How Patient Demographics, Imaging, and Beliefs Influence Tissue-Type Plasminogen Activator Use
A Survey of North American Neurologists

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Background and Purpose—Understanding physician decision making is increasingly recognized as an important topic of study, especially in stroke care. We sought to characterize the process of acute stroke decision making among neurologists in the United States and Canada from clinical and epistemological perspectives.

Methods—Using a factorial design online survey, respondents were presented with clinical data to mimic an acute stroke encounter. The history, examination, computed tomographic (CT) scan, CT angiogram, and CT perfusion were presented in sequence, and respondents rated their diagnostic confidence and likelihood of treatment with tissue-type plasminogen activator after each element. Patient age, race, sex, and CT perfusion imaging results were randomized, whereas the rest of the clinical presentation was held constant.

Results—We collected 715 responses, of which 473 (66%) were complete. Diagnostic certainty and likelihood of treatment with tissue-type plasminogen activator rose incrementally as additional clinical data were provided. Diagnostic certainty and treatment likelihood were strongly influenced by the clinical history and the CT scan. Other factors such as physicians’ personal beliefs or biases were not influential. Respondents’ accuracy in interpreting CT angiographic and CT perfusion images was variable and generally low.

Conclusions—Diagnostic certainty and likelihood of treatment with tissue-type plasminogen activator increase with additional clinical data, with the history being the most important factor for diagnostic and treatment decisions. Respondents had difficulty in interpreting the results of CT perfusion scans although they had little impact on treatment decisions. We did not identify treatment bias based on patient age, race, or sex. (Stroke. 2016;47:2051-2057. DOI: 10.1161/STROKEAHA.116.013344.)

Key Words: bias (epidemiology) □ diagnosis □ stroke □ therapeutics □ tissue-type plasminogen activator

In modern medicine, physician decision making is often imagined as a rational and algorithmic process in which physicians consciously process clinical data,12 applying best evidence from randomized clinical trials in a straightforward fashion.3,4 However, a large body of literature drawing from psychology,5 economics,6 sociology,7 anthropology,8 history,9,10 philosophy,11 and implementation science12 suggests that physician decision making is often more complex, meaning that it is not fully explained by evidence alone.13 Values, beliefs, biases, and uncertainties likely contribute alongside medical knowledge.14

In acute stroke decision making, complex and impactful decisions are made under time pressures. Despite a robust body of clinical evidence supporting the efficacy of intravenous tissue-type plasminogen activator (tPA) for acute ischemic stroke,15,16 rates of use seem to be low17,18 and variable.19-22 For example, tPA use seems to be influenced by patient sex,23-25 race,26-29 and age.30-33 It is unclear to what extent these disparities are due to physician decisions or systems factors. Therefore, we sought to study neurologists’ decision making in acute stroke management.

Acute stroke decision making surrounding intravenous tPA use can be understood to include decisions about diagnosis, prognosis, and treatment. Anthropological fieldwork has suggested that the diagnosis of stroke depends on clinical and radiological data.34 Advanced imaging data (from computed tomographic [CT] angiography and CT perfusion [CTP]) has been shown to increase diagnostic sensitivity and clinical confidence.35 However, acute stroke decisions may not rely...
exclusively on clinical and radiological parameters. In a recent survey, Canadian neurologists endorsed being less likely to offer treatment with intravenous tPA to patients who were older, demented, or more severely affected.\textsuperscript{36}

We hypothesized that acute stroke decision making is a complex process incorporating scientific data, experience, and uncertainty and that may be influenced by physician beliefs and biases. Particularly, we hypothesized that neurologists would be less likely to offer tPA to older patients, to women, and to blacks, concordant with widely recognized inequalities in healthcare delivery in the treatment of stroke,\textsuperscript{37} as in other conditions.\textsuperscript{38,39}

### Methods

#### Survey Design

We characterized the process of acute stroke decision making using a factorial design online survey, in which certain elements of the clinical case are held constant, whereas others are varied to determine their differential influence (online-only Data Supplement).\textsuperscript{40} Respondents were presented with quanta of clinical data in sequence (history, examination, CT scan, CT angiogram, and CTP) to mimic an acute stroke encounter. After each element was presented, respondents were asked to rate their diagnostic confidence and likelihood of offering treatment with tPA, each on a 0 to 100 scale. In addition, a series of questions about the diagnostic and treatment decision-making processes were included. Demographic data about respondents were also collected.

The clinical examination was presented as a videotaped vignette of a standardized encounter where the patient demonstrated a left middle cerebral artery pattern of deficits (mild aphasia, face, and arm greater than leg weakness) for a National Institutes of Health Stroke Scale score of 5. This severity was chosen as it was felt to represent a point around which variance in clinical practice would likely be greatest.\textsuperscript{41} The clinical deficit was held stable across 8 vignettes, whereas the patient’s age (60 versus 80 years), race (white versus black), and sex (men versus women) were varied randomly. All vignettes were filmed under the same conditions at the Kanbar Center for Simulation, Clinical Skills, and Telemedicine Education at the University of California San Francisco. Respondents were randomized to observe only 1 of the 8 possible vignettes.

Respondents were presented with images from an unenhanced CT, CT angiogram, and CTP images, without an interpretation. CT scan and CT angiogram results were held constant for all respondents: the CT angiogram, and CTP images, without an interpretation. CT scan and CTP images were portrayed as they may vary per question.

Survey Population

The target population included neurologists in private and academic practice in Canada and the United States, with and without subspecialty training in stroke or vascular neurology. Based on a review of the available literature, we determined that a sample of 600 respondents would be required to achieve a statistical power of 80% to detect a 10% difference for each of patient age, sex, and race.

Survey Distribution

A link to the online survey was distributed electronically (Qualtrics, Provo, UT). Participants were reached in 2 ways: (1) direct contact via email addresses collected from publicly available websites and directories (1125 addresses); (2) presentation of a link distributed to association list serves (American Academy of Neurology Stroke, Education, and Ethics lists, Canadian Neurological Sciences Federation, Canadian Stroke Consortium, California Neurological Society, Indiana Neurological Society, North Carolina Neurological Society). For those respondents who received direct email invitations, reminders were sent to nonresponders at 30 and 60 days. The survey was launched on January 10, 2014, and was closed on June 4, 2015. The survey was closed because of declining response rates and after an interim statistical analysis suggested that additional responses would not change results. Respondents were presented with information on consent, and their participation in the study was taken as an indication of their consent to participate.

#### Pilot Testing

The survey was pilot tested on 12 neurologists and stroke fellows in the Calgary Stroke Program and Ottawa Stroke Program. Adjustments were made based on their feedback, and their responses were not included in the final analysis.

Statistical Analysis

All available responses were included in the analysis, including those with incomplete data. Analysis was completed in SPSS version 20 (IBM Co, Armonk, NY) and in StatCrunch (Pearson Education, Old Tappan, NJ). Responses were reported descriptively, and associations between predictors (patient and respondent demographics, beliefs, and imaging) and outcomes (diagnostic certainty and treatment likelihood) were evaluated using paired and independent sample \( t \) tests where appropriate. Specifically, \( t \) tests were applied to compare differences in absolute diagnostic certainty and treatment likelihood, as well as to compare differences in changes in these parameters based on the randomized clinical factors (eg, patient age, sex, race, CTP). All tests of hypotheses were 3 sided and were conducted at significance level of 0.05. Equality of variances was tested for and the appropriate \( t \) test was conducted accordingly. \( \chi^2 \) tests of independence were used to explore differences between proportions.

### Results

#### Responses

We collected 715 responses, of which 473 (66%) were complete. We obtained 222 responses from 1125 email invitations, for a response rate of 20% through this method. We cannot provide an overall response rate, as we do not know the denominator for all list serves and associations that distributed the survey. Accounting for complete and incomplete surveys, 532 (75%) respondents passed the point where randomized clinical data were presented. We included every received response in our analysis; therefore, the number of responses may vary per question.

Survey Respondents

Respondents were predominantly men (75%), practicing in the United States (67%), and between the ages of 31 and 50 years (60%). Nearly half (48%) of all respondents had subspecialty training in stroke or vascular neurology, and 58% had at least 10 years of experience in clinical practice (Table 1).

Diagnosis and Treatment

In general, diagnostic certainty and likelihood of treatment increased incrementally with additional clinical data (Figure 1). Of note, the average diagnostic certainty and likelihood to treat with tPA after the clinical history alone (sudden onset of right-sided weakness and speech difficulty) were 83% (SD=13) and 76% (SD=29). The final mean diagnostic...
certainty after all clinical data was 98% (SD=9), and the final mean likelihood of treatment was 93% (SD=19). Respondent sex, age, years of practice, subspecialty training, and country of practice were not associated with significant differences in final mean diagnostic certainty or mean likelihood of treatment for all comparisons. Respondents identified the clinical sources they routinely use in their real-world acute stroke decision making (Table 2), and those factors that might influence their use of tPA (Table 3).

**Biases**

Overall, there was no significant impact of patient age, race, or sex when comparisons were drawn between the differences in diagnostic certainty and treatment likelihood. Comparisons were performed via t tests for each variable and each patient to attempt to isolate the impact of individual demographic factors (age, race, and sex). ANOVAs were then used to look at all other possible combinations. Although t tests identified a significant decrease in diagnostic certainty and treatment likelihood among those respondents who viewed the vignette depicting the older, black female patient (−7.6%; P=0.01), no such difference was reflected in the ANOVAs and no similar effect was seen for other patient or factor comparisons.

**Beliefs**

Respondents were nearly evenly split on whether a severe left middle cerebral artery stroke was a fate worse than death, with 48% saying yes and 52% saying no. The majority of respondents (78%) identified their clinical experience as the most important factor determining their attitude about life after a left middle cerebral artery stroke. This opinion was not associated with a significant difference in terms of diagnostic certainty or likelihood of treatment with tPA. The vast majority of respondents (98%) agreed that tPA is an effective treatment for stroke, citing the medical literature (60%) and clinical experience (33%) as the most important factors contributing to that belief. There was no significant difference in final treatment likelihood between those who did (mean 93%; SD=20%) and did not (93%; SD=14%) endorse a belief in tPA efficacy (P=0.978).

**Advanced Imaging**

Respondents’ diagnostic certainty and likelihood to treat with tPA rose incrementally and significantly after viewing the CT scan, CT angiogram, and CTP (Figure 1). When asked to interpret the imaging, 75% of respondents correctly identified an occlusion on the CT angiogram and 78% correctly identified a cerebral blood volume/cerebral blood flow mismatch on CTP, but only 32% correctly identified a matched region of reduced cerebral blood volume and cerebral blood flow. Respondents with subspecialty training were significantly more likely to accurately interpret the matched CTP images (44% versus 19%; P<0.0001) although their accuracy was still low.

There was a small but statistically significant difference in the likelihood of treatment with tPA among those respondents who viewed the mismatch (mean, 95%; SD=16%) and those who viewed the match (mean, 91%; SD=22%) on CTP (P=0.05). This difference was driven by those neurologists with subspecialty training, who were significantly less likely to offer treatment with tPA when viewing the matched CTP (mean, 88%; SD=28% versus 94%; SD=16%; P=0.04). Those respondents who accurately identified the matched deficit also reported lower likelihoods of tPA use (mean, 87%; SD=28% versus 93%; SD=19%) although this was not statistically significant (P=0.08). Eleven respondents rated a very high final diagnostic certainty (>90%) and a very low final likelihood of treatment (<20%) in response to the matched CTP deficit.

**Discussion**

This study supports the view that acute stroke decision making may incorporate many factors (Table 3) although respondents’ decisions did not seem to reflect these elements in this testing environment. According to our model, diagnostic certainty and treatment likelihood increase with additional clinical data and demonstrate a positive association (Figure 2). The patient’s clinical history seems to be the most important single factor in decision making. Respondents had difficulty interpreting the results of CTP scans although they had little impact on treatment decision making. Although we did not identify treatment biases based on patient age, race, or sex, limitations to our methodology mean that this does not guarantee their absence in the real-world context.
Limitations
This study has several limitations. First, the study environment is necessarily artificial and may not accurately reflect decision making in the field. However, our methods maintained patient confidentiality, allowed for the isolation of individual factors, and generated data about physician decision making quickly and cost-effectively. Second, our response rate was low despite a large sample size. Low and declining response rates are increasingly encountered in physician surveys despite rigorous methodology; response rates below ours are common.42 Third, our respondent population was limited to neurologists, and likely over-represented Canadian neurologists and neurologists with subspecialty training in stroke. Most importantly, our respondents provided very high diagnostic certainties and treatment likelihoods (ie, a ceiling effect), thereby limiting the range between responses and compromising our ability to identify differences between them. We had expected greater variability in responses as a modest stroke severity (National Institutes of Health Stroke Scale score of 5) best differentiates between treated and untreated ischemic stroke according to the Get With the Guidelines registry.41 Respondents’ very high rates of confidence may have reflected a form of priming, in that they had been invited to participate in a survey of acute stroke decision making. Selection bias may also have contributed, as neurologists more familiar with stroke and tPA may have been more likely to complete the survey. Ultimately, additional studies of acute stroke decision making could further vary factors such as physician specialty, stroke severity, time of onset, or degree of early ischemic change to refine our understanding of this process.

Diagnosis–Treatment Relationship
Our study demonstrated a positive association between diagnostic certainty and treatment likelihood ($r=0.66; P<0.001$). The notable exception to this association came from those few respondents who endorsed a very high diagnostic certainty and a very low likelihood of treatment, in response to the matched CTP map. In situations where the disease is not benign (like acute stroke), we would expect most physicians with high diagnostic certainty to offer treatment; at the same time, the likelihood of treatment is unlikely to exceed diagnostic certainty where the treatment itself carries risk (Figure 2).

Treatment Decision Making
Respondents identified the CT scan (50%) and the clinical history (15%) as the factors most important to treatment

Table 2. “Which of the Following Elements Is Routinely Used in tPA Decision Making in Your Hospital?” (n=499)

<table>
<thead>
<tr>
<th>Factor</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical history</td>
<td>99</td>
</tr>
<tr>
<td>Clinical examination</td>
<td>98</td>
</tr>
<tr>
<td>Unenhanced CT scan</td>
<td>97</td>
</tr>
<tr>
<td>CT angiogram</td>
<td>49</td>
</tr>
<tr>
<td>CT perfusion</td>
<td>25</td>
</tr>
<tr>
<td>MRI scan</td>
<td>14</td>
</tr>
<tr>
<td>MR angiogram</td>
<td>6</td>
</tr>
<tr>
<td>MR perfusion</td>
<td>4</td>
</tr>
</tbody>
</table>

CT indicates computed tomography; MRI, magnetic resonance imaging; and tPA, tissue-type plasminogen activator.
The incremental increase in treatment likelihood produced by the CT scan (Figure 1) is consistent with its importance in ruling out intracerebral hemorrhage and identifying early ischemic change. However, on direct questioning, only 83% of respondents identified the CT scan as a potential contributor to their decision making, suggesting that perhaps they did not understand the question. Other factors, such as the physical examination (82%), clinical experience (55%), and belief in the efficacy of tPA (32%), were similarly recognized as important to decision making by fewer respondents than expected (Table 3).

Beliefs Without Impact
Our respondents were divided based on the question of post-stroke quality of life and less so on the benefits of tPA although these beliefs had no distinguishable effect on their decision making. It is counterintuitive to think that neurologists who do not believe in the efficacy of tPA are just as likely to use it, though this finding may suggest that physicians’ decisions are more reflective of guidelines or local practice than of their personal beliefs.

Biases and Patient Demographics
The use of a factorial video vignette system was intended to explore potential biases related to patient demographic factors. This methodology was chosen because of previous experiments in other physician groups since the mid-1990s that have consistently demonstrated that women and members of minority groups are less likely to receive standard care. A landmark study of cardiologists’ decision making published in the New England Journal of Medicine in 1999 applied a very similar methodology and found that blacks and women—and especially black women—were less likely to be referred for cardiac catheterization when presenting with acute chest pain. A large body of literature has pointed to disparities in the delivery of acute care to patients with stroke; our study

![Figure 2](http://stroke.ahajournals.org/)

**Figure 2.** Relationship between diagnostic certainty (%) and treatment likelihood (%). A plot of every decision-point as a relationship between diagnostic certainty (%) and treatment likelihood (%) shows a linear association between them ($r=0.66$; $P<0.001$).
would suggest that physician decision making is contributing less to these disparities than larger systems issues such as patient awareness and access. Given persistent concerns about inequality in the care of patients with stroke, we encourage further study in this domain.

Advanced Imaging
Our results suggest that neurologists (and particularly non-specialists) have significant difficulty directly interpreting images from CTP studies. Our respondents were more likely than might be expected to offer tPA to patients with a matched defect, even when they accurately identified that match. This finding may point to a lack of understanding of CTP imaging, or to skepticism about the validity of CTP findings. Only 25% of our respondents endorsed using CTP in their routine stroke decision making. In the clinical context explored by our study, and given the current status of perfusion science, CTP would seem to add little to treatment decision making. Based on our results, more work will be needed to ensure the reliable interpretation of CTP and its optimal incorporation into acute stroke decision making. We did not investigate magnetic resonance imaging diffusion and perfusion.

Conclusions
Efforts to improve practice are most likely to be successful if they are informed by a detailed understanding of the practices that are targeted for change. Disparities seem to exist in the care of patients with acute stroke, but it is unclear to what extent these disparities are related to individual physician decision making. Therefore, we applied an online survey model with the aim of arriving at a description of the real-world decision making of neurologists in the care of patients with acute stroke. Our results demonstrate the importance of the patient history and the unenhanced CT scan, with less significance attributed to patient demographics, physician beliefs, and advanced imaging. Additional studies may be strengthened by the perspectives elaborated here, with particular attention to the role of CTP and biases in acute stroke decision making.

Acknowledgments
We acknowledge the support of the following institutions and organizations who kindly distributed the survey to their memberships: The Canadian Stroke Consortium, The Canadian Neurological Federation, The American Academy of Neurology, The California Neurological Society, The Indiana Neurological Society, and the North Carolina Neurological Society. We are particularly grateful to all those neurologists who took the time to participate in this study.

Sources of Funding
This work was funded by a Clinician-Fellowship grant from Alberta Innovates Health Solutions (MCFS) and by a Graduate Scholarship from the Ottawa Hospital Research Institute (MCFS).

Disclosures
Dr Shamy reports research funding from the University of Ottawa, which is unrelated. Dr Kim reports research funding from the National Institutes of Health (NIH)/National Institute of Neurological Disorders and Stroke (NINDS), NIH/National Center for Advancing Translational Sciences (NCATS), SanBio Inc, and Biogen, all of which is unrelated. Dr Smith reports having received travel expenses and honoraria for lectures and educational activities from the American Heart Association, Alzheimer Association and Canadian Conference on Dementia; has served on a Data Safety Monitoring Board for Massachusetts General Hospital; is an Assistant Editor of Stroke; is a member of the Editorial Board of the Journal of the American Heart Association; and has received research funding from the National Institute of Neurological Disorders and Stroke (R01 NS062028), Canadian Institutes of Health Research, Alberta Innovates—Health Solutions, Canadian Partnership Against Cancer, Heart and Stroke Foundation of Alberta, and the Alzheimer Society of Canada.

References


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*Stroke*. 2016;47:2051-2057; originally published online June 30, 2016; doi: 10.1161/STROKEAHA.116.013344
*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/47/8/2051

Data Supplement (unedited) at:
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Text of Survey Administered to Study Participants

You are the neurologist on call for stroke at your hospital.

You have been called to the emergency department to assess a patient who presents with the sudden onset of right-sided weakness and aphasia. The patient was last seen well 60 minutes ago.

A quick review of the patient's history and records reveals no medications or laboratory values that would be considered contraindications to tPA.

You will briefly examine the patient, and then will obtain a CT scan with CT Angiography and CT Perfusion.

After each new piece of information becomes available, you will be asked to comment on your diagnostic certainty and likelihood of treatment.

1. Given ALL the information available up this point (the clinical history), how likely is the diagnosis of acute ischemic stroke?

[Respond on scale 0-100]

2. Given ALL the information available up to this point (the clinical history), how likely are you to administer IV tPA to this patient?

[Respond on scale 0-100]

Please watch the patient's neurological examination.

[Watch 1 of 8 randomized videos of patient examination]

3. Given ALL the information available up this point (the history and physical examination), how likely is the diagnosis of acute ischemic stroke?

[Respond on scale 0-100]

4. Given ALL the information available up to this point (the history and physical examination), how likely are you to administer IV tPA to this patient?

[Respond on scale 0-100]

Here are images from the patient's unenhanced CT scan.

5. Given ALL the information available up this point (the history, examination and CT scan), how likely is the diagnosis of acute ischemic stroke?

[Respond on scale 0-100]

6. Given ALL the information available up to this point (the history, examination and CT scan), how likely are you to administer IV tPA to this patient?

[Respond on scale 0-100]

Here is a composite (MIP) image from the patient's CT Angiogram.

7. Given ALL the information available up this point (the history, examination, CT scan and CTA), how likely is the diagnosis of acute ischemic stroke?

[Respond on scale 0-100]

8. Given ALL the information available up to this point (the history, examination, CT scan, and CTA), how likely are you to administer IV tPA to this patient?

[Respond on scale 0-100]
Here are images from the patient’s CT Perfusion scan.

[Randomized to view matched CBV: CBF or mismatched CBV:CBF images]

9. Given ALL the information available up this point (the history, examination, CT scan, CTA and CTP), how likely is the diagnosis of acute ischemic stroke?

[Respond on scale 0-100]

10. Given ALL the information available up to this point (the history, examination, CT scan, CTA and CTP), how likely are you to administer IV tPA to this patient?

[Respond on scale 0-100]

11. Based on your interpretation of the CT Angiogram,

There was an intracranial occlusion
There was not an intracranial occlusion
You were not sure about the presence of an intracranial occlusion

12. Based on your interpretation of the CT Perfusion study,

There was a perfusion mismatch
There was not a perfusion mismatch
You were not sure about the presence of a perfusion mismatch

13. Which of the following elements is routinely used in tPA decision-making in YOUR hospital? You may select more than one.

Clinical History
Clinical Examination
Unenhanced CT Scan
CT Angiogram
CT Perfusion
MRI Scan
MR Angiogram
MR Perfusion

14. Which element of the case was MOST important to the certainty with which you made your diagnosis?

Clinical History
Patient demographics
Clinical examination: motor findings
Clinical examination: language findings
Unenhanced CT scan
CT Angiogram
CT Perfusion

15. Which element of the case was MOST important to the certainty with which you established your treatment plan?

Clinical History
Patient demographics
Clinical examination: motor findings
Clinical examination: language findings
Unenhanced CT scan
CT Angiogram
CT Perfusion

16. Thinking about your diagnosis and management plan, what do you predict THIS PATIENT’s outcome to be at 90 days?
mRS 0: No disability
mRS 1: Some disability, but able to complete all functions
mRS 2: Mild disability that impairs at least one function
mRS 3: Moderate disability but able to ambulate independently
mRS 4: Moderately severe disability, unable to ambulate independently
mRS 5: Severe disability, bedbound
mRS 6: Death

17. In your opinion, is a severe left MCA stroke (aphasia, hemiplegia, dysphagia and incontinence) a fate worse than death?

Yes
No

18. Which of the following is MOST IMPORTANT to your opinion about stroke and death expressed above?

Your clinical experience with stroke and stroke patients
Your personal experience with stroke and stroke patients
Information from the medical literature
Institutional practice guidelines
Peer opinions at your institution

19. In your opinion, is IV tPA an effective treatment for acute ischemic stroke?

Yes
No

20. Which of the following is MOST IMPORTANT to your opinion about tPA efficacy?

Your clinical experience with stroke and stroke patients
Your personal experience with stroke and stroke patients
Information from the medical literature
Institutional practice guidelines
Peer opinions at your institution

21. Which of the following factors may influence your use of IV tPA? Select any and all that apply.

Patient Age
Patient Sex
Patient Race
Results of the physical examination (ie. NIHSS score)
Results of the unenhanced CT scan (ie. ASPECTS score)
Results of the CT Angiogram
Results of the CT Perfusion Scan
Your clinical experience with stroke patients
Your personal experience as the family member or friend of a stroke patient
Uncertainty surrounding the diagnosis of acute ischemic stroke
Uncertainty surrounding the prognosis of acute ischemic stroke
Uncertainty surrounding the interpretation of CT Perfusion scans
Your age
Your sex
Your race
Your beliefs about post-stroke quality of life
Your beliefs about the efficacy of IV tPA
None of the above

22. What is your age?

30 or under
31-40
41-50
23. What is your sex?
Female
Male

24. What is your race?
Asian
African-American or Black
Caucasian
Hispanic
Other

25. How long have you been practicing as a neurologist?
Less than 10 years
10-20 years
Greater than 20 years

26. Do you have subspecialty training in stroke or vascular neurology?
Yes
No

27. In what country do you currently practice?
Canada
United States
Other

Thank you for completing this survey. Your participation is greatly appreciated.