Formation and Function of Acute Stroke–Ready Hospitals Within a Stroke System of Care Recommendations From the Brain Attack Coalition

Mark J. Alberts, MD; Lawrence R. Wechsler, MD; Mary E. Lee Jensen, MD; Richard E. Latchaw, MD; Todd J. Crocco, MD; Mary G. George, MD; James Baranski, BS; Robert R. Bass, MD; Robert L. Ruff, MD; Judy Huang, MD; Barbara Mancini, RN; Tammy Gregory, BA; Daryl Gress, MD; Marian Emr, BS; Margo Warren, BA; Michael D. Walker, MD

Background and Purpose—Many patients with an acute stroke live in areas without ready access to a Primary or Comprehensive Stroke Center. The formation of care facilities that meet the needs of these patients might improve their care and outcomes and guide them and emergency responders to such centers within a stroke system of care.

Methods—The Brain Attack Coalition conducted an electronic search of the English medical literature from January 2000 to December 2012 to identify care elements and processes shown to be beneficial for acute stroke care. We used evidence grading and consensus paradigms to synthesize recommendations for Acute Stroke–Ready Hospitals (ASRHs).

Results—Several key elements for an ASRH were identified, including acute stroke teams, written care protocols, involvement of emergency medical services and emergency department, and rapid laboratory and neuroimaging testing. Unique aspects include the use of telemedicine, hospital transfer protocols, and drip and ship therapies. Emergent therapies include the use of intravenous tissue-type plasminogen activator and the reversal of coagulopathies. Although many of the care elements are similar to those of a Primary Stroke Center, compliance rates of ≥67% are suggested in recognition of the staffing, logistical, and financial challenges faced by rural facilities.

Conclusions—ASRHs will form the foundation for acute stroke care in many settings. Recommended elements of an ASRH build on those proven to improve care and outcomes at Primary Stroke Centers. The ASRH will be a key component for patient care within an evolving stroke system of care. (Stroke. 2013;44:3382-3393.)

Key Words: acute stroke • cerebrovascular disease • stroke

See related article, p 3289.

For the past 10 years, the organization of acute stroke care in the United States has moved in the direction of stroke centers. The concept is that stroke centers, by providing vital infrastructure, expertise, protocols, and monitoring care in accordance with nationally recognized guidelines and performance expectations, provide improved care and lead to better outcomes. At present, there are 2 recognized levels of stroke centers: Primary Stroke Centers (PSCs) and Comprehensive Stroke Centers (CSCs). Each provides high levels of care to patients with a variety of strokes in a range of geographic and clinical settings.

Several recent studies have affirmed the benefits of PSCs and CSCs in improving outcomes for admitted patients. The Joint Commission and other national, regional, and state agencies have developed and implemented certification programs for PSCs and CSCs. There are close more than 1000 PSCs certified by The Joint Commission, and many others certified by other entities, such as the Healthcare Facilities Accreditation Program, Det Norske Veritas, and various state health departments. Last year The Joint Commission began a formal program to certify CSCs. It is anticipated that there will be ≥100 to 200 CSCs in the United States for the next few years.

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From the Department of Neurology and Neurotherapeutics, University of Texas Southwestern, Dallas (M.J.A.); Department of Neurology, University of Pittsburgh, PA (L.R.W.); Department of Radiology and Medical Imaging (M.E.L.J.), Department of Neurology (D.G.), University of Virginia, Charlottesville; Department of Radiology, UC Davis Medical Center (R.E.L.); Department of Emergency Medicine, West Virginia University, Morgantown (T.J.C.); Centers for Disease Control and Prevention, Atlanta, GA (M.G.G.); National Stroke Association, Englewood, CO (J.B.); National Association of EMS Officials, Falls Church, VA (R.R.B.); Department of Neurology, VA Medical Center, Cleveland, OH (R.L.R.); Department of Neurosurgery, Johns Hopkins Hospital, Baltimore, MD (T.J.C.); Centers for Disease Control and Prevention, Atlanta, GA (M.G.G.); National Stroke Association, Englewood, CO (J.B.); National Association of EMS Officials, Falls Church, VA (R.R.B.); Department of Neurology, VA Medical Center, Cleveland, OH (R.L.R.); Department of Neurosurgery, Johns Hopkins Hospital, Baltimore, MD (T.J.C.); Centers for Disease Control and Prevention, Atlanta, GA (M.G.G.); National Stroke Association, Englewood, CO (J.B.); National Association of EMS Officials, Falls Church, VA (R.R.B.).

The findings and conclusions in this manuscript are the opinions of the authors and may not necessarily represent the official position of the Centers for Disease Control and Prevention and the National Institute of Neurological Disorders and Stroke.

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Correspondence to Mark J. Alberts, MD, Department of Neurology and Neurotherapeutics, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390-8897, E-mail Mark.Alberts@UTSouthwestern.edu

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Recent studies have shown that ≥50% of the US population is not within 60 minutes of a PSC. The corollary is that there are many hospitals in areas of the country with low population densities. These hospitals each admit a relatively small number of patients with stroke each year (perhaps <25–75 per year), although cumulatively they admit a relatively large percentage of all patients with an acute stroke. Hospitals in such circumstances may be less likely to have the resources to become a PSC and may lack the experience and expertise to provide ongoing care in some if not many cases of acute stroke. However, among these various hospitals, there is a need to distinguish between those that offer enhanced care and expertise for acute stroke versus those with only basic or no organized abilities and expertise.

Considering the unpredictable and emergent nature of stroke, it is prudent to have some provision to deliver acute stroke care in all settings. To address these concerns, the Brain Attack Coalition (BAC) believes that there should be another level of stroke center that distinguishes and defines those smaller hospitals that have the basic capabilities (personnel, expertise, processes and resources) to provide acute stroke care from those that lack such resources.

We propose a new designation for hospitals that are not PSCs, yet can provide timely, evidence-based care to most patients with an acute stroke—the Acute Stroke–Ready Hospital (ASRH; some have called these Stroke-Ready Hospitals). The vision and intent of the ASRH is to provide initial diagnostic services, stabilization, emergent care and therapies to patients with an acute stroke who are seen in their emergency department (ED). They would then arrange for appropriate patients to be transferred to another hospital, that is, a PSC or CSC, that would provide ongoing, definitive care. After the acute event has resolved, it is expected that most patients would return to their local facilities and healthcare professionals for outpatient care and perhaps rehabilitation.

The goals of this publication are to define the key elements of an ASRH, present options for performance measures, and discuss how an ASRH would operate within a stroke system of care that encompasses a variety of geographic areas, populations, hospitals, cities, and levels of medical resources and expertise. The American Heart Association (AHA)/American Stroke Association (ASA) has published policy recommendations for stroke systems of care, some of which are applicable to the operations of an ASRH.

### Methods

We performed a literature search using Medline of articles published from January 2000 to early January 2013 to identify studies and guidelines that defined and validated elements of acute care that seemed important for patients with an acute stroke. Key words for the search included, stroke care, stroke centers, acute stroke teams (ASTs), stroke protocols, stroke therapies, stroke outcomes, and similar elements. We also included search items related to teletechnologies in stroke care, such as telemedicine, telestroke, teleradiology, etc. In addition to original articles, we also reviewed care guidelines from other documents or organizations that are relevant for acute stroke care (ie, AHA Acute Stroke Guidelines, American Academy of Neurology Stroke Care Guidelines). Components of a PSC that were included in the initial and revised PSC recommendations were also included, although they were modified on the basis of resources likely to be available at most ASRHs.

The importance and use of these care elements were graded using the modified grading system that the BAC developed for the revised PSC guidelines. This grading system recognizes not only specific therapies, but also elements of care, such as personnel, protocols, and diagnostic procedures (see Table I in the online-only Data Supplement). Each of these elements was further reviewed by the membership of the BAC (see Appendix for member organizations and representatives) for their inclusion on the basis of medical, logistical, and financial considerations at an ASRH. Healthcare professionals from other groups were also given the opportunity to review and to comment on the ASRH recommendations.

### Results

There are some key elements of a PSC that an ASRH should provide because they are essential for the care of patients with an acute stroke in any setting (Tables 1 and 2). These can be divided into 9 specific care areas and 3 ancillary or support areas. Specific details of these elements are modified on the basis of characteristics of an ASRH, such as its location, staffing levels, financial issues, etc. Each of these elements is described in detail, along with some suggested performance metrics.

### ASRH Care Elements

#### Acute Stroke Team

An acute stroke team (AST) is a key element for any ASRH. Prior studies have shown the importance of such a response team to provide organized care in a safe and efficient manner. The presence of an AST is an independent predictor of the ability to administer intravenous tPA and reduced mortality. These teams may also be factors in the improved outcomes of patients with stroke at a stroke center.

The staffing of the AST at an ASRH should include a minimum of a nurse (or nurse practitioner or physician assistant) and a physician. It is important for each member of the AST to have, at minimum, some basic training in acute stroke care. Examples of such training might range from a nurse (or advanced practice nurse) with prior experience in a neuroscience intensive care unit, an ED nurse who has completed continuing education courses in areas of acute stroke care, and physicians who have attended regional or national courses dealing with acute stroke care. (Although a neurologist or neurosurgeon would be ideal members of the AST, their availability at rural locations would probably be limited.) Higher levels of physician expertise in stroke care can be provided via a telemedicine link with another facility. Even if this is done, in most circumstances, it is recommended that there be ≥1 physician onsite to supervise patient care, order medications, and deal with emergent issues.

Members of the AST should be available and on call 24 hours a day, 7 days a week. The AST should respond to suspected patients with an acute stroke who are in the ED or an inpatient unit at the ASRH. Although their presence in the hospital is preferred, members of the AST may reside outside of the hospital as long as they can be at the bedside within 15 minutes of being called. In some facilities, members of the cardiac code team might be trained to respond to patients with an acute stroke. The hospital should support the development of a call-log or registry for the AST that captures key data points, such as the number of calls, response times, and patient diagnoses, treatments, complications of treatment, and disposition.
It is recommend that physician and nurse members of the AST receive ≥4 hours/y in education related to cerebrovascular disease, with an emphasis on acute care, diagnosis, and treatment. This is an extrapolation from the educational requirements for a PSC. It represents a 50% reduction in the level of education recommended at a PSC for key medical personnel, which we think is reasonable on the basis of anticipated staffing levels at a typical ASRH facility.1,18

The inclusion of an AST with 24/7 availability is an essential element for an ASRH and is a class I, level A recommendation. The need for 4 hours of education per year is supported as a class IIA, level B recommendation.

**Stroke Protocols**

A written stroke protocol is an essential element to ensure that all patients with stroke receive organized care in a safe and an efficient manner.16,20–22 Such protocols also ensure that important care elements are not omitted, and that prohibited medications or treatments are not administered. These protocols should include standardized order sets that deal with aspects of acute diagnosis, such as checks of vital signs and neurological function, blood tests, and brain imaging studies. These protocols should encompass care in the ED and in-hospital (if appropriate). They should be developed by a multidisciplinary team and reviewed and revised at least annually to reflect changes in medical knowledge, care standards, and guidelines.23 Such protocols should address all types of strokes (ie, ischemic, intracerebral hemorrhage [ICH], subarachnoid hemorrhage).

The protocols could be paper-based or computer-based depending on the standard practice at a specific facility. In general, the BAC supports the use of electronic medical records (including medical orders) because they reduce errors and can be easily modified as diagnostic and treatment paradigms evolve.24 Written or (preferably) electronic stroke protocols are an essential element of an ASRH and are a class I, level A recommendation. These should be used for ED and inpatient care.

**Emergency Medical Services**

In most community settings, a patient with an acute stroke is taken to the hospital by emergency medical service (EMS) personnel. The ability of EMS personnel to recognize patients with a possible stroke, to communicate their findings to the receiving hospital, and to stabilize and transport such patients is essential to the effective role of an ASRH within a stroke system of care. Studies have shown that patients with stroke who activate EMS by calling 9-1-1 are more likely to receive intravenous tissue-type plasminogen activator (tPA) and to be more rapidly diagnosed and treated.25

Because EMS is frequently the entry point for patients with stroke into the stroke system of care, we think that it is appropriate for us to comment on the critical relationship between the ASRH and the local EMS system(s). We acknowledge and

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**Table 1. Comparison of Elements in an Acute Stroke–Ready Hospital and Primary Stroke Center**

<table>
<thead>
<tr>
<th>Element</th>
<th>ASRH</th>
<th>PSC</th>
<th>Comment*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute stroke team</td>
<td>15-min response time</td>
<td>15-min response time</td>
<td>Minimum of 2 members</td>
</tr>
<tr>
<td>Stroke protocols</td>
<td>Revise annually</td>
<td>Revise annually</td>
<td>Applies to all types of strokes</td>
</tr>
<tr>
<td>Emergency medical services</td>
<td>Training in field assessment tools for stroke</td>
<td>Training in field assessment tools for stroke</td>
<td>At least 2 h of stroke-related education annually</td>
</tr>
<tr>
<td>Emergency department</td>
<td>Written protocols for treatment and stabilization; 4 annual h of stroke education</td>
<td>Written protocols for treatment and stabilization; 8 annual h of stroke education</td>
<td>Physician and nurse education for key staff</td>
</tr>
<tr>
<td>Laboratory testing, ECG/chest radiograph</td>
<td>Test results available within 45 min of ordering</td>
<td>Test results available within 45 min of ordering</td>
<td>Testing available 24/7</td>
</tr>
<tr>
<td>Brain imaging*</td>
<td>Test completed and read within 45 min (60 min for MRI)</td>
<td>Test completed and read within 45 min (60 min for MRI)</td>
<td>Head CT or MRI acceptable; service available 24/7</td>
</tr>
<tr>
<td>Stroke unit</td>
<td>Not required unless patients are admitted</td>
<td>Required for admitted patients; should include protocols and telemetry</td>
<td>Specific monitoring protocols even if not admitted</td>
</tr>
<tr>
<td>IV tPA†</td>
<td>Door-to-needle time of ≤60 min</td>
<td>Door-to-needle time of ≤60 min</td>
<td>IV tPA available 24/7</td>
</tr>
<tr>
<td>Neurosurgical services‡</td>
<td>Available within 3 h</td>
<td>Available within 2 h</td>
<td>Can be onsite or by transfer of patient</td>
</tr>
<tr>
<td>Initiation of telemedicine link</td>
<td>Within 20 min of when it is deemed medically necessary</td>
<td>Respond within 20 min of link request if serving as a hub</td>
<td>Type of link will vary by service vendor; same response times for receiving hub CSC</td>
</tr>
<tr>
<td>Telemedicine/teleradiology equipment</td>
<td>Onsite to transmit</td>
<td>Onsite and offsite to receive</td>
<td>Applies to a CSC if they will be a hub site</td>
</tr>
<tr>
<td>Transfer of patients to PSC or CSC</td>
<td>Patient leaves within 2 h of ED arrival (or once medically stable)§</td>
<td>Not applicable in most cases unless transferred to a CSC</td>
<td>Mode of transportation will vary</td>
</tr>
</tbody>
</table>

ASRH indicates Acute Stroke–Ready Hospital; CSC, Comprehensive Stroke Center; CT, computed tomography; ED, emergency department; IV tPA, intravenous tissue plasminogen activator, and PSC, Primary Stroke Center.

*Comments apply to the ASRH recommendations unless otherwise noted.
†See Performance Metrics section for further details.
‡Neurosurgical coverage might include having a neurosurgeon at the hospital or transfer of the patient to another facility where a neurosurgeon is available and can be onsite.
§Exceptions include factors beyond the control of the ASRH, such as weather delays, mechanical issues, etc.
understand that the organization, as well as the medical and regulatory oversight of EMS, is highly variable in the United States. However, EMS authorities must ensure that there are written protocols that detail how a patient with a suspected stroke is triaged, treated, and transported to the closest most appropriate hospital. The effect of this in terms of acute treatment has been documented in a recent publication.26

Because our recommendations refer to ASRHs as part of a stroke system of care, we think it is justified for us to comment about elements of EMS because they might affect and interact with patients with acute strokes and the ED. A recent AHA Policy Statement addresses these issues in more detail.26a

It is recommended that EMS personnel have specific training in the recognition of patients with a possible stroke, including the use of ≥1 accepted field assessment tools (eg, Cincinnati Stroke Scale, Los Angeles Prehospital Stroke Scale).27 Training in acute stroke diagnosis and treatment should occur at least annually, with a minimum educational exposure of ≥2 hours/y. Other key elements include the establishment of a time of onset, the use of concomitant medications, and other major medical conditions. Data from recent studies have shown that EMS communication and notification of the ED when a potential patient with stroke is en route can shorten door to imaging and door to needle times, both of which are key parameters in receiving intravenous tPA therapy.28

After initial evaluation and treatment in the field, EMS should transport the suspected patient with stroke to the nearest ASRH unless there is a PSC or CSC within 20 miles or <15- to 20-minute transportation time.29 The exception to this triage paradigm is if the patient has some other emergent medical problem (cardiac arrest, severe hypotension) that mandates diversion to the nearest hospital for life-saving resuscitation. The AHA/ASA guidelines also recommend that patients with an acute stroke be preferentially transported to the nearest stroke center.2 Furthermore, local EMS rules and regulations may restrict transportation times and triage options.

Several states and many cities (FL, IL, [Chicago], MD, and TX, among others) have passed laws and regulations that mandate preferential triage of patients with stroke to the nearest PSC or CSC.26 Although preferential triage usually applies to urban settings (because there are relatively few PSCs or CSCs in rural areas) in theory, if not practice, it should apply to all parts of a state. We are hopeful that when ASRHs proliferate, similar rules will be developed and enforced for preferential diversion of patients to the nearest ASRH in a rural setting.

In many settings, EMS personnel in the field receive orders via radio from medical control officers, typically physicians. In these settings, the medical control officers should have sufficient training and expertise in acute stroke diagnosis and care. Although local regulations may vary, the BAC recommends that these medical personnel receive ≥4 hours/y of education related to cerebrovascular disease.

A well-trained and organized EMS is a key component for a stroke system of care that includes ASRHs. EMS providers should have protocols that address the assessment, triage, treatment, and transportation of patients with a suspected acute stroke. Notification of the ED by EMS of an en route patient with stroke is also recommended. EMS should transport a patient with an acute stroke to the nearest stroke center, whatever its level. All of the above are class I level A recommendations. Medical control officers should have ≥4 hours of annual education related to cerebrovascular disease (class IIa, level C).

Emergency Department

The vast majority of patients with an acute stroke will enter the ASRH via the ED. It is essential that ED personnel (physicians and nurses) have stroke protocols in place for the acute diagnosis, stabilization, monitoring, and treatment of patients with all types of stroke. In addition to standard orders that are likely to be included in the stroke protocols, ED protocols should include detailed instructions for the administration of intravenous tPA for ischemic stroke and the reversal of anticoagulation for patients with an intracranial hemorrhage. The use of a standardized assessment score or scale, for example, National Institutes of Health Stroke Scale, for the initial assessment and monitoring of patients is highly recommended. Other elements might include protocols for the treatment of raised intracranial pressure. Recent studies have shown that EDs that are part of a PSC have improved care processes26; it is hoped that this will also be seen at an ASRH.

For EDs at ASRHs with a low volume of patients with stroke (1 every few weeks), consideration should be given to running mock stroke codes with various clinical scenarios. This might serve to keep personnel up-to-date with current protocols, refresh their memories, and deal with any logistical issues that could affect stroke care. This also applies to the AST at hospitals with low stroke volumes.

As with all physicians and nurses at an ASRH who deal directly with patients with an acute stroke, ED personnel should have a minimum of 4 hours/y of educational time that is related to the care of patients with cerebrovascular disease. Prior studies have shown that continuing medical education of the medical staff is an independent predictor of receiving intravenous tPA, which is an important medical therapy for acute ischemic stroke.26 This requirement might be met in a variety of ways, including online continuing medical education credits, attendance at grand rounds, lunch-time lectures, regional and national meetings, and various educational courses.

The existence of a well-organized ED with trained personnel is a key element of an ASRH and is supported by a class I, level A recommendation. The use of a standardized stroke assessment scale or scales, and emergent care protocols, is a key element for ED care at an ASRH (class I, level A recommendations).

Laboratory Testing

The ability to perform and to complete basic laboratory testing on patients with a stroke is essential for several reasons: (1) it is useful for diagnosing metabolic and infectious disorders that can masquerade as a stroke syndrome, (2) it is important to ensure that patients with stroke can be treated with the proper acute medications, and (3) it is needed to determine the possible causes of some types of stroke. Basic tests, such as a complete blood count, chemistries, coagulation studies, pregnancy test (where indicated), troponin, and an ECG, should be performed on all patients with a suspected stroke.2 More advanced testing in the ED, such as a toxicology screen and a chest radiograph, might be helpful in some cases. An ASRH
must be able to complete basic laboratory tests, an ECG, and chest radiograph (if needed) within 45 minutes of them being ordered. The above test results should not delay the initiation of intravenous tPA therapy in most cases.5

The availability of standard laboratory testing with rapid completion times is a key component of an ASRH and is supported by a class I, level A recommendation.

**Brain Imaging**

The importance of brain imaging to support the diagnosis of stroke, to determine the type of stroke, and to exclude other disease that might present with stroke-like signs and symptoms is an essential function of an ASRH. In most cases, the first (and perhaps only) imaging study readily available will be a noncontrast head computed tomographic scan. This type of scan is usually sufficient to rule out other conditions that could present with stroke-like symptoms, such as a subdural hematoma, large abscess, or tumor. When performed acutely, a head computed tomography (CT) will often be either negative or show only subtle changes in cases of ischemic stroke, especially if the stroke is small or acute. A head CT is sensitive and accurate for the diagnosis of most types of hemorrhagic stroke (ie, ICH, subarachnoid hemorrhage). Other tests, such as a CT angiogram, can rapidly determine if there is a large-vessel occlusion. Advanced techniques, such as CT perfusion, can assess areas of brain with likely ischemia.31

MRI with diffusion imaging is more sensitive than head CT for detecting small areas of ischemia, as well as early ischemic changes.32 MRI can also be useful for diagnosing diseases that could produce stroke-like symptoms, such as demyelinating processes, small metastatic tumors, and cavernous angiomas. MRI is also useful for differentiating acute, subacute, and chronic ischemic lesions and hemorrhages. The use of brain MRI is now recommended in several guidelines for imaging in suspected patients with stroke and is a new required element for a PSC.33

For an ASRH, it is recommended that brain imaging with a noncontrast head CT or MRI be performed and read within 45 and 60 minutes, respectively, of being ordered. (Advanced brain imaging with MRI should be reserved for complex cases and should not be done routinely if it will delay the use of intravenous tPA in acute ischemic stroke.) Reading and interpreting emergent scans can be performed by onsite personnel or via a teleradiology process. In such cases, the technical capabilities of that system must be adequate to ensure proper resolution of the images to permit the diagnosis of lesions, such as a subtle subarachnoid hemorrhage and small subdural hematoma, that could affect or change acute therapy.34–37 The specific technical aspects of these systems are discussed in more detail (Table 3). In all circumstances, it is essential that the interpreting physician be provided with sufficient clinical information and details to ensure an accurate interpretation and diagnosis. Whether the interpretation is done onsite or remotely, the formal reading results should be communicated to the treating physician(s) within the time frames noted above.

Acute brain imaging capabilities and interpretation services must be available on a 24/7 basis. Personnel interpreting such scans should be board-certified radiologists or other physicians with experience and expertise in reading head CTs and brain MRIs.

The ability to complete and to interpret emergent brain imaging (head CT or MRI) within a specified time period is a key component for an ASRH and is supported by a class I, level A recommendation.

**Emergent Therapies**

An ASRH should be able to deliver several acute therapies that can improve outcomes for patients with a variety of strokes. Examples include intravenous tPA for acute ischemic stroke, measures to reverse coagulopathies in patients with hemorrhagic strokes, steps to control and reduce elevated intracranial pressures in appropriate patients, control of seizures, treatment of blood pressures that are too high or too low, and stabilization of other vital functions and metabolic derangements (Table 2).3 Other related aspects of emergent therapy would include an assessment of initial neurological function, as well as stroke severity.

The ASRH should have protocols and policies in place that define treatments in all of the above domains of care. These protocols should be updated and revised at least annually using current published care guidelines from organizations, such as the AHA, ASA, American Academy of Neurology, the American Association of Neurosurgery and the Congress of Neurological Surgeons, as well as other organizations. The use of telemedicine/telestroke and related technologies may aid the treating clinicians and help guide therapy if the bedside expertise of the available healthcare providers is in need of augmentation.36,37

In some cases, a drip and ship approach will be used, meaning that treatment will be initiated at the ASRH and continued while the patient is transported to a PSC or CSC for ongoing care. In such cases, it will be important for the medical professionals at the receiving hospital to communicate directly with

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**Table 2. Examples of Emergent Care and Treatment Elements of an ASRH**

<table>
<thead>
<tr>
<th>Care Element</th>
<th>Purpose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stabilize vital signs</td>
<td>Prevent clinical deterioration</td>
<td>Oxygenation and blood pressure management are key elements</td>
</tr>
<tr>
<td>Diagnose stroke type</td>
<td>Determine acute treatment options</td>
<td>May use teleradiology/telestroke</td>
</tr>
<tr>
<td>Assess stroke severity</td>
<td>Important for acute treatment options and outcomes</td>
<td>Different scales based on stroke types; serial assessments needed</td>
</tr>
<tr>
<td>IV tPA protocol</td>
<td>Improves outcomes for acute ischemic stroke</td>
<td>Standard of care</td>
</tr>
<tr>
<td>Reversal of coagulopathy</td>
<td>Prevent expansion of hemorrhage</td>
<td>Various treatment options</td>
</tr>
<tr>
<td>Treatment of elevated ICPs</td>
<td>Prevent neurological worsening</td>
<td>Medical and surgical options</td>
</tr>
<tr>
<td>Treatment of seizures</td>
<td>Prevent medical complications</td>
<td>IV agents may be needed</td>
</tr>
</tbody>
</table>

ASRH indicates Acute Stroke–Ready Hospital; ICP, intracranial pressure; and IV tPA, intravenous tissue plasminogen activator.
the medical staff at the ASRH before and after the transfer to share baseline clinical information and provide feedback about the effectiveness of the initial treatment, accuracy of diagnosis, and the patient’s ultimate clinical outcome.38

An ASRH should have written protocols that detail available emergent therapies and reflect current treatment guidelines. Specific performance measures, such as door-to-needle times, for intravenous tPA and other therapies should be developed. The protocols should be revised at least annually based on recent changes in care guidelines and new medical care standards. The staffs at the ASRH and any receiving hospital should develop protocols that enhance clear and concise communication and feedback. These are class I, level A recommendations (for treatment protocols) and class IIa, level C (for communication protocols).

**Stroke Unit**

There are abundant data from individual studies and meta-analyses that stroke units improve outcomes and reduce inhospital complications.39–41 However, it is anticipated that many of the patients with stroke at an ASRH will not be admitted to that facility but will be transferred to a nearby PSC or CSC after they are stabilized. Thus, the need for most ASRHs to have a formal stroke unit is somewhat mitigated.

If the ASRH does envision admitting some of these patients, then they should develop a formal stroke unit. Details of the elements of a stroke unit are discussed in the recently published revised PSC guidelines.3 Although there may be some patients with stroke who are unlikely to benefit from a stroke unit (for example, a patient with end-stage dementia and a new stroke, terminal cancer and a new stroke, patients who will be getting palliative or hospice care), most patients will benefit from the intense nursing care and protocols common to stroke units, telemetry monitoring, and similar interventions. These are the essential elements of a stroke unit.

Although the size and location of a stroke unit at an ASRH may vary, at a minimum it should include dedicated and well-trained nursing personnel, multichannel telemetry monitoring, care protocols (for example, swallow evaluation, deep vein thrombosis prophylaxis), neurological assessment tools and scales, and tracking of outcomes.3

An ASRH that has the elements described above along with a stroke unit is essentially equivalent to a PSC and should seriously consider developing all of the elements of a PSC and seek formal certification as a PSC. This is based on abundant data showing improved treatments and outcomes for patients at a PSC.5,8

If an ASRH intends to admit many or most patients with an acute stroke, it is a class I level A recommendation that the facility develop a stroke unit with elements and procedures similar to those of a stroke unit at a PSC.

**Neurosurgical Services**

Some patients who present to an ASRH will need acute or eventual neurosurgical evaluation and treatment, particularly those with large ischemic strokes, cerebellar strokes, ICH, and subarachnoid hemorrhage.42–45 Because of geographic and staffing issues, a neurosurgeon may not be readily available at many if not most ASRHs, and it is unlikely that such hospitals would have the infrastructure and support services to provide ongoing care to many of these patients (ie, operating room and neuroscience intensive care unit). This is an area where teletechnologies and urgent transfer of patients after they are stabilized would be most appropriate and effective. Some of the care elements discussed above should be used to stabilize such patients before transportation for definitive care.

Considering the remote locations of some ASRHs, and other logistical challenges with emergent transfer, we recommend that neurosurgical services be available to such patients within 3 hours of when it is deemed necessary. This availability encompasses transporting the patient to a facility with a neurosurgeon readily available or having a neurosurgeon go to the ASRH. (By comparison, a PSC should have neurosurgery services available within 2 hours.) There should be a written neurosurgery call schedule and a clear triage and transportation plan for those patients in need of acute neurosurgical services. This includes a written agreement between each ASRH and ≥1 hospital that has neurosurgery coverage on a 24/7 basis consistent with the PSC or CSC recommendations.3,4

The presence of a neurosurgery coverage plan, call schedule, and a triage and transportation plan is a class I level C recommendation.

**ASRH Ancillary or Support Elements**

**Administrative Support and Leadership**

Any hospital seeking to become an ASRH will need the support of hospital administration. This will include organizational support, financial resources, and political assistance. Specific areas in need of change might include enhanced staffing of the ED, improvement of infrastructure, investment in teletechnologies, partnering with other facilities to enhance transfer of patients, and educational programs, among others. Staffing salaries should be modified to reimburse key members of the ASRH care team properly, especially those taking 24/7 call. It is recommended that a senior administrator take ownership of the ASRH effort, organize and prioritize key programmatic elements, and provide the resources to ensure a successful program. At most hospitals, stroke is a leading programmatic element, and neuroscience intensive care units. This is an area where teletechnologies and urgent transfer of patients after they are stabilized would be most appropriate and effective. Some of the care elements discussed above should be used to stabilize such patients before transportation for definitive care.

Another important element is medical leadership of the program. Although leadership by a neurologist or neurosurgeon might be beneficial or even optimal in many cases, the distribution of these specialists is likely to limit their availability at many ASRH facilities. Other specialists who might lead such a program include emergency medicine physicians, internists, and radiologists, among others. In some settings, advance practice nurses have been successful in leading a stroke center. Whoever the leader is he or she should have demonstrated experience in the care of patients with cerebrovascular disease. This might include completion of a fellowship or other specialized training in the area of cerebrovascular disease, attendance at national courses, prior experience in a neuroscience intensive care unit, etc. The medical director of an ASRH should have ≥4 hours/y of educational time in cerebrovascular disease.
The medical and hospital leadership should develop and implement programs and meetings (ideally peer-review) to assess overall care, treatments, outcomes, and complications. The frequency of such meetings will be determined and defined by the governance of each facility consistent with their overall policies.

Administrative support for the staff and infrastructure of an ASRH is a key element for its success. The ASRH should have a designated medical director with experience in acute stroke care (the above are class IIa, level C recommendations). Regular assessments of care and complications should be conducted consistent with local and facility policies (class IIa, level C recommendation).

**Teletechnologies**

Because of the relatively isolated location of most ASRHs, the use of a telestroke type of technology will be needed at many of these facilities. (There might be some facilities that determine that they have sufficient neurological and neuro-imaging expertise readily available; in such cases, the need for telestroke systems might be mitigated). There are a variety of teletechnologies currently used for the diagnosis and treatment of patients with a known or suspected stroke (and other conditions). These technologies range from a simple oral telephone conversation to a multimodal live interactive physical examination with real-time viewing of the patient and their neuroimaging studies.

A live or interactive telestroke assessment typically includes both audio and video components. There are recommended technical standards for these types of interactions (Table 3).36,37,44 Meeting these standards will ensure that high-quality data are used to make important treatment decisions. These standards apply to the sending (ASRH) facility, as well as the receiving (PSC or CSC) facility. In most cases, these systems consist of a portable computer system that can be wheeled into a patient room in the ED. A related link can then be established for the transmission of radiology images. At the receiving facility, a laptop or desktop computer will likely be sufficient to meet the diagnostic needs. Some clinicians have discussed using a smartphone-type platform to receive such images. It is unclear if the small screen of these devices will offer the needed size and resolution for accurate interpretation of head CT images on a consistent basis although early reports are encouraging.45

There are a number of studies in the literature that support the efficacy and safety of telestroke in improving care and increasing the appropriate use of emergent medications, such as intravenous tPA.46–48 The medical professionals providing remote medical guidance should have training and expertise that is equivalent to that of someone at a PSC or CSC. It is important to remember that telestroke is envisioned as a useful tool for the diagnosis and treatment of patients with all types of cerebrovascular disease. It should be viewed as a solution or tool to be used for the absence of onsite physicians with special expertise (in cerebrovascular disease) in an emergency situation. However in most cases, the ongoing medical care beyond the acute period (at either the ASRH or another facility) for patients with active cerebrovascular disease should be provided by trained medical personnel at that facility who can be at the patient’s bedside.

There is general agreement that a telestroke link should be fully established (live audio and video connection) within 20 minutes of when it is deemed necessary based on the clinical scenario of a specific patient. This time frame is consistent with diagnostic and treatment time epochs as recently published and should be sufficient to meet a 60-minute door-to-needle time for intravenous tPA therapy.2 In other less urgent cases, the time frame for establishment of a telestroke link might be longer.

Although the technical aspects of the telemedicine/telestroke link are important, of equal, if not greater, importance is a well-designed support system. This includes contractual agreements between the ASRH and the consulting facility (typically a PSC or CSC), expectations for response times, training and expertise of personnel at the consulting facility, as well as financial and legal considerations. Many of these issues have been addressed for many established telemedicine/telestroke programs and systems.48–50 Although the specific terms of any agreements will vary with each group of institutions, they should include specific time performance measures (for example, how long it takes to establish a telemedicine link), as well as reimbursement for taking telemedicine calls and participating in remote consultations. There should be ongoing assessments of diagnostic accuracy and treatment outcomes, including complications and delays in treatment.

The use of telemedicine technologies at most ASRHs is a key component to provide acute care and its general use is supported by many studies; this is a class I, level A recommendation. It is recommended that such telemedicine programs be supported by a written contractual agreement that addresses performance standards, legal issues, and reimbursement (class IIa, level C). A telemedicine link should be established within 20 minutes of when it is deemed medically necessary by the ASRH staff (class IIa, level C recommendation).

**Table 3. Examples of Technical Parameters for Telemedicine Systems Related to Stroke**

<table>
<thead>
<tr>
<th>Imaging or Data Element</th>
<th>Requirement</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speed</td>
<td>20 frames/s or higher</td>
<td>Bidirectional audio and video</td>
</tr>
<tr>
<td>Resolution</td>
<td>720p at 1 Mbps</td>
<td>1080p preferred for images</td>
</tr>
<tr>
<td>Latency</td>
<td>≤500 ms</td>
<td>Dependent on type of connection</td>
</tr>
<tr>
<td>Images</td>
<td>Full color</td>
<td>Full zoom and pan features</td>
</tr>
<tr>
<td>Screen size</td>
<td>≥13 inches or more</td>
<td>iPhone size may not be sufficient</td>
</tr>
<tr>
<td>Security</td>
<td>Encryption needed</td>
<td>Meets state and Federal standards</td>
</tr>
<tr>
<td>Connections/ formats</td>
<td>Fixed ISDN or IP (private or public)</td>
<td>DICOM for images</td>
</tr>
<tr>
<td>Redundancy</td>
<td>≥1 back-up system</td>
<td>Applies to sender and receiver facility</td>
</tr>
</tbody>
</table>

DICOM indicates digital imaging and communications in medicine; IP, internet protocol; and ISDN, integrated services digital network.

*Different telemedicine systems may have various technical parameters and requirements; the above are examples of some of the key parameters and performance levels.35–37,44

**Transfer of Patients to a PSC or CSC**

It is anticipated that many or most patients with stroke seen initially at an ASRH will require emergent transportation to a
PSC or CSC. It is recommended that such transfers occur, that is, the patient leaves the ASRH, within 2 hours of the patient presenting to the ASRH, which is ample time in most cases for the initial diagnosis, stabilization, discussions with family and outside facilities, and the arrangement of transportation. In some cases, the actual transfer will occur well before 2 hours. In other cases, the patient might require a longer stay at the ASRH if they are medically unstable. Even in such cases, transfer to a PSC or CSC with more resources should occur as soon as possible because a higher level of care may ultimately benefit even the unstable patient.

There should be ≥1 written transfer agreements between the ASRH and a PSC and a CSC (although a CSC alone is sufficient) that contains key information, such as contact personnel, phone numbers, hours of operation, transportation options, etc. These agreements should be comprehensive and address transfer of patients on a 24/7 basis, consistent with local rules and regulations. If past experience shows that the receiving hospital(s) is often on bypass or diversion because of lack of bed space, then additional receiving hospital(s) should be part of the transfer agreement(s). Specific transfer criteria and expectations for care en route should also be part of the transfer agreement or be detailed in documents that are exchanged between the institutions. We are aware that in some areas, a formal agreement may not be allowable because of legal considerations. In such cases, there should still be an informal arrangement with protocols that detail the logistical aspects of emergent transfers.

Some patients will be transferred while they are receiving various acute medications or shortly after such medications are administered (so called drip and ship). This treatment paradigm has been used in many cases of intravenous tPA therapy and may be applicable to other therapies, such as neuroprotective agents and perhaps coagulopathy reversal treatments. A recent study of national data suggested that 17% of patients treated in the United States with intravenous tPA receive such therapy using a drip and ship protocol. Recent studies suggest that such an approach using intravenous tPA for acute ischemic stroke is as safe and efficacious as treatment at a regional stroke center. We are unaware of any published data about en route complications of intravenous tPA infusion for acute ischemic stroke. In all drip and ship cases, close attention and documentation should be provided about the type of therapy, dosing, time of initiation, completion, and complications.

For the interfacility transfer of all patients with an acute stroke, detailed and well-formulated protocols based on best practices should be used. During the transfer, the patient must be accompanied by medical personnel who have training and expertise directly related to the therapy being used.

There are some patients and circumstances in which the transfer of a patient might be superfluous. This might include patients who are obviously moribund, those who decline further treatments, end-of-life situations (severe dementia and diffuse cancer), and patient or family refusal, among others. The option of transfer from the ASRH should be offered to all patients in whom further medical therapy can reasonably be expected to lead to improved outcomes and reduced complications.

There should be a detailed, written transfer agreement, arrangement, or understanding (depending on state regulations and laws) between the ASRH and ≥1 PSC and 1 CSC (a CSC alone is also sufficient). This agreement should ensure 24/7 ability to transfer all appropriate patients consistent with local rules, regulations, and policies. There should also be a written document with ≥1 transportation vendor that cover both ground ambulance and air ambulance transfer options. These should address how to facilitate the safe and efficient transfer of patients between facilities on a 24/7 basis. These are class IIA, level B recommendations. A drip and ship approach for acute therapies, particularly, intravenous tPA, seems to be safe, effective, and feasible (class IIA, level B).

**Performance Metrics**

It is important for ASRHs to have well-defined performance metrics to ensure that they are providing high level care to all patients with stroke. Past studies have shown that the collection of such metrics and their incorporation into quality improvement programs can increase compliance with various guidelines and enhance patient care. There are some standard metrics that should apply to all ASRHs, such as door-to-needle time for intravenous tPA and other acute therapies, door-to-imaging times, and door-to-physician assessment.

As noted in Table 1, several of the required elements of an ASRH have specific performance times. Most of these elements as applied to a PSC have an 80% compliance requirement, meaning that a PSC must comply with the recommendation in 80% of the cases. For the ASRH, the level of compliance for the elements in Table 1 should be ≥67%. This is meant to reflect the geographic, logistical, staffing, and financial challenges that some ASRHs may face, as well as resource limitations that exist at some ASRH facilities. Overall, however, the performance metric or standard is identical or similar to that of a PSC, yet the compliance rates have been somewhat modified.

Many of the disease performance measures used at a PSC apply to elements of inpatient care, such as deep vein thrombosis prophylaxis, use of antithrombotics, etc. Some of these elements will not be applicable to patients at an ASRH because they will typically not be admitted to that facility. Considering the features of an ASRH, some novel performance measures might be developed. Examples include door-to-door times for patients who are transferred to an outside facility, door-to-computer link time for cases where a teletechnology is used, and protocol violations for the use of intravenous tPA and other acute therapies (Table 4). An assessment of initial stroke severity with some type of scale (National Institutes of Health Stroke Scale for ischemic stroke and ICH score of intracerebral hemorrhage), is another element that may be helpful for determining patient eligibility for various treatments, as well as adjusting outcomes.

In cases when a stroke patient is not transferred to a PSC or CSC, some of the performance measures that are used at these facilities should be adapted and modified for use at the ASRH. Examples include deep vein thrombosis prophylaxis, use of antithrombotics within 48 hours of admission,
clearly delineate when and how patients with specific types of
ties. Examples include laws in some states that mandate that
and perhaps research (in some cases). This level of organi-
support and oversight, education, outcomes, rehabilitation,
centers (ASRH, PSC, CSC), as well as EMS, government
level of care in the most expeditious and efficient manner.

The goal is to make sure that a patient receives the proper
resources, administrative oversight, or a combination of the
Such a system can be organized on the basis of geography,

ASRH Certification and Stroke Systems

ASRH Certification
Various states and regions are already incorporating the
ASRH tier of hospital facilities into their overall systems of
care. This is especially important in states where there are legis-
late mandates that direct EMS to transport patients to the
nearest stroke center facility. In such cases, it is important that
the public and medical personnel are confident that a hospital
that defines itself as an ASRH actually meets the requirements
of an ASRH as defined in this document and other similar
publications. Prior studies have shown that self-certification is
neither objective nor accurate.5

On the basis of these concerns, the BAC strongly endorses
an ASRH certification program or designation process that
incorporates the following elements: (1) certification be-
formed by an outside, independent organization with no
direct or financial relationship or interests with the ASRH,
(2) certification includes an onsite assessment of the facility,
personnel, and protocols, and (3) the process includes col-
lection and analysis of ≥4 disease performance metrics.3 It is
recommended that such a certification visit be performed at
least every 2 to 3 years, but with annual data collection and
analyses.

ASRHs in a Stroke System of Care
The ASRH is one component of a larger stroke system of care.38
Such a system can be organized on the basis of geography,
resources, administrative oversight, or a combination of the
above. The goal is to make sure that a patient receives the proper
level of care in the most expeditious and efficient manner.

Any stroke system of care will include all levels of stroke
centers (ASRH, PSC, CSC), as well as EMS, government
support and oversight, education, outcomes, rehabilitation,
and perhaps research (in some cases). This level of organi-

Table 4. Possible Performance Metrics for an ASRH

<table>
<thead>
<tr>
<th>Element</th>
<th>Metric</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV tPA use in eligible patients</td>
<td>Percentage of eligible patients treated with IV tPA</td>
<td>Measured by TJC for PSCs and CSCs</td>
</tr>
<tr>
<td>Stroke severity scale done in ED</td>
<td>Percentage of patients with documented score</td>
<td>Important to guide therapy and severity adjust outcomes</td>
</tr>
<tr>
<td>Time to first brain image</td>
<td>Door to image time</td>
<td>Applies to all stroke types</td>
</tr>
<tr>
<td>Door-to-needle time for IV tPA</td>
<td>ED arrival to IV bolus initiation</td>
<td>National quality standard</td>
</tr>
<tr>
<td>Time to begin coagulation reversal therapy</td>
<td>Time from diagnosis of cerebral hemorrhage to beginning therapy</td>
<td>May be a CSC performance metric; only applies to hemorrhagic strokes</td>
</tr>
<tr>
<td>Time to initiate telemedicine link</td>
<td>Time from diagnosis to establishment of link</td>
<td>Link to predesignated PSC or CSC</td>
</tr>
<tr>
<td>Time to initiate patient transfer</td>
<td>Time from door to transport</td>
<td>Applies to air or ground transfers</td>
</tr>
</tbody>
</table>

ASRH indicates Acute Stroke–Ready Hospital; CSC, Comprehensive Stroke Center; ED, emergency department; IV tPA, intravenous tissue plasminogen activator; PSC, Primary Stroke Center; and TJC, The Joint Commission.

anticoagulants for patients with stroke because of atrial fibril-
ation, and proper patient and family education. Information
should also be collected about the proper (or improper) use of
the transfer and transportation protocols.

strokes of various severities are triaged via EMS and sent to
the most appropriate facility.

Further aspects of a stroke system of care are addressed in a
recently published Policy Statement commissioned by the AHA/
ASA.24 This document includes many other aspects of care within
a stroke system, including transfer of patients, hospital bypass reg-
ulations, medical and legal issues, financial concerns, etc.

Discussion
The concept of an organized stroke system of care has evolved
since its introduction ~2 decades ago. We now have some data
supporting improved outcomes (death and disability) when
patients with stroke are cared for at either a PSC or a CSC.5,8
Yet many patients with stroke will enter into the healthcare
system via EMS and a hospital in a small city or rural area.
The development of a network of ASRHs will increase the
chances that such patients will receive appropriate acute care
in a timely and effective manner, thus increasing their chances
of having a better outcome.

Many of the elements of an ASRH are similar to those of
a PSC, which is understandable because these are basic pro-
cedures and steps in acute stroke care and they have been
shown to improve the efficiency of such care and improve out-
comes.5,8,16 In developing the requirements and performance
measures for an ASRH, we have chosen to retain some of the
metrics used for a PSC. However, we realize that because
of logistical and other limitations at the hospitals that will
become ASRHs, there needs to be some flexibility in terms
of compliance with these care metrics. Although The Joint
Commission has, in general, used an 80% compliance goal
for a PSC in terms of meeting the various requirements and
metrics, we think that a 67% compliance rate is a reasonable
level for most ASRHs. This goal might be higher for some ele-
ments, such as documentation of stroke severity.

In most cases, the ASRH would be in a remote location
and not in a densely populated urban or suburban area where
there might be a nearby PSC or CSC. The ASRH concept is
not intended to compete with a hospital that is a PSC or CSC
in the immediate area. In such cases, a patient with an acute
stroke should be taken to the nearest PSC or CSC that
is consistent with current AHA/ASA and EMS guidelines, as
well as many local and state EMS policies.2,29 Although exact
distances and times might vary by location and clinical factors,
it seems reasonable that in cases where an ASRH is within 20
miles or 15 to 20 minutes of a PSC or CSC, the patient should be taken directly to the nearby PSC or CSC. These times and distances might vary somewhat by local factors, but the above parameters are generally applicable.

A common concern is the cost associated with becoming an ASRH. As defined above, the ASRH might not involve any significant additional expenses in terms of infrastructure or personnel, with the exception of telemedicine infrastructure, training, and staffing. Many of these patients are already coming to the hospital or a nearby hospital; thus, there is no anticipated net increase in the number of patients in the entire system. There may be an increase in patient volumes at some ASRHs if EMS chooses to bypass some or all non-ASRH facilities and directly transport the patient to the ASRH. Obviously the hospital will bill for any care provided and be reimbursed according to various factors, such as primary diagnosis, patient insurance status, level of care provided, etc. There are no data to suggest that the care of patients with stroke is a source of financial stress for most hospitals.56,57

One exception may be reimbursement of patients who receive intravenous tPA at an ASRH and are then transported to another hospital (ie, drip and ship). Under current Medicare rules, a Medicare patient cannot be billed by the treating ASRH hospital to receive the enhanced diagnostic-related group for patients with stroke treated with intravenous lysines because they are not admitted to that hospital. Likewise, the hospital that they are transferred to may not be allowed to bill for diagnostic-related groups 061 to 063 because they never administered the intravenous tPA. This may be less of an issue for patients with private insurance.

The reality is that nationwide only 5% to 7% of patients with stroke receive treatment with intravenous tPA, so the overall financial burden of this loophole seems to be small in most cases.58 A similar concern might occur with reversal of anticoagulation for patients with an ICH seen in the ED of an ASRH, as well as other acute therapies that might be developed in the future. Hospitals that frequently use the drip and ship paradigm (sending and receiving facilities) might see an adverse financial effect. To the extent that this and other technicalities could financially affect some hospitals, public and private payers may choose to review the effect of current policies.

We have suggested some performance metrics for an ASRH. As this process moves forward, it is possible that The Joint Commission, AHA/ASA, Healthcare Facilities Accreditation Program, Det Norske Veritas, and perhaps other groups will define additional metrics that are associated with improved care and outcomes. For example, the inclusion of a stroke severity assessment may be important for adjusting patient outcomes and determining the appropriateness of various therapies. This is an important element because various agencies are trying to compare outcomes across different hospitals, hospital systems, and regions.

The ASRHs will form the base of any local or regional stroke system of care.36 We anticipate that ≥1000 hospitals throughout the United States (and perhaps ≥2000) will become ASRHs and interact with nearby PSCs and CSCs to ensure that patients are rapidly treated and triaged to receive the level of care most appropriate to their condition. Because the healthcare system in the United States emphasizes efficient care and improved outcomes, a robust and multitiered stroke system of care will be a vital component, and ASRHs will become a key element in such systems.

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Disclosures

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References


Formation and Function of Acute Stroke–Ready Hospitals Within a Stroke System of Care Recommendations From the Brain Attack Coalition


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### Supplemental Table I

**Literature Grading System**

<table>
<thead>
<tr>
<th>Class of Recommendation</th>
<th>Explanation</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Benefits of treatment, test, intervention or personnel, clearly outweigh any risks</td>
<td>This treatment, test, intervention, or personnel should be used</td>
</tr>
<tr>
<td>IIa</td>
<td>Benefits of treatment, test, intervention, or personnel likely outweigh any risks</td>
<td>It is reasonable to use treatment, test, intervention, or personnel</td>
</tr>
<tr>
<td>IIb</td>
<td>Benefits of treatment, test, intervention or personnel is possibly greater than the risks</td>
<td>It may be reasonable to consider this treatment, test, intervention or personnel in some cases</td>
</tr>
<tr>
<td>III</td>
<td>Risks may be equal to or greater than any benefits</td>
<td>Treatment, test, intervention, or personnel should not be used</td>
</tr>
</tbody>
</table>

**Level of Evidence**

| A                       | Treatment or test validated in multiple studies/populations, meta-analyses, or circumstances | Very consistent treatment effects or test sensitivity and specificity |
| B                       | Treatment or test studied in studies/populations or circumstances with some limitations | Treatment effects promising but somewhat limited; testing results less robust |
| C | Treatment or test examined in few or very limited studies/populations or clinical circumstances; case series, expert opinion | Treatment or test recommendation based largely on expert opinion or is considered the standard of care; may be a need for further studies/data |

See reference #3 for details