Timing, Intensity, and Duration of Rehabilitation for Hip and Stroke Fracture

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Workshop Summary

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A workshop on rehabilitation for stroke and hip fracture was held August 4 by the National Center for Medical Rehabilitation Research at the NIH. The workshop focused upon key clinical and methodological issues for study: timing, intensity, and duration of rehabilitation. Stroke and hip fracture were included together because these two diagnoses are responsible for the majority of inpatient rehabilitation bed days (and expense) for the elderly. Current medical practice has been heavily influenced by reimbursement rules, with comparatively little empirical research on optimal treatment schedules. Serious methodological and logistical issues confront investigators who seek to address this issue. The purpose of the workshop was bring together rehabilitation clinician-investigators, epidemiologists, and policy analysts to discuss the steps necessary to carry out clinical trials that determine optimal therapy schedules.

Much common ground was found between the investigations necessary and the problems faced by investigators in determining optimal therapy schedules for patents with hip fracture and stroke: key issues such as patient selection, trial design, ethics of assignment, characterization of therapies, measurement of outcomes and financing of trials. In contrast, the problem faced by health policy makers is to allocate resources among patients fairly. The current funding model incorporates specific pricing and seeks to encourage competition between providers, but does not incorporate the other features necessary for the distributive effects of market economics to work fairly, i.e., fungible products or services, and accurate information symmetrical between providers and purchasers. Outcome measures do not appear to drive either appropriate allocations of services to patients or payments to providers. Data on schedules and outcomes for rehabilitation are needed for the development of a system that is "self-interested"—one where choices that benefit patients also benefit physicians and benefit the health care system as a whole.

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Overview of Stroke Rehabilitation

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The rehabilitation needs and goals for individuals with stroke vary considerably. For some, the goal may be to return to full independence and resume all previous life activities. For others, the goal may be merely to return home with family assistance. The challenge for the health care system is to determine what type of rehabilitation, in what setting, meets these individual needs in a cost-effective fashion. While there is a general acceptance that rehabilitation is at least modestly beneficial in promoting improvement in important functional areas such as mobility, performance of self-care and community activities, important questions remain about the effectiveness of individual treatment strategies, as well as the organization and intensity of rehabilitation services. The effectiveness of stroke rehabilitation must also take into account the natural recovery from stroke. The most rapid neurological and functional recovery occurs in the first one to three months after stroke, [1,2,3] although some individuals can show improvement beyond this time. Individual patient characteristics also are associated with poorer functional outcome. [4,5] These include older age, severe initial functional deficit, persistent urinary incontinence, severe cognitive deficits, severe medical co-morbidities, and disability prior to the stroke. For persons with moderate or severe disability, the availability of a caregiver also facilitates the ability to live in the community post-stroke. The World Health Organization in 1989 recommended that selection for rehabilitation should be based on the prognosis for recovery of function in three main groups of patients: a) those who will recover well (with or without rehabilitation); b) those who will not recover well; and c) those who will need rehabilitation for maximal recovery [6]. Unfortunately, it is still difficult to ascertain which patients will fall into these groups with certainty, and advances in rehabilitation methods may change the boundaries.

Rehabilitation services may be provided in a variety of care settings. Rehabilitation is often provided during the acute hospitalization following stroke. Later, services may be received in rehabilitation hospitals or units, skilled nursing facilities, outpatient programs, or home health programs. These rehabilitation “levels of care” are distinguished by the types and intensity of services provided, the type of patients served, and the overall philosophy

and focus of the program. In general, the most intensive services are provided in rehabilitation hospitals and units, and the least intensive in home health programs.

Guidelines for post-stroke rehabilitation were published in 1995, by the Agency for Health Care Policy Research. [4] However, because of lack empirical evidence, many of the recommendations were based on expert opinion, and therefore might be considered more of a codification of current practice than absolute guidelines. Stroke patients are judged to be candidates for formal rehabilitation if they have two or more significant disabilities, are medically stable, able to learn, have physical endurance to sit supported for one hour, and are able to participate in active rehabilitation treatments at least to some extent. Patients who meet these threshold criteria, but require moderate-to-total assistance in mobility or performing basic activities of daily living (ADL's) are candidates for an intense inpatient program if they can tolerate three or more hours of physical activity each day, or less intense programs if they can not. Patients meeting threshold criteria and requiring only supervision or minimal assistance in mobility or ADL's are usually candidates for home or outpatient rehabilitation if the home environment and support are adequate, or for a skilled nursing facility if they are not. Johnston and colleagues have suggested that the AHCPR guidelines may be unreliable for accurate prediction of best location for rehabilitation and may need further development. [7] In 65 percent of stroke survivors more than one type of placement was appropriate.

Regardless of guidelines, what is clear is that there is enormous variation in the delivery of rehabilitation services to stroke patients. There is suggestive evidence that this is financially, rather than medically, driven. In a 1993 RAND study, there were significant differences in utilization of post-acute services based on the size of the acute care hospital, whether it was in a rural or urban area, and other factors. [8] In a large analysis of Medicare claims, Lee, Huber and Stason found that 73 percent of stroke survivors received some kind of rehabilitation during the first six months post-stroke, including 16.5 percent that were admitted to an inpatient rehabilitation hospital or unit. [9] Many patients received rehabilitation sequentially in more than one care setting. Geography seemed to determine much of the variation in the kind of services individuals received. For example, 10 percent of stroke survivors were admitted to rehabilitation hospitals in Florida vs. 31 percent in Houston. The percentage of stroke survivors admitted directly to skilled nursing homes varied from 14 percent in Newark to 41 percent in Minneapolis. 19 percent of stroke survivors in Minneapolis received home health services vs 57 percent in Miami. Such findings unambiguously

demonstrate that the United States has a problem with inconsistent post-stroke rehabilitation practice. The differences are too large to be attributable to demographic, clinical or environmental factors and suggest that either patients in some areas are receiving too few services, or patients in other areas are receiving too many services.

Another bothersome observation has been the almost experimental growth in post-acute care of all types in the 1980's and 1990's. For example, between 1986 and 1994 hospital-based skilled nursing facilities (SNF's) grew by 200 percent, free-standing SNF's grew 24 percent, and home health agencies grew 25 percent [10]. The growth was similar for hospital based rehabilitation programs. During the same period, rehabilitation hospitals grew 149 percent, and distinct rehabilitation units in acute care hospitals grew 71 percent. [11] The nature of this rise cannot be explained by the demographic aging of the population or increased severity of illness. To many observers, the rapid rise of post-acute services was attributed to the favorable reimbursement climate for these services, and suggested a pattern of over-utilization. The primary reason for the explosive growth was the passage of the Tax Equity and Fiscal Responsibility Act (TEFRA) by the U.S. Congress in 1982. This resulted in the introduction of Diagnostic Related Groups (DRG's). Payment to hospitals for inpatient care was radically altered. Whereas hospitals were previously paid by Medicare on a fee-for-service basis, under the DRG system reimbursement was fixed according to diagnosis and was largely independent of resource utilization and length of stay. Reimbursement for post-acute care services was excluded from DRG prospective payment, and remained cost-based. A common financial strategy for hospitals was to maximize revenue by discharging Medicare patients quickly from the acute hospital and admitting them to a post-acute facility, such as rehabilitation unit or skilled nursing facility.

Another illustration that financial factors rather than patient criteria determine the rehabilitation setting, comes from a study of stroke patients covered by Medicare fee-for-service and HMO plans. [12] After controlling for possible confounding variables, HMO patients were significantly more likely (41.8 percent) than fee-for-service patients (27.9 percent) to be discharged from acute care to a nursing home. In summary, the practice variation in stroke rehabilitation care appears to be due to a confluence of factors, including Medicare fee schedules, proportion of individuals enrolled in Medicare HMO's, local practice patterns, and perhaps the regional availability of certain types of rehabilitation services.

Reimbursement for rehabilitation services are currently in the process of dramatic change. The Balanced Budget Act (BBA) of 1997 created a prospective payment system (PPS) for all post-acute rehabilitation. The major objective of the BBA is to reduce Medicare outlays by $115 billion between 1998 and 2003. Different components of post-acute care will be affected at different times. Skilled nursing facilities were the first to be affected in July 1998. Home health rehabilitation came under PPS in October 2000. Rehabilitation hospitals and units will not be affected until April 2001, or later, while outpatient rehabilitation will not feel the full effects of PPS until at least 2002. How PPS will affect admission patterns for stroke survivors is not yet clear.

Physicians are justifiably concerned whether placement of patients in certain post-acute care settings compromises quality of care. Unfortunately, studies comparing clinical outcomes among different care delivery systems are relatively few. In a non-randomized comparison of stroke patients receiving rehabilitation in a traditional rehabilitation hospital and in a free-standing SNF, greater gains in functional abilities were found in patients treated in the rehabilitation hospital, but the cost for successful discharge to the community was twice as high as the SNF. [13] In a carefully performed study Kramer et al., [14] evaluated approximately 1000 carefully selected Medicare patients with stroke who had been admitted to a rehabilitation hospital or a skilled nursing facility. Patients were studied prospectively and followed for six months. When outcomes were adjusted for premorbid residence and function, care-giver availability, comorbid illness, and other important variables, stroke patients admitted to rehabilitation hospitals were more likely to have favorable outcomes than those treated in SNF's. A recent study demonstrated that Medicare stroke patients enrolled in HMO's were less likely to be admitted to rehabilitation hospitals and received less specialty physician care than Medicare stroke patients enrolled in fee-for-service systems. [15] Medicare HMO stroke patients had poorer short-term functional outcomes and were less likely to reside in the community at one year, consistent with the lower intensity of rehabilitation and less specialty physician care they received. Available evidence, at least for stroke, suggests that outcomes in SNF facilities are less favorable than those in rehabilitation hospitals, but the cost is 50-64 percent lower in SNF facilities. [13, 16]

There are even fewer studies comparing outcomes of persons treated in other post-acute settings. One study in the United Kingdom found similar abilities to perform household and community activities in stroke patients treated with home rehabilitation, compared to those treated in hospital-based outpatient facilities. [17] Hui and associates in

Hong Kong reported greater functional improvement in elderly stroke patients treated in an outpatient day hospital setting compared to an inpatient ward service. [18] In a recent study from Australia, patients with stroke were randomized to early hospital discharge followed by home-based rehabilitation or "conventional" post-stroke rehabilitation on a geriatric ward or rehabilitation ward. [19] Clinical outcomes did not differ between the groups at six months, but the mean cost for the home-based program was $8,040 compared to $10,054 for the conventional program. [20] Similar outcomes between groups of stroke patients randomized to home intervention versus conventional rehabilitation were also found in a study in Quebec, Canada. [21] However, patients in both the Australian and Canadian studies already had very good function at the time of randomization. Most rehabilitation professionals would argue that such patients would have a good outcome regardless of rehabilitation setting. At least one study suggested that the quality of life of care-givers of stroke patients discharged to early home care was worse than the care-givers of stroke patients who had conventional rehabilitation. [22]

European studies on stroke consistently demonstrate superior patient outcomes in stroke units combining acute and rehabilitation care provided by dedicated clinical staff. [23,24,25] However, direct comparison of these units with stroke care in the U.S. is difficult because payment systems force very different patterns of practice, e.g., rapid discharge from acute care.

Thus, across all rehabilitation providers internationally, the optional duration, intensity and methods of rehabilitation for different stroke patients are still controversial issues.

A new set of rehabilitation tools is currently in development and in clinical trials. Functional neuroimaging and transcranial magnetic stimulation are providing new insights into brain plasticity. For example, it appears that certain patterns of neural network reorganization are correlated with motor recovery following stroke. We are just beginning to learn how to manipulate neurologic plasticity with pharmacologic agents and behavioral training programs. Specific drugs to enhance motor recovery and novel therapy approaches such as constraint-induced therapy and partial body weight suspension with treadmill training are now in clinical trials. It is quite possible that this new interest in evidence-based rehabilitation interventions may provide information to help us choose which patients benefit most from stroke rehabilitation and the best treatment methods and locations of care.

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Trials in Stroke Rehabilitation

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Most of the studies on stroke care and rehabilitation outcomes have been performed in countries with socialized medical systems. Such systems provide comprehensive models of acute, subacute and chronic care with centralized monitoring of medical and financial records. Their unified cost-accounting and record-keeping systems make it easy to test alternate stroke care delivery models and measure their impact on outcome. Such data are most likely to reflect the actual cost of care, with minimal bias towards artificially shifting health care costs from one setting to the next.

The Cochrane Library's meta-analysis of organized inpatient care for stroke is the most comprehensive, up-to-date, and unbiased review of prospectively randomized stroke outcome studies available.[1] This analysis includes a total of 2,500 patients in 20 trials, 12 formally randomized, eight quasi-randomized. These studies examined differences in outcome for patients randomized to receive rehabilitation services on general medical units compared to comprehensive multidisciplinary stroke rehabilitation units. Patients in both settings received medical, nursing, and rehabilitation services. The difference was in the interdisciplinary team approach to care on the designated stroke rehabilitation unit, and the enhanced quality of care provided on the specialized stroke-care unit. The total amount of therapy time provided did not differ for the two care settings; however the time from stroke onset to mobilization was significantly shorter for the designated stroke-care units. Patients assigned to care in a stroke unit demonstrated a decreased risk for death or dependency.[1] This effect was most evident for inpatients with severe stroke.[1] The benefit of acute inpatient rehabilitation was greatest for patients with more severe strokes requiring inpatient rehabilitation hospital stays of three-to-eight week's duration.[1]

Patients in the U.S. with severe strokes who are likely to require more than four weeks of inpatient rehabilitation are often sent directly from an acute care hospital to nursing home based subacute rehabilitation care.[2] The randomized prospective studies referenced above show that these are the patients most likely to benefit from acute inpatient

rehabilitation.[1] Subacute rehabilitation care for severe stroke victims is a uniquely U.S. care pattern, and is driven by cost containment, not by quality-of-care data. A recent U.S. study demonstrated that stroke patients admitted to acute rehabilitation hospitals were 3.3 times more likely to be discharged home than patients admitted to subacute rehabilitation facilities, and that patients admitted to subacute rehabilitation facilities were 6.8 times more likely to be discharged home than patients admitted to skilled nursing facilities without subacute rehabilitation.[3]

Studies from Australia and Canada have focused on the value of inpatient versus home rehabilitation.[4,5] Review of their entry criteria shows that the patients studied had only mild stroke-related deficits (Barthel index >80). Unless these patients lived alone, had impaired safety awareness, or had other extenuating medical comorbidities, they would have been considered too high-level to be admitted into inpatient rehabilitation in the U.S. For these patients, home care appears to be as effective as inpatient rehabilitation, and far less costly. Acute inpatient rehabilitation services are best focused on more impaired patients, especially those requiring medical and nursing supervision and assistance with hydration, nutrition, bowel, bladder, cardiopulmonary and cognitive-behavioral management.[2]

While there is general consensus that stroke rehabilitation reduces morbidity and improves functional recovery, it is not known which components of rehabilitation care are most critical.[6] Is daily therapy by a physical therapist better than daily therapy directed by a physical therapist but provided by a therapy assistant? What rehabilitation techniques are best, for which patients, when, and for how long?

There is no longer any serious question of the value of focused stroke rehabilitation. The major issue at present is how to provide it as cost-effectively as possible. This has given rise to HCFA-RAND algorithms for determining stroke severity and burden of care. Initial HCFA-RAND Function Related Group (FRG) algorithyms used only Functional Independence Measure (FIM) Mobility subscores (FIMM) and age parameters to estimate length of stay.[7] They defined five FRG categories, designated FRG-11 to FRG-15. A more recent HCFA-RAND publication uses FIMM scores converted into Minimum Data Set Post Acute Care (MDS-PAC) data scores. The algorithms specifying how these data transformations were made are not yet available.

It was originally assumed that self-care and mobility scores encompassed neurologic impairment. This has proven to be a false assumption. Reference to the figure below shows an analysis of patients in the lowest HCFA-RAND FRG category, FRG-11 based on their neurologic impairments. In this figure, patients are separated into three groups, those with: 1) isolated motor weakness (M); 2) motor weakness plus either hemisensory deficit or hemianopic visual deficit (MS/MV); 3) motor deficit + hemisensory deficit + hemianopic visual deficit (MSV). Repeated measures ANOVA shows that outcomes for the three groups, all within the same FRG-11 category, are significantly different ($p = 0.04$). Similar differences in outcome can also be shown for FRG-12 ($p = 0.01$) and FRG-13 ($p = 0.02$).

The Figure below shows that FRG-11 contains at least three clinically significant groups of neurologic impairments. If prospective payment is based solely on functionally defined categories, then there will be an incentive to reject patients with MS/MV or MSV neurologic impairments. Outcome analyses will appear to show improved outcome for each FRG when, in fact, the only change has been in patient selection. Patients with MS/MV and MSV impairments respond well to acute inpatient rehabilitation, but may be rejected because they adversely affect outcome statistics (final FIM, change in FIM, length of stay) and Medicare reimbursement.

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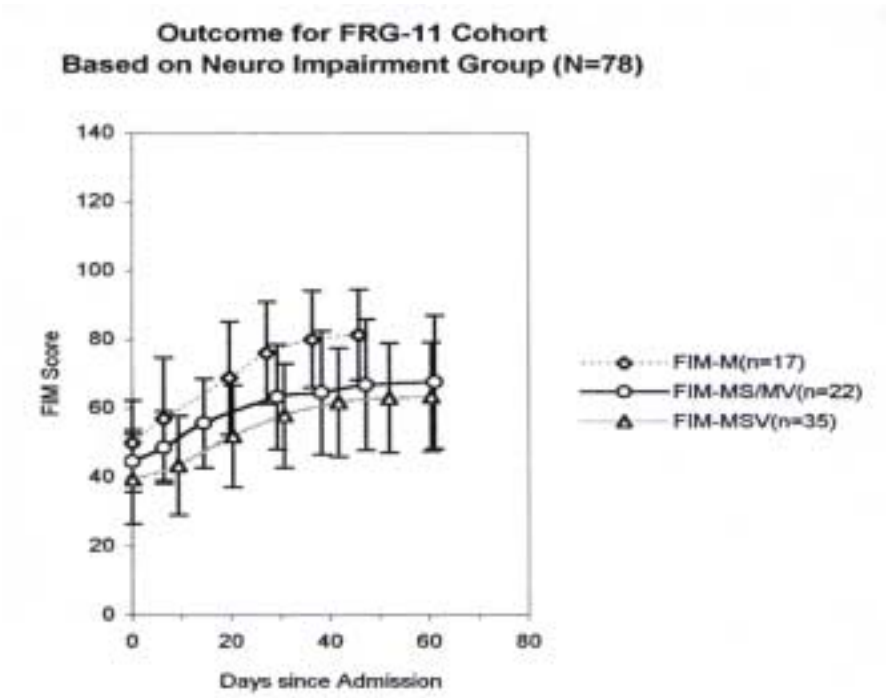
Outcome for FRG-11 Cohort
Based on Neuro Impairment Group (N=78)
FIM Score
140
120
100
80
60
40
20
0
0
20
40
60
80
Days since Admission
FIM-M(n=17)
FIM-MS/MV(n=22)
FIM-MSV(n=35)

Comorbidities in Stroke:

Issues in Clinical Trials

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Comorbidities in stroke can include pre-existing medical conditions, post-stoke complications, and acute exacerbations or manifestations of chronic diseases. Such comorbidities may have a causal, consequential or coincidental relationship to stroke. For instance, hypertension and diabetes are well known risk factors for stroke, while depression, pain syndromes and deep venous thrombosis are equally well known consequences of stroke. Comorbidities occur more commonly in stroke patients than in age-matched controls, their presentations may be more subtle and unusual, they may be more refractory to treatment and take longer to resolve. Implications for rehabilitation include delay of initiation of rehabilitation, prolonged duration of rehabilitation, and affects on the services delivered. For example, because of comorbidities, therapists may be restricted in the time some patients can tolerate in therapy and in the kinds and locations of physical activities in which they can engage.

Standard comorbidity scales, such as the Charlson and Apache scales, were not designed with stroke patients in mind, nor were they designed to be used in the rehabilitation or post-acute settings. Therefore, they may fail to adequately capture data relevant to the care of these patients. Similarly, data obtained through retrospective review of medical records for ICD-9 codes is subject to both diagnostic and coding biases. Nonetheless, multiple studies [1,2,3] demonstrate that patients with greater numbers of comorbidities have longer lengths of stay, greater stroke severity, and poorer outcomes. In an ongoing study at the Rehabilitation Institute of Chicago, we have constructed a prospective database for analysis of patients in stroke rehabilitation. The database contains 128 pre-existing and acute medical complications and 83 rehabilitation medical complications. To date, we have analyzed data from over 1900 patients. 75 percent of patient have at least one complication. Urinary tract infection, pain and depression are among the most common rehabilitation complications, while feeding tubes, urinary tract infections and pneumonia

were among the most common acute care complications. Pre-existing conditions and medical complications are significant independent factors in predicting discharge function, rehabilitation length of stay, and mean charge per patient. Thus, pre-existing medical conditions and medical complications must be considered in the design and analysis of clinical trials in stroke rehabilitation.

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Table 1. RIC-RRTC Stroke Database: Preexisting Conditions

Condition	Number	Percent
Hypertension	**1351**	**69%**
Smoking	**892**	**46%**
Diabetes	**520**	**27%**
Coronary Artery Disease	**389**	**20%**
Osteoarthritis	**253**	**13%**
Myocardial Infarction	**209**	**11%**
Cataracts	**195**	**10%**
Congestive Heart Failure	**187**	**10%**
Atrial Fibrillation	**169**	**9%**

Total Number of Stroke Patients Studied = 1944

Table 2. RIC-RRTC Stroke Database: Acute Care Complications

Condition	Number	Percent
Feeding Tube	**526**	**27%**
Urinary Tract Infection	**409**	**21%**
Pneumonia	**286**	**18%**
Hypertension	**189**	**10%**
Tracheostomy	**186**	**9%**
Pressure Sores	**162**	**8%**
Hydrocephalus	**152**	**8%**
Seizures	**151**	**8%**
Gastrointestinal Bleed	**70**	**4%**

Total Number of Stroke Patients Studied = 1944

Table 3. RIC-RRTC Stroke Database: Rehabilitation Medical Complications

Complication or Condition	Number	Percent
Urinary Tract Infection	**569**	**30%**
Joint or Soft Tissue Pain	**300**	**16%**
Depression	**235**	**12%**
Hypertension	**200**	**10%**
Electrolyte Abnormalities	**141**	**7%**
Acute Urinary Retention	**95**	**5%**
Pneumonia	**91**	**5%**
No Complications	**473**	**25%**

Total Number of Stroke Patients Studied = 1903

Table 4. Preexisting and Medical Complications as a Predictor of:

- **Mean Charge Per Day**

Factors	*B*	p Value	Adjusted R^2
Tracheostomy	.197	<.0001	.206
No. Rehab Complications	.089	.001	
NIHSS:			
11-15	.086	.006	
Congestive Heart Failure	.078	.002	
Feeding Tubes	.068	.01	

Table 5. Preexisting and Medical Complications as a Predictor of:

- **Discharge Function (FIM™)**

Factors	*B*	p Value	Adjusted R^2
NIHSS:			.481
6-10	-.163	<.0001	
11-15	-.343	<.0001	
16-27	-.409	<.0001	
Feeding Tubes	-.159	<.0001	
No. Rehab Complications	-.128	<.0001	
Pressure Sore	-.091	<.0001	
Prior Stroke	-.070	<.0001	

Factors Affecting Functional Outcome After Stroke

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A comprehensive review of the medical literature from 1950 to the present reveals more than 220 studies investigating factors affecting functional outcome after stroke. Unfortunately, rigorous randomized, controlled trials are extremely limited in this area of research. Presently, a critical review of the available literature remains the best available technique to determine the association of demographic factors, clinical features, and rehabilitation interventions with post-stroke functional outcome. [1,2,3]

Only one *demographic factor* demonstrated a strong (consistent) association with poorer functional outcome at hospital discharge and follow-up, age greater than 65 years; however numerous factors were weakly (inconsistently) associated with poorer functional outcome at hospital discharge and follow-up, including: lower educational level, poor social supports, non-married, unemployment, a history of prior stroke, presence of coronary artery disease (angina or prior myocardial infarction, and presence of diabetes mellitus. The following demographic factors did not demonstrate an association with stroke outcome; financial resources, and a history of hypertension, congestive heart failure, or peripheral vascular disease. Insufficient research has been reported for the following demographic factors to assess their association with functional outcome after stroke: gender, race, and a history of transient ischemic attacks (TIA's), acute or chronic pulmonary disease, arthritis, anticoagulant use, or tobacco use.

The presence of the following *clinical features* in the first one-to-four weeks after stroke was strongly (consistently) associated with poorer functional outcome at rehabilitation discharge and follow-up: bowel incontinence, bladder incontinence, sensory deficits, motor deficits, balance deficits, visual deficits, perceptual deficits, cognitive deficits, aphasia, and global functional deficits. There was a weak (inconsistent) association between the following clinical

features in the first four weeks after stroke and poorer functional outcome: presence of hypotension in the first 24 hours, right-sided strokes, abnormal admission serum glucose, elevated admission white blood cell count, elevated admission erythrocyte sedimentation rate, abnormal admission electrocardiogram, and dysphagia. The following clinical features did not demonstrate an association with stroke outcome: presence of hypertension in the first 24 hours, overall severity of concurrent medical illness, etiology of stroke, and admission hemoglobin A1C, platelet count, hemoglobin, or hematocrit. Insufficient research has been reported for the following clinical features to assess their association with functional outcome after stroke: abnormal serum potassium, albuminuria, CT findings, multimodal evoked potentials, and dysarthria.

The following *rehabilitation interventions* after stroke have a strong (consistent) association with improved functional outcome after stroke: early initiation (within 72 hours post-stroke) of rehabilitation services and rehabilitation provided in an interdisciplinary versus multidisciplinary inpatient setting. There was a weak (inconsistent) association between the following rehabilitation interventions and improved functional outcomes after stroke: use of specialized versus generalized ("functional") types of therapy services and greater intensity of therapy services. Insufficient research has been reported for the following rehabilitation interventions to assess their association with functional outcome after stroke: specific types of non-inpatient rehabilitation services.

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Chronic Stroke:

Therapeutic Interventions

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The conventional wisdom is that individuals suffering from a stroke reach a recovery plateau within the first six months after the event. However, new studies demonstrate that these individuals can, in fact, make substantive gains in their functional abilities if provided with specific therapies long after this period. Unfortunately, most stroke patients finish their time-limited subacute course of rehabilitation with few specific instructions on physical activity, and even fewer resources to support their continued involvement in therapeutic exercise programs. Compared with age- and sex-matched sedentary controls, chronic stroke patients are significantly disabled in terms of their aerobic metabolism. When exercise capacity was measured by open circuit spirometry during bicycle ergometry in chronic stroke patients, VO_2 during peak exercise (VO_2 peak) was only 15.8 mL/kg/min, half that predicted by normative data. [1] Our group reported comparable low VO_2 peak levels based on treadmill testing in older stroke patients that are more representative of the age profile for stroke. [2] Further, the aerobic requirements of hemiparetic gait are elevated 1.5 - 2 fold in stroke patients compared to controls. Collectively, these studies show stroke patients have elevated energy demands associated with biomechanically deranged gait, amplified by poor fitness. As a group, stroke patients require at least two-thirds of their peak exercise capacity for slow ambulation - indicating diminished physiological reserve in basic sub-maximal effort ADL tasks. [3,4] The following discussion details several interventions that have attempted to improve physical function in chronic stroke patients, including recent research from our institution.

Resistive strength and conventional rehabiliation training after stroke: A number of investigators [5-9] have examined the potential benefits in stable, chronic stroke patients of exercise regimens that include established techniques of resistive strengthening (either isotonic or isokinetic, in a variety of concentric or eccentric modes) or standard applications of physical and/or occupational therapy. These studies varied greatly in their designs and

outcome measures, but all purported to demonstrate modest increases in strength and/or function over differing post-treatment time frames.

Aerobic Exercise (AEX) to improve exercise capacity after stroke: There are few published studies of AEX training in chronic stroke patients. An early study demonstrated 12 weeks bicycle ergometry increased Self-Concept Scores, estimated oxygen uptake during peak exercise, and function in most patients [10]. In a randomized study of 10 weeks adapted bicycle ergometry in chronic stroke patients, AEX increased peak VO_2 by 14 percent, with no improvement in controls receiving only range of motion exercises. [1] Though Fugl-Meyer scores were positively related with gains in VO_2 peak, there were no differences in functional outcome scores in the AEX treatment group. These studies show AEX improves fitness in stroke patients, but do not establish that cycle or wheelchair ergometry can improve functionality. Our initial studies show that treadmill training increases VO_2 peak, while reducing the energy demands of hemiparetic gait, thereby improving physiological fitness reserve. [11] Studies in our laboratory and others provide evidence that gait, balance, and strength also improve, suggesting treadmill AEX training represents an efficacious training modality to improve functional mobility after stroke.

Treadmill training to improve physical function after stroke: The history of repetitive task-oriented training to improve locomotor function goes back to early animal models showing recovery of phasic hindlimb stepping in thoracic despinalized cats with treadmill training. [12] Based on such animal models, partial weight suspension (PWS) treadmill training was first applied in spinal cord injured patients, and later considered for gait retraining in hemiplegic stroke. In a non-controlled study, 25 PWS treadmill training sessions in nine severely affected non-ambulatory stroke patients improved mobility scores and gait temporal-distance parameters. [13] PWS, initially with removal of 30 percent of body weight, was not required after day six of training in seven of nine cases, but harness support and assistance in stepping was needed because these were severely disabled patients. These findings, and a report by Visintin, [14] suggest PWS treadmill is an effective training modality, particularly in more severely gait-impaired stroke patients during the early stroke recovery period. Studies show that in early stroke recovery, PWS treadmill is an important bridge to full weight bearing treadmill exercise in about two thirds of more severely affected patients.

These studies support a model that task-oriented training, such as treadmill AEX, may optimize locomotor re-learning in chronic stroke. Our data show that task-oriented AEX can be administered safely and effectively using a progressive treadmill AEX training model with handrail support to improve fitness and motor function in most elderly stroke patients. Treadmill was selected as a training modality because sensory stimuli from the moving belt may facilitate gait symmetry, while enabling AEX intensity for cardiovascular conditioning at low gait velocities using inclines. [11] To test this, we compared gait symmetry during treadmill vs. floor walking in 6 stroke patients [15]. Motion analysis showed stance and swing duration symmetry improved at matched self-selected and fastest comfortable walking speeds - a reversal of the classic asymmetry of hemiparetic gait. Treadmill walking resulted in 13 percent decrease in cadence at both speeds, indicting increased stride length compared to the overground condition.

The effects of treadmill training were examined in neurologically stabilized chronic stroke subjects in several studies by our group, including tests of mobility, rapid stepping, and lower limb strength. A "Get-Up and Go" ambulation task [16] was used to determine temporal gait events in five stroke patients before and after treadmill training. With training, time to perform "get-up and return-to-sit" decreased by 25 percent, cadence increased 10.2 percent, while stance / swing ratios diminished 9.0 percent for the paretic and 11.7 percent for the non-paretic limb. Improvements were greatest in more impaired patients. These findings suggest treadmill training improves floor walking, mobility in and out of a chair, and gait symmetry in chronic stroke patients. Our group also studied the effects of AEX on cadence, stance and swing times during rapid stepping-in-place. [16] 14 stroke patients were assessed by motion analysis utilizing custom sandals with foot contact microswitches. Six months treadmill AEX produced a 41 percent increase in cadence. After training, mean percent time in stance phase (65 percent) and swing phase (35 percent) were identical in paretic and unaffected limbs, indicating restoration of weight bearing temporal symmetry during stepping. Hence, treadmill training resulted in improved volitional lower extremity motor control of stepping. In addition, effects of treadmill training on leg strength in chronic stroke patients were examined by measuring torque in concentric, eccentric, and passive (reflexive) actions at 30, 60, 90, 120 deg/sec angular velocities in flexion and extension across the paretic and unaffected knee. Passive mode testing (no volitional muscle activation) measures resistance with movement that consists of reflexive (spasticity) and viscoelastic forces. Treadmill AEX increased torque-generating profiles in both quadriceps and hamstrings, with greater relative gains in paretic than unaffected

leg. [17, 18] We found that treadmill training increased dynamic leg strength across a wide range of movement velocities that are normally used in walking. Since the unaffected limb showed similar relative improvements, which may contribute to improved function, we cannot determine whether these gains are due to reversal of deconditioning, neural plasticity, or a combined effect. Findings suggest that chronic LE motor deficits and spasticity may be reversed in part by treadmill, but not stretching exercises.

UE forced-use training in chronic stroke: In 1977, the hypothesis that functional limitations in the paretic UE are reinforced by chronic inactivity emerged as a model of "learned non-use." [19] A number of subsequent investigations have shown that constraint induced "forced-use" training can improve function in the paretic UE of chronic stroke patients. [20, 21] Studies demonstrate that two consecutive weeks of six-to-eight hours daily training using the paretic limb for performance of selected ADL tasks ("shaping"), while the unaffected UE is restrained, improves paretic UE function. The benefits carry over to improved home usage of the limb, and are sustained at least two years beyond training cessation. These findings demonstrate that chronic hemiparetic deficits of the UE are not immutable, and can be improved by forced-use training even years after the putative window of neurological recovery after stroke. Our recent findings that bilateral active and passive arm training with rhythmic cueing improves paretic UE function in chronic hemiparesis raises the possibility that rhythmic training programs involving both limbs may further facilitate motor re-learning following stroke. [22]

Critical to improving outcomes for stroke patients is an advanced understanding of what mechanisms are responsible for improvements in function induced by exercise training late after stroke depicted in the above discussion. Are these effects primarily due to a peripheral mechanism, e.g., alteration of muscle fiber and type or a central effect due to reorganization within the central nervous system? How much of the effects are due to cardiovascular conditioning? Recent and exciting applications of central nervous system measurement techniques including functional MRI and transcranial magnetic stimulation by our institution and others may help answer these questions.

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Rehabilitation Following Hip Fracture

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Compared to stroke literature, there is minimal research about rehabilitation and hip fracture. We do know that older adults who sustain a hip fracture, as a group, have significant residual physical disability.[1,2] Improved medical management has resulted in significant decreases in mortality and length of hospitalization. Non-weight bearing status has declined dramatically with the advent of internal fixation. Yet, the residual disability remains.[3,4] The goals of the orthopedic surgeon have largely guided the management of patients in the initial rehabilitation course after hip fracture—alignment of bone fragments, stability of the fixation and fracture healing.[5] Rehabilitation goals are different—restore pre-fracture function. More specifically, rehabilitation goals include increased aerobic capacity and endurance; balance and locomotion improvement; improvement in abilities to perform self-care and home management; a reduction in tissue swelling and inflammation reduction in pain; reduction in needed supervision; and decreased risk of recurrence.[6]

Current practice suggests that 8-to-18 visits per episode of care are provided for patients with impaired joint mobility, muscle performance and range of motion associated with fracture; and 12-to-60 visits for patients with hip arthroplasty.[5,6,7] Functional training involves ADL training, assistive and adaptive device training, home management task adaptation and environmental task adaptation. Treatment includes patient instruction, therapeutic exercise, functional training in community and work, manual therapy, prescription and application of devices and equipment, and use of electrotherapeutic and mechanical modalities or physical agents. Therapeutic exercises entail aerobic or resistive exercise, aquatic therapy, gait and locomotion training, stretching, balance and coordination training, relaxation, postural awareness, and proper body mechanics. In the first week post surgery, it is common for patients to engage in range of motion exercises, weight-bearing locomotion as tolerated, pivot transfers, isotonic ankle exercises and isometric gluteal and quadriceps exercises. By four-to-six weeks post fracture, endosteal and

bridging calluses have formed, and patients are engaging in active range of motion exercise around the hip and knee and active resistive exercise as tolerated. By eight-to-12 weeks, moderate stability from the callus is achieved, and patients are engaged in weight bearing transfers and ambulation and weaning from assistive devices. Eight-to-12 weeks is also the time frame for the completion of rehabilitation.

Nonetheless, a significant level of residual disability remains in patients who have sustained a hip fracture. For example, in a small study of 18 patients over 90 years old with hip fracture, only eight returned home and only ten became independent ambulators.[8] Koval et al,[9] suggested that intensive case management could improve patient outcomes. A comparison of outcomes in a single facility of patients treated before and after 1990, showed a dramatic increase in the utilization of rehabilitation going from 9 percent prior to 1990 to 64 percent in 1993. A concomitant decrease in length of stay, but no differences in walking, independence or performance of ADL accompanied this increased service utilization. More home-based intervention does not necessarily produce better functional outcomes. Tinetti et al.[10] reported only marginal improvements in upper extremity strength and qualitative gait scores in patients provided with a program of self-care and home management skills as opposed to usual care.

Questions that need research include the following: What are modifiable risk factors for hip fracture? What is involved in bone and muscle healing?; What is strength training?; What is the optimal frequency, intensity and duration of therapies?; What is the appropriate timing for different interventions? Can we stratify or classify patients and tailor specific interventions for particular needs? Several studies [11,12] demonstrate improvements in function for patients provided with exercise programs seven months to one-year post-operatively. Do these investigations suggest that some aspects of rehabilitation should be delayed? What is the optimal timing for the intervention?

It is unclear why a repaired femoral fracture results in such a compromised health care outcome. Research is needed at all levels, i.e., from pathophysiology to handicap, to address the concerns of this burgeoning population of elders.

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Functional Changes after Hip Fracture

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World-wide there are about 1.6 million hip fractures annually.[1] In the U.S. approximately 340,000 individuals over the age of 65 are hospitalized annually for hip fracture.[2] The great proportion of hip fractures in the U.S. occur in elderly white women. By 2050, we estimate the number of hip fractures in the U.S. will rise to about 700,000 annually, with a world-wide incidence of about 3.9 million.[1,3] The mortality after hip fracture in the U.S. is between 18 and 33 percent.[4-8] The amount of disability and dependency varies according to the area of measurement, but between 25 and 75 percent of patients do not return to pre-morbid levels of functioning.[9-13] Direct costs in the U.S. associated with hip fracture is over $5 billion annually.[3,14]

Most of the published work is descriptive rather than mechanistic. The Baltimore Hip Studies have followed sequential cohorts of patients with hip fracture since 1983. One measure of the impact of a disease or condition is its effect on mortality. We found that patients with hip fracture as compared with an age cohort matched for baseline function and co-morbidities, had an excess of nine deaths per hundred at the end of five years.[15] Even those patients who had no co-morbidity experience a major increase in mortality and this excess continues to increase after the second year following fracture. We are just beginning to study in detail the causes of these excess deaths.

To illustrate the impact of hip fracture on patients' functional abilities, consider that of patients who previously had no limitations, at one year post fracture, 20 percent had difficulty pulling their pants on and 90 percent had difficulty climbing stairs.[16] The recovery curves for hip fracture appear to resemble those for stroke, perhaps retarded by a few months. At two months post fracture, almost all patients had some dependency in walking 10 feet. However, even at 24 months after fracture, up to 50 percent of patients need some assistance walking 10 feet.[16] Cognition, affect, and upper extremity function improve for the first four months after hip fracture and then reach a plateau.

Balance, gait, and lower extremity ADLs improve at a slower rate and do not reach plateau until 10-to-14 months post fracture.[16]

One of the underlying physiological events that occurs with hip fracture is loss of bone density and muscle mass. The average woman loses between 4.5-to-5 percent of bone density in the first year after fracture, as compared with the average rate of 1 percent for post menopausal women.[17] Half of this loss occurs within the first 60 days after fracture, probably because of immobility. Muscle mass decreases by about 6 percent within the first 60 days, and there is an increase of 3.5 percent in fat mass over the year.[17]

Depression is common after hip fracture, may persist, and can have severe, debilitating effects.[18] Anesthesia technique may be quite important.[19] Our own work suggests that patients who receive general anesthesia may have better outcome than those who receive local anesthesia, a counter-intuitive result. These studies provided a basis for identifying rehabilitation goals and areas for post-fracture interventions. We need careful study of interventions, both acute and rehabilitative, to decrease the rate of bone and muscle loss post fracture and to improve patients' level of function.

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Methodological Issues in Clinical Trials

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Clinical practice in rehabilitation faces the same challenges that most fields in medicine face: developing an evidence-based practice. The primary method to investigate therapies for evidence-based medicine is randomized clinical trials. Random assignment is crucial to obtain meaningful results, and the technology for randomization is now easily available. Investigators must clearly declare their population, treatment, outcome and analysis intentions prior to the study. The inclusion criteria for the study population should specify individuals according to the time and course of a particular disease or condition. This population should be potentially sensitive to the intervention for study. The population should also be representative of the larger population that the investigator wishes the results to generalize to. Exclusion criteria should be used to exclude individuals not likely to benefit from the intervention or unable to participate in the study.

The resources necessary for recruitment must be adequate to obtain a study population large enough to provide a power of 0.9 for the primary outcome measure. Secondary outcomes should be tested at a more stringent alpha-level. Cross-over should be taken into account in the power calculations and has a very major effect on the sample size required. Investigators should do everything in their power to minimize cross-over. Double-blinding is especially valuable for minimizing cross-over. Losses to follow-up are a bit less damaging; but clearly, following patients to ascertain outcomes is a crucial component of clinical trials. Investigators can stratify their randomization, but this may be unnecessary if the clinical trial has more than 200 participants.

The intervention itself must be standardized and clearly defined, e.g., the specifics of physiotherapy intervention. Face-to-face investigator meetings are essential in clinical trials, especially in multi-site trials. Standardized methods that specify not only what is done, but who does it and how its done are valuable in assuring uniformity of methods across sites and in reporting results. The unit of randomization need not be the same as the unit of intervention. For

example, individuals can be randomized to group interventions. Note also, that the rigor of standardized performance required to prove a point in a clinical trial may not be required once the result is moved into clinical practice.

We should expect surprises in clinical trials—that's why we do them. We don't know the answers. We need to have adequate follow-up for patients, and we need to measure primary outcomes that are meaningful to patients. Everyone entered into a clinical trial should have the potential to benefit from participation in it. Composite outcomes and surrogate outcomes are popular, but have many potential problems. Intermediate outcomes can be helpful, especially in understanding pathophysiology, but are no substitute for primary outcomes.

Analysis plans need to be written in advance and must be organized around intention-to-treat. Adjusted analyses are not a substitute for adequate power. Interim analyses are necessary to provide safety findings to data and safety monitoring boards. Informed consent for entering into clinical trials is a crucial issue. Investigators can be assisted by their Institutional Review Boards. Finally, the cost of clinical trials is an important issue. Investigators must build in adequate personnel not only to perform the intervention, but to follow patients and analyze outcomes.

Cognitive Therapy

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Much if not all of the cerebral cortex is devoted to cognition and, consequently, cortical strokes inevitably compromise some aspects of cognition. Cognition refers to the brain's coding of information it receives through the sensory apparatus, for the purpose of acting on the information, remembering it, or communicating about it. The cortex is a mosaic of specific coding and transcoding networks that overlap in their spatial extent. Obviously, then, a stroke's impact on cognition will be determined by which networks are affected and to what degree. Thus, cognition should not be treated as a unitary entity when designing clinical trials.

A cognitive disorder such as aphasia (acquired language loss) or hemispatial neglect is subject to description and theoretical analysis at the impairment/skill level and at the functional limitation level. In designing clinical trials, two key desiderata are: (1) whether the therapeutic intervention targets the impairment/skill level or the functional limitation level; and (2) whether a focal or global therapy approach is more appropriate. Focal cognitive therapies target specific skills or impairments one at a time. Such therapies set important constraints on research design, especially with regard to subject selection and selection of outcome measures. In clinical trials of a focal therapy, criteria for subject inclusion are typically strict and the therapy procedures are applied uniformly to all subjects. The prediction is for improvement in the particular impairment or skill level targeted and not necessarily in more global outcome measures.

Global therapies, by contrast, target multiple skill areas in tandem, or they bypass the skill level completely to get at the functional limitation level. A clinical trial investigating a global therapy would typically accept a more heterogeneous sample of patients, would use procedures of a more individualized nature, and would predict improvement on a broader array of outcome measures. The individualized character of global therapies need not

compromise their scientific value. The clinical and research literature contains many examples of global therapies that are formulated in terms of algorithms that can be systematically applied and replicated across sites and studies.

There is accumulating evidence in the aphasia treatment literature that a combination of focal and global approaches may be most beneficial for patients. There is also evidence that patients with aphasia may continue to improve through learning-based approaches long into the course of recovery. Given this information, it becomes important to evaluate alternative models of providing rehabilitation through the entire course of the recovery process.

Physical/Occupational Therapies in Clinical Trials

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In thinking about measurement of rehabilitation outcomes we must confront a strong bias that we have had. While the NCMRR model (and others) proposes clear relationships between impairment, disability and societal outcomes, we have implicitly assumed that these relationships are linear, i.e., that differences at the level of pathophysiology will translate transparently into differences in these other domains. Clearly, a whole repertoire of movements and compensatory strategies is available to individuals who have suffered loss of motor skills secondary to stroke. What we are measuring in functional terms is the individual's capacity to perform tasks using this repertoire, and this can not be predicted simply by a measure of the individual's physical impairment, for example, loss of strength. In fact, we probably cannot measure functional level by simply summing up the number and degree of impairments, because strategies are often combined to produce new outcomes. We have all observed how performance may change in different environments, e.g., hospital and home. Consider how motivation and role may change disability, for example going from a patient to a family participant.

To place some of these issues in the context of clinical trials, I will review some of the issues we faced in our study of constraint-induced therapy for stroke. The primary outcome measure was to be brain activation as measured by fMRI, PET and trans-cranial magnetic stimulation. The rehabilitation contribution was designed to provide a standardized treatment program to all admitted and compare the outcome of this program which was administered during a two week hospitalization. We measured the ability to perform standard motor tasks and activity levels as determined by completion of questionnaires (Wolf Motor Function Test, Motor Activity Log, Assessment of Motor and Process Skills). Patients were randomly assigned to either constraint of the unaffected side plus shaping therapies for utilization of the affected limb, or to no constraint to the unaffected side and receipt of range of motion and symptom treatment for the affected upper extremity.

One of the first problems we faced was that while we prospectively established therapies, patients had very different baseline levels of activity and interests. Confounding variables might include what they did in their leisure time because they were able to participate in activities ad lib. Some went to the gym to play basketball, while others preferred to be sedentary. Would leisure activity influence outcome? Are those who are more inclined to participate in vigorous activity likely to have different outcomes? The small number of patients involved probably does not permit analysis of this problem

Some of the methodological decisions that we faced include: whether to use observed activity or/and self-reported activity; treatments delivered by calibrated staff or non calibrated staff; individual vs. group treatments; predetermined therapies or individualized therapies; and whether primary outcomes should be more physiological or functional. At a minimum, investigators must be conscious of these issues and choose the research strategy most appropriate to their question.

I have accepted the usefulness of self-reports, but suggest that we must use standardized assessments with trained, calibrated evaluators, as well. Patients should be observed performing tasks that are functional and which identify their skills as well as their weaknesses. In our own study, there were small, and not clinically significant differences in the motor performance tests between patients in the constraint-induced vs. traditional therapy groups. However, patients in both treatment groups improved significantly in performing social interactive games, such as checkers, after a two-week hospitalization. The differences between the two groups were most marked, and significant, when they were compared using the self-report. Whether this reflects the “true” functional difference or whether this is influenced by hopefulness or other beliefs, is not known. The differences in outcomes using two generically different measures needs to be assessed and should be anticipated in study designs.

We learned several things from this study. One important issue is, and while we all discuss the need for a homogeneous sample, that if the sample is too restrictive, it may result in a prohibitively long recruitment process. The second is the power and selecting an adequate sample size. When there is clinical variation and many tests, this must be large enough to correct for small numbers. A third issue is when do we intervene with our “test”

interventions. We do not yet know enough about the trajectory of brain plasticity and recovery from stroke—the extent to which it is modifiable and the optimal time and intensity for different interventions. We know even less about optimal sites for delivery of treatment. Conceptually, this study did challenge our concept of randomized trials and the use of standard treatments as a way of answering questions about treatment efficacy. Efficacy trials of rehabilitation treatments may need to follow a different model than the traditional prospective, randomized trial and devise schemes based on levels of performance that are individually tailored to patients using strict criteria for intervention based on a patient's performance and disease profile, rather than a group standard. Outcomes should be a mix of observed, calibrated measures and self-reports, if we are to learn about relationships between impairments and functional limitations or functional capacity.

Workshop Discussion Conclusions:

1) All questions regarding rehabilitation of stroke and hip fracture do not require randomized clinical trials. Many important questions, such as the interaction of age with outcome, can be best answered with large-scale observational studies.
2) Reaching consensus on appropriate outcome measures for studies on stroke and hip fracture can advance the field. These measures should be meaningful for clinicians, patients, and payers.
3) Crucial for implementation of high-quality clinical trials is the development of a precise taxonomy and specification of rehabilitation interventions. We can not measure whether a rehabilitation intervention works unless we know exactly what the intervention is.
4) Trials of interventions targeted at impairments vs. interventions targeted towards specific functions are necessary. These interventions are not necessarily equivalent nor are effects at these levels necessarily related in simple ways.
5) Randomized clinical trials may cause clinical practice to evolve even as they are underway. This is not altogether bad, and probably unavoidable.
6) Large-scale demonstration projects may be very useful for measuring the effects of different systems of care, but the resources available for these demonstration projects are very limited.
7) Trials of rehabilitation interventions should encompass measurements of the entire system of care—acute care, inpatient rehabilitation, outpatient, and home therapy services.
8) Under the Executive Order signed by the President, the Health Care Financing Administration will reimburse providers for the routine costs of medical care for Medicare and Medicaid beneficiaries enrolled in clinical trials. Investigators may access information from the HCFA Web site at: www.hcfa.gov/quality/8d.htm. This policy provides an opportunity for investigators who wish to perform clinical trials in rehabilitation. NCMRR will be very interested to fund quality applications for clinical trials in rehabilitation. NIH funds may be requested for experimental interventions, data collection and analysis.
9) Many issues can and must be addressed to enable the execution of high quality large-scale clinical trials in rehabilitation of stroke and hip fracture. NCMRR intends to fund clinical trial planning grants to assist investigators in these efforts. A Request for Applications for these grants can be accessed at:

http://grants.nih.gov/grants/guide/rfa-files/RFA-HD-01-022.html. Information on other funding opportunities available through NCMRR can be obtained at: http://www.nichd.nih.gov/about/ncmrr/funding.htm.