier assessment and educational intervention to increase tPA use in community hospitals and their associated emergency departments is underway, with completion anticipated in 2010. (The INSTINCT Trial, NIH R01 NS50372). The intervention under assessment incorporates many of the above elements in its design.

Assuming 500,000 ischemic strokes per year in the United States¹⁰⁸, an efficient educational / behavior change process which could generate a modest 4% increase in appropriate tPA delivery could translate to an additional 20,000 treated patients per year. This potentially returns a minimum of 2,200 stroke victims (11%) to the community normal - with added improvement across the entire spectrum of neurologic outcomes for patients who do not achieve normal status.²⁰

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Figure 1.

Barriers to Physician Adherence to Practice Guidelines in Relation to Behavior Change (From: Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. *Jama* 1999;282(15):1458-65)

Table 1
Summary of Major Differences in Thrombolytic Trials in Stroke

Study	Location	Drug	Dose	Time	Exclusion criteria
Atlantis A ²⁴ (1991-93)	US	rt-PA	0.9 mg/kg (max: 90 mg)	0-6	Blood pressure (BP)
NINDS ²⁰ (1991-94)	US	rt-PA	0.9 mg/kg (max: 90 mg)	0-3 (1:59) [*]	Blood pressure
MAST-I ²² (1991-95)	Italy, UK, Portugal	streptokinase	1.5 million u	0-6 hours	
ECASS I ²⁶ (1992-94)	Europe	rt-PA	1.1mg/kg (max: 100mg)	0-6 (4:24) [*]	CT evidence of early infarct; age
MAST-E ²³ (1992-94)	France, UK	streptokinase	1.5 million u	0-6 h (4:36) ^{**}	Mild stroke
ASK Trial ²⁵ (1992-94)	Australia	streptokinase	1.5 million u	0-4 (3:28)	Age; minor stroke
Atlantis B (1993-98)	US	rt-PA	0.9 mg/kg (max: 90 mg)	3-5 (4:36) ^{**}	Blood pressure; age
ECASS 2 ²⁷ (1996-98)	Europe ANZ [*]	rt-PA	0.9 mg/kg (max: 90 mg)	0-6	BP; CT evidence of early infarct; age

^{*} mean;

^{**} median time onset-to-treatment;

Table 2
Content Suggestions for Barrier Specific CME Sessions

Identified Barrier(s)	Suggested CME Content
Awareness of tPA Use Guidelines	Compare / Contrast Guideline Development, Data & Recommendations <ul style="list-style-type: none"> • AHA/ASA • ACEP • AAEM
Agreement with Guidelines	Review guideline source data and post-approval data <ul style="list-style-type: none"> • NINDS tPA Stroke Study • NINDS tPA Stroke Study re-analysis • STARS, CASES, SITS-MOST • Cleveland Use of tPA
Self-efficacy for tPA Delivery	<ul style="list-style-type: none"> • Neurological assessment skills • Use of the NIH Stroke Scale • EP diagnostic accuracy in stroke • Use of local treatment protocols • Promotion of electronic aids (HandiStroke[®]) • Simulation training: mock stroke codes
Outcome Expectancy	<ul style="list-style-type: none"> • Review NINDS short and long-term outcome data • Review other post-approval study outcome data • Use local cases for evaluation and review
Overcoming Inertia of Previous Practice	<ul style="list-style-type: none"> • Use of local opinion leaders in interactive session • Present local performance data • Create competition between stakeholders • Review coding/billing process and financial impact
External Barriers	Identify and address hospital-specific external barriers