

---

## Research Plan (COOR)

---

### A. *PTClinResNet*, a physical therapy clinical research network, has three Specific Aims:

**A1. The first aim is to generate evidence to evaluate the efficacy of physical therapist interventions focused on resistance exercise for muscle strength through one multi-site phase III and three phase I, controlled randomized clinical trials. Specifically:**

*Project 1 (phase III): Strength-training effectiveness post stroke (STEPS):*

1. We aim to determine whether functional outcomes are improved with strength training as an adjunct to body weight supported treadmill training (BWSTT) in persons with chronic post-stroke hemiparesis; and
2. We aim to determine whether functional outcomes are improved with locomotor-based strength training (LBST) compared with muscle-specific strength training (MSST) as an adjunct to BWSTT; and
3. We aim to determine whether functional outcomes are improved with LBST as compared with BWSTT.

*Project 2 (phase I): Pediatric endurance development and limb strengthening (PEDALS):*

1. We aim to evaluate the effect of a 12-week stationary bicycling training program in children with CP on outcomes including:
  - a. torque generating capacity of the knee extensors and flexors
  - b. cardiorespiratory endurance for mobility
  - c. functional performance and
  - d. health-related quality of life
2. We aim to determine whether children with CP who participate in a cycling intervention using locomotor-based strength training on a stationary bicycle will demonstrate greater improvements in joint torque production, cardiorespiratory endurance during walking, functional ability and health-related quality of life than a matched control group of children with CP that does not participate in the cycling intervention.

*Project 3 (phase I): Muscle specific strengthening effectiveness post lumbar microdiscectomy (MUSSEL)*

1. We aim to assess the immediate and long term effects of muscle specific strengthening on decreasing pain and improving function and quality of life in people status-post lumbar microdiscectomy. Our three working hypotheses are:

Hypothesis 1: Compared to patient education only, a focused intervention of muscle specific strengthening will result in *immediate* improvement in function, quality of life, and will reduce pain and disability in people status-post microdiscectomy.

Hypothesis 2: Compared to patient education only, a focused intervention of muscle specific strengthening will result in *long-term* improvement (i.e., 6 months – 5 years) in quality of life, and will reduce pain and disability in people status-post microdiscectomy.

Hypothesis 3\*\*: Compared to patient education only, a focused intervention of muscle specific strengthening will result in *immediate* improvement in muscle performance as assessed by muscle activation during exercise and symmetry in size of back muscles.

\*\*This hypothesis will be tested using MRI data and funded from an alternate source

***Project 4: (phase I): Strengthening and optimal movements for painful shoulders in chronic spinal cord injury (STOMPS)***

1. We aim to investigate the effectiveness of a shoulder exercise program combined with instruction to optimize the technique for performance of transfers and wheelchair propulsion on the reduction of shoulder pain with performance of activities and on the health-related and overall quality of life in patients with chronic spinal cord injury.
2. We aim to compare the effectiveness of a combined intervention on shoulder pain, function, and quality of life to a group receiving education regarding shoulder pain management. The role of prior and current physical activity on these outcomes will also be studied.

**A2. The second aim is to create the infrastructure necessary to develop and sustain clinical trials research in physical therapy. Specifically:**

1. We aim to identify the key elements essential to clinical trials research in physical therapy and build them into the infrastructure for the present multi-site projects and as a model and platform for sustained future efforts supporting programmatic physical therapy clinical trials research. Key elements include: a model to organize questions and cross-study collaborative measurement strategies; development of a partnership with biostatistical and data management expertise; and establishment of an administrative structure for the management of a large-scale, multi-site and collaborative enterprise.
2. We aim to use the infrastructure of *PTClinResNet* as a test-bed for at least one and possibly two additional clinical trial research proposals either as an extension of one of the four RCTs or a new, but related, proposal. This is one of the long-term objectives of *PTClinResNet*.

**A3. The third aim is to provide education and training opportunities for present and future clinician-researchers in physical therapy and for the physical therapy practice community at-large in its support of evidence-based practice. Specifically:**

1. We aim to provide a summer clinical research rotation for up to two entry-level DPT students per funding year during the students' final year of a 3-year entry-level DPT education program. Each student will rotate through at least two sites during the clinical research rotation.
2. We aim to mentor at least four entry-level DPT students and/or recent graduates of entry-level professional preparation programs (per funding year) through their involvement as authors and collaborators with consultant Ph.D-level faculty and researchers in the evidence-based practice electronic publication, *Infusions: Research into Practice*. For the duration of the funding period, this independent publication will partner with *PTClinResNet* to address the literature underlying the four projects described in this proposal, providing education to the physical therapy community-at-large regarding the state of evidence for muscle-specific and task-specific resistance training in the patient populations addressed by the study projects. The Editor-in-Chief (Lewthwaite), Senior Editors (Winstein, Kulig), and Editorial Board member (Thompson) also play key roles in *PTClinResNet*.

**B. Introduction and Overview of the Clinical Research Network**

**B1. Design of the Network**

*PTClinResNet* is designed pseudo-hierarchically with an umbrella coordination center that provides a common scientific, administrative, education and training infrastructure for four randomized controlled clinical trial (RCT) projects (1 phase III, 3 phase I) across seven effective sites illustrated in Figure B1.

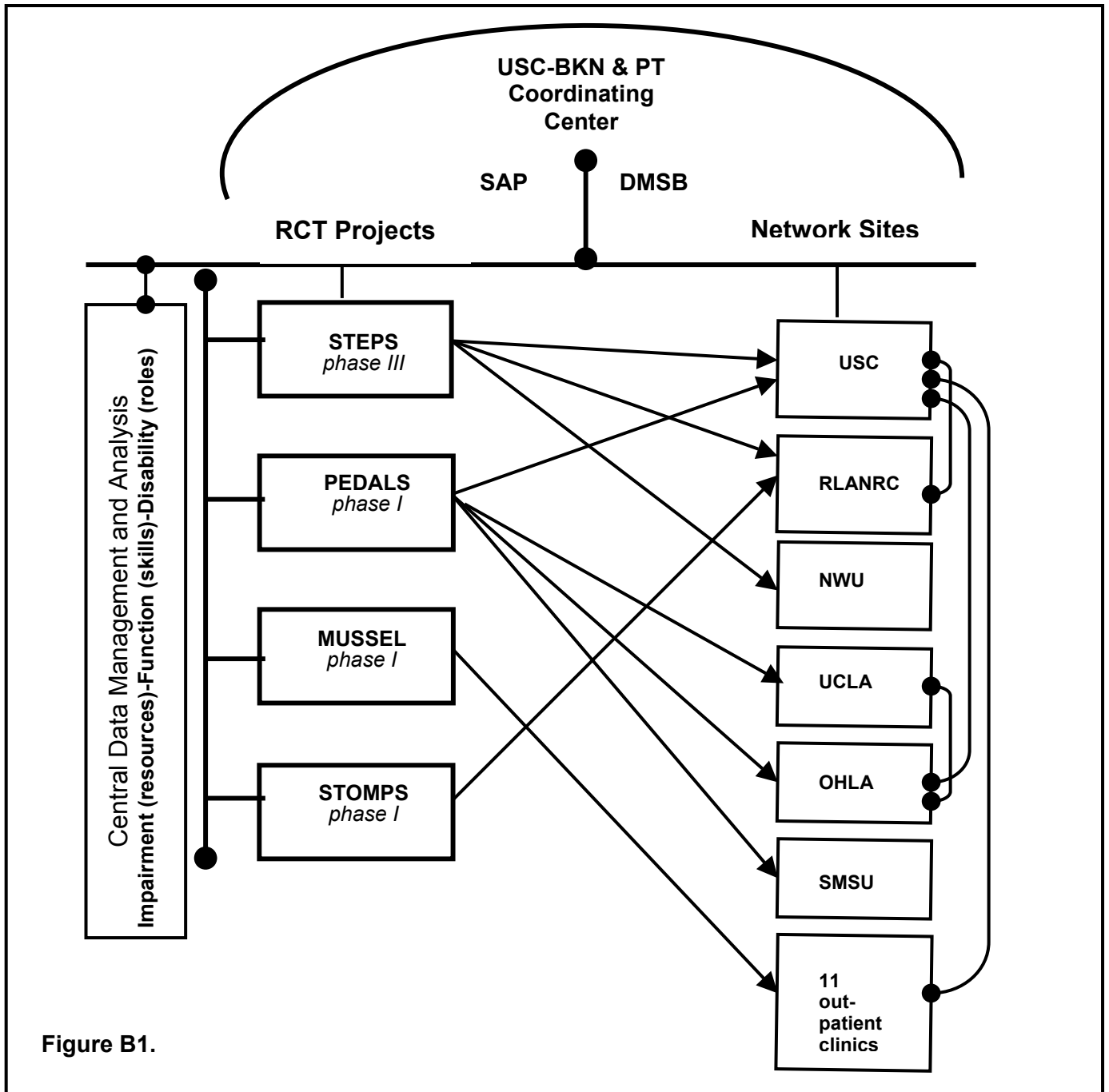


Figure B1.

**Figure B1:** Illustrates the structure of *PTClinResNet* with the umbrella coordination center providing oversight, data management, education, training, and fiscal management for the four projects (left column) that will unfold across seven effective sites (right column). In reality, there are more than seven sites as the bottom box represents 11 different out-patient orthopedic clinics in the Greater Los Angeles Area including USC PT Associates. SAP = Scientific Advisory Panel; DMSB = Data Monitoring and Safety Board; STEPS = Strength training effectiveness post stroke; PEDALS = Pediatric endurance development and limb strengthening; STOMPS = strengthening and optimal movements for painful shoulders in chronic spinal cord injury; MUSSEL = Muscle-specific strengthening effectiveness post lumbar microdiscectomy; USC = University of Southern California, Department of Biokinesology and Physical Therapy; RLANRC = Rancho Los Amigos National Rehabilitation Center; NWU = Northwestern University, Department of Physical Therapy and Human Movement Sciences; UCLA = University of California at Los Angeles, Department of Orthopedics; OHLA = Orthopedic Hospital of Los Angeles; SMSU = Southwest Missouri State University, Department of Physical Therapy. Each of the 11 OP clinics are listed in the MUSSEL project in section E (Project three) of the proposal. The right outside brackets illustrate the currently existing institutional and/or collaborative links between sites.

## B2. Thematic and Structural Rationale for *PTClinResNet* (Specific Aim # 1)

### a. Clinical Research in Rehabilitation is a New Focus:

Clinical trials research in rehabilitation is a relatively new area of focus for clinician-scientists in rehabilitation fields such as physical therapy, physical medicine, occupational therapy, and clinical psychology (Tate et al., 1999). In response to a growing need for evidence-based practice in this area of research and less than four years ago (December, 1998), the National Advisory Board on Medical Rehabilitation Research of the NIH-NICHD-NCMRR clinical practice programs conducted a 2-day workshop titled: *Clinical Trials In Rehabilitation* (ref). The workshop was open to a relatively small group of clinical trial researchers (34 invited participants including Barbeau, Duncan, Winstein, and Wolf, from the physical therapy research community, 15 presenters, and an additional 9 panel members representing scientists and consumers). The workshop was divided into four main sessions: 1) Outcome measures, 2) Clinical trial design and selected disorders, 3) Challenges in rehabilitation clinical trials, and 4) Recommendations. To a large extent, the formation, mission and design of *PTClinResNet* is motivated by an understanding of the principles, challenges, and barriers of clinical trials research in rehabilitation consistent with conclusions that emerged from that workshop.

The physical therapy profession is at a critical juncture in its development. As the profession manages its transition to doctoral level education and autonomy in practice in the United States, it must also ensure that the emerging clinical science of physical therapy reaches maturity. Maturity in this case will require a critical mass of research programs that are engaged in the process of defining optimal physical therapy interventions based on clinically-relevant evidence. Arguably, the development and refinement of clinical practice emanating from the bench to bedside continuum will support this professional maturity. Thus far, the profession has developed a core set of research institutions (including those represented in this CRN proposal) that have engaged in research to identify the basic mechanisms involved in impaired muscle performance, movement dysfunction, the characteristics of disability, and the clinical implications. Furthermore, leading clinical scholars and innovators have developed systematic diagnostic and intervention approaches applicable to many conditions that physical therapists encounter. The next critical step, and the one that we propose to coordinate through *PTClinResNet*, is to link these various forms of research together through the 1) implementation of four randomized controlled trials (RCT) of physical therapy interventions in a diverse set of disability conditions, 2) creation of an infrastructure to develop and sustain clinical trials research in physical therapy, that includes support for the generation of the idea, design, and pilot data and 3) provision of education and training opportunities in the process of clinical research in physical therapy, all through an integrative coherent collaboration. Our approach for *PTClinResNet* to conduct one phase III and three phase I RCTs has benefits in that it will allow both short term efficacy

results and long term development of new trials (that might spring from the phase I trials) and could be funded elsewhere once they are seeded by Foundation support.

**b. Establishment of a Clinical Research Network (CRN) for Physical Therapy:**

It is perhaps surprising, yet sobering to realize that most, if not all, of what constitutes practice in physical therapy today has not been evaluated through systematic clinical trials research. To our knowledge, there are only two funded, phase III randomized clinical trials (RCT) in physical therapy to date (both currently ongoing). One is the phase III NIH RCT initiated in 2000 to study the efficacy of upper extremity training with constraint-induced movement therapy in patients with stroke-related brain damage in the subacute stage of recovery (n = 240); the other is the phase III NIH RCT initiated in 1999 to study the efficacy of locomotor training with body-weight support in individuals with spinal cord injury in the subacute stage of recovery (n = 237). In a recent review published in *Current Opinion in Neurology*, Barbeau and Fung, provide an excellent synopsis of the role of rehabilitation in the recovery of walking in the neurological population (Barbeau & Fung, 2001). In their review, they systematically identify studies that have passed through the scientific experimental development process from discovery phase to the preclinical phase and finally phase I, II, III and IV clinical trials (Table B2a). In so doing, they describe the important steps to evaluate the efficacy and effectiveness of new interventions that will have an important impact on neurorehabilitation over the next decade.

Developmental Steps	Description-Criteria
Discovery Phase	A new therapeutic effect is reported to improve recovery
Preclinical studies	Studies that provide research evidence of the potential therapeutic effect.
Clinical Trials	
Phase I	Small scale clinical trials to establish the feasibility and safety with a limited number of patients.
Phase II	Clinical trial that usually takes between 2 to 4 years with a broad sample of patients to establish effectiveness (note: this should be 'efficacy' or effectiveness) of intervention.
Phase III	To demonstrate efficacy (note: this should be efficacy or 'effectiveness') of intervention in a large scale, well controlled randomized and multi-center clinical trial.
Phase IV	The object is to detect long-term effects and complications of investigational interventions. No studies have been done in the field of rehabilitation science. It normally takes 7 to 11 years to complete the scientific process from discovery to phase IV and costs several million dollars.

**Table B2a:** Describes the logical steps of progression from discovery phase to a preclinical phase followed by clinical phases I, II, III, and IV in order to establish an evidence-based practice. Adapted from Barbeau & Fung, 2001. The CRISP (NIH-Computer Retrieval of Information on Scientific Projects) database recently added two new terms: **Clinical Trials, Phase I** are clinical studies performed to evaluate the safety of diagnostic, therapeutic, prophylactic drugs, devices, or techniques in a small number of volunteer subjects or patients. **Clinical trials, Phase II, III, IV** broadly include controlled clinical studies performed to evaluate an experimental intervention in comparison with a standard or control intervention or comparing two or more existing treatments, e.g., evaluation of the efficacy or effectiveness and safety of diagnostic, therapeutic or prophylactic drugs, devices or techniques. The definition includes pharmacologic, non-pharmacologic, and behavioral interventions given for disease prevention, prophylaxis, diagnosis, or therapy. Community trials and other population-based intervention trials are also included.

One might ask why there have been so few RCTs in physical therapy and why relatively few (if any) of our therapeutic interventions have passed through the scientific experimental development process. Recently, the Institute of Medicine and the NIH Directors office appointed commissions to study problems in clinical research. The major obstacles identified by these commissions were: economic disincentives, insufficient support for clinical research by NIH, shortage of qualified investigators, inadequate development of new investigators, and cultural barriers between clinical practice and the basic and clinical research communities. One mechanism that has proven effective in the past at both the generation and fostering of clinical research in medicine has been the clinical research network (CRN). This mechanism holds promise for physical therapy as evidenced by this call for proposals: "The Foundation for Physical Therapy (Foundation) seeks to establish a Clinical Research Network (CRN) that promotes collaborative research to evaluate the effectiveness of physical therapist practice, and to implement the Clinical Research Agenda established in 2000 [Clinical Research Agenda for Physical Therapy. *Phys Ther* 2000; 80:499-513.]" Indeed, *PTClinResNet* has assembled a group of well-qualified, experienced and talented investigators, each with a relevant research track record (see section B2d below) and with a superb set of consultants and scientific advisory panel. Our unique group brings both the experience and knowledge needed to successfully design and implement the proposed plan.

The first specific aim of *PTClinResNet* is to generate evidence to evaluate the efficacy of physical therapy interventions. To do this, we propose four projects, one multi-site phase III RCT and three phase I RCTs. ***In each case, and with a diverse set of disabilities, we focus on identifying and testing strategies for improving function and reducing disability through interventions designed to enhance muscle performance through a dynamic task-oriented or muscle-oriented approach.*** These studies are expected to provide a foundation for a comprehensive set of investigations that will determine the optimal intervention strategies to be used by physical therapists for a variety of conditions and provide evidence that the intervention strategies are effective in real clinical settings. The ultimate goal is to provide clinically relevant evidence in support of the Clinical Research Agenda (2000) and upon which the next edition of the Guide to Physical Therapist Practice can be based. As one of the well-known barriers to clinical research is insufficient support, future studies will require additional funding from other agencies, such as the National Institutes of Health and National Institute of Disability and Rehabilitation Research, and will be conducted by a widening clinical research network.

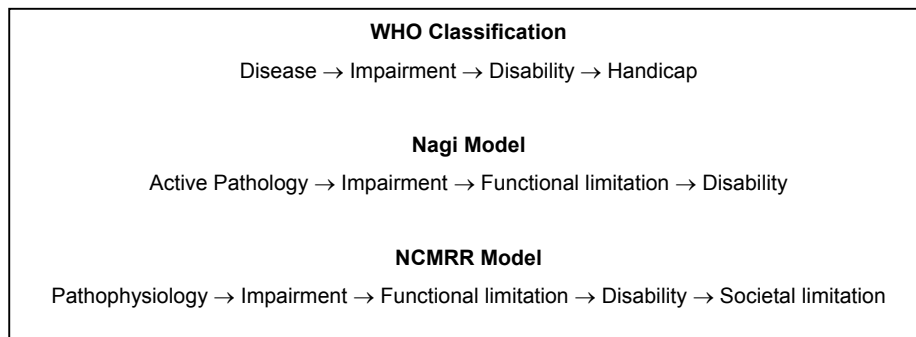
The fundamental idea upon which *PTClinResNet* is based is that one of the most important and robust ways that physical therapists improve the function of their clients, and by logical deduction, reduce their disability (but see recent discussion in Keysor & Jette, 2001) is by designing interventions that focus on improving muscle performance (e.g., joint torque output) and movement ability. Theories of disablement (see *Guide to Physical Therapist Practice, 2001*) have emphasized that disease pathology does not directly lead to disability. Instead, disability results indirectly from a complex set of interacting factors operating at different levels (Jette & Verbrugge, 1994). The Institute of Medicine (IOM) revised its disablement model in 1997 to show both the interactions of the person with the environment and the potential effects of rehabilitation and the enabling process (Brandt & Pope, 1997). The revised model shows a bi-directional interaction between the components, in which improvement in one component (e.g., impairment) has an effect on the development or progression of a preceding (e.g., pathophysiology) as well as forthcoming component (e.g., functional limitation). ***For PTClinResNet, and across the four RCTs, improvements in muscle performance are expected to mitigate functional deficits and disability to the extent that muscle weakness is the linchpin in impairment---function---disability "maps" (and muscle strengthening viable) for each diagnostic group.*** The response of muscle to overload conditions is arguably one of the most robust

research and practice expectations, used to great effect—at least at impairment levels—in informed physical therapy and human performance interventions (e.g., Bearne et al., 2002; Krebs et al., 1998; Landers et al., 2001; Ploutz-Snyder et al., 2002). Further, recent research has focused on the central effects of these “peripheral” changes linked to suspected task-level performance such as functional mobility skills. Jette and colleagues (Jette et al., 1998) used a cross-sectional dataset to examine the relationships among physiologic impairments, functional limitations, and disability in a moderately disabled sample of 207 community-dwelling older adults. Their multivariate analyses showed that most of the association of muscle strength and balance with disability was through the intermediary role of mobility limitations (Jette et al., 1998).

Each of the four RCTs is designed to determine the effects of a specific exercise intervention on the mitigation of functional deficits and disability. In the case of our phase III project (STEPS), where there has been significantly more prior research useful to design the intervention, we are asking if it is best to target the mobility task (dynamic-task specific-BWSTT) in combination with some form of resistance exercise (functional strengthening-limb-load pedaling vs traditional muscle-specific strengthening with PRE). For the other phase I projects (MUSSEL, PEDALS, and STOMPS), the specific resistance exercise intervention has been chosen using a deductive process from best evidence and considering current clinical practice. For example, the benefits of stationary cycling exercise are assumed for CP (UCPREF, 1999), and have a scientific basis in connection with the central pattern generation of locomotion (Visintin & Barbeau, 1994), and cardiopulmonary endurance. However, surprisingly, the benefits of such an exercise intervention have not been explored systematically in children with CP. Likewise, the beneficial effects of a muscle-specific strengthening program in individuals who have undergone microdiscectomy makes logical sense from the literature, but again, this has not been explored systematically for individuals with this disabling condition.

**c. The Disablement Model Provides a General Framework for PTClinResNet**

The use of disablement models as an organizing framework for research and practice in physical therapy and other rehabilitation professions was one of the key conceptual developments of the 1990’s (Jette, 1994). Various models of disablement have been developed and explored, including the World Health Organization (WHO) model, the Nagi model (Nagi, 1965), and the National Center for Medical Rehabilitation Research (NCMRR) model (NIH-1993, NCMRR) and the IOM (Brandt & Pope, 1997) as described above. These models are illustrated in Figure B2a.



**Figure B2a-** Different Models of the Disablement Process

Despite their differences in terminology, each of these models provides a framework for analyzing the various impacts of acute and chronic conditions on the functioning of specific body systems, basic human performance, and people’s functioning in necessary, expected, and personally desired roles in society (Jette, 1994). Indeed, the terminology selected for the *Guide to Physical*

*Therapist Practice* is based on the Nagi disablement model, and “is the model for understanding and organizing practice” (p. S19, Guide, 2001). The Nagi disablement model (Nagi, 1965), adopted by the Institute of Medicine in its 1991 report, *Disability in America* (Pope & Tarlov, 1991) defines four distinct levels in the process of disablement: pathology, impairment, functional limitations, and disability. The *Pathology* level defines the disease or movement disorder (e.g., multiple sclerosis, cerebral palsy, ACL tear). *Impairments* are defined at the organ-system level by a loss of structure or function (e.g., paresis, spasticity, limited range of motion); *functional limitations* are defined at the person-level by a loss of the ability to function in ways considered normal for human beings (e.g., walking, eating, remembering); *disabilities* are defined at the *societal-level* by a disadvantage for the person created by the intersection of the impairment or functional limitation with the environment or the person’s role in society (e.g., participation in home, work and recreation).

A newer version of the WHO model was recently released (December, 2000). This model, referred to as ICDH-2, has revised terminology with refined definitions for each level and bi-directional effects (*Impairment* ↔ *activity* ↔ *participation*), but the three basic levels beyond the ‘pathology’ (i.e., organ, person, and society) still exist (see Figure B2b). The refinements in definition are beneficial for characterizing function where the quality of, or duration of, the activity is lacking.

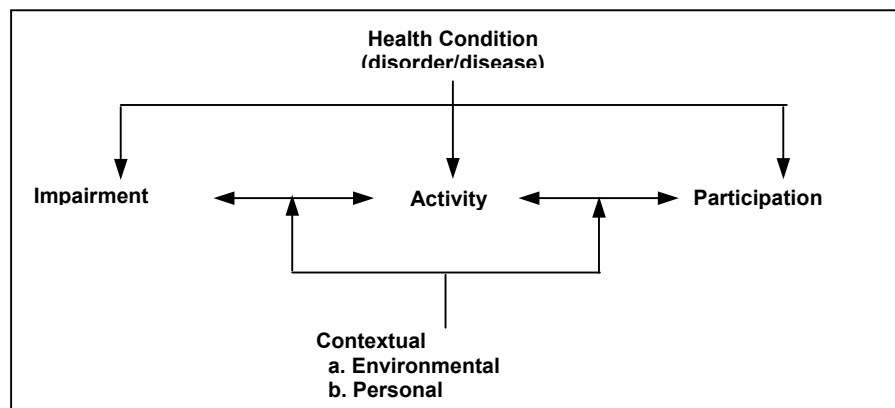


Figure B2b. The ICDH-2 Model of Disablement

Further, the potential negative connotation associated with “disability” and “handicap” in the original model led to the development of new terms, “activity” and “participation” to define the person and societal level of impact, respectively. Recently, Gordon (Gordon, 2000) proposed the Top-Down model of rehabilitation as the reverse or mirror image of disablement (see Figure B2c) and focusing on the enablement process characteristic of physical therapy intervention.

With health care cost containment and a minimal, but growing, body of evidence demonstrating the efficacy of physical therapy treatment (e.g., Pohl et al., 2002), the clinical outcomes research focus has shifted along the disablement continuum (Jette, 1995). Clinical outcomes research in rehabilitation medicine has progressed from earlier work focused exclusively on the *impairment* level; to more recent work that focuses on the *functional limitations and/or disability level* with the development of such scales as the Functional Independence Measure (FIM) which captures the burden of care (i.e., how much assistance is required to accomplish a set of motor and cognitive activities). Jette (1995) suggests a paradigm shift in clinical outcomes research from descriptive studies at each level to that which provides “direct evidence of the degree to which physical therapy that affects an impairment (e.g., muscle force) will also reduce disability and improve the functional outcomes of the patient (i.e., in activities such as transfers, walking ability, and improved quality of life)” (p. 968).

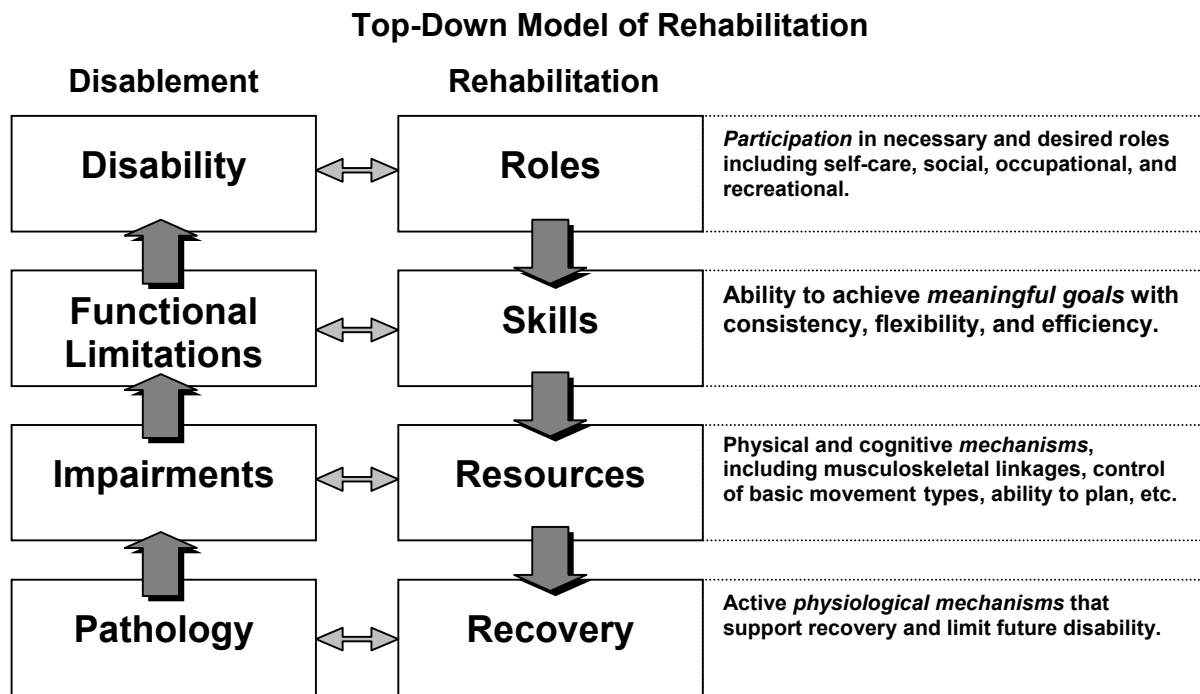


Figure B2c: Top-Down Model of Rehabilitation (Gordon, 2000)

One of the faulty though implicit assumptions regarding the impact of a treatment directed at the impairment level is that if one observes a positive change from a particular intervention at the impairment level (e.g., paresis), this will also increase function and decrease disability. Similarly, the assumption has been made that if one characterizes the recovery pattern of motor control (Duncan et al., 1992), this leads to predictions of disability outcomes. It is now more commonly understood that impairments do not directly predict disabilities. Indeed, the supposition of weak or non-existent impairment—function—disability linkages (resulting in lack of recognition of impairment roles in these more distal outcomes) may be seen as equally damaging to effective rehabilitation practice. The need to understand the effectiveness of physical therapy interventions in the broadest sense includes not only its effect on the individual in terms of impairment (i.e., muscle function) and functional limitation (e.g., walking velocity), but also its effect on health-related quality of life (HRQL) and quality of life (QOL) in general. **For each PTClinResNet project, we have chosen a common set of psychometrically sound primary outcome measures at these three levels of disablement (i.e., impairment, functional limitation, HRQL).** A common conceptual framework for PTClinResNet is a focus on the impairment-to-disability relationship and interactions. We suggest here that the question for rehabilitation research is not to determine the impairments *or* the disability; but instead to test models of the pathogenesis of disablement. More importantly and directly related to this proposal, by using the Top-Down Model (Gordon, 2000), we propose to test models of enablement in which the *relationships and interactions* between impairments and disability are discovered through effective resistance exercise intervention strategies (Jette, 1995). **Overall, and for each of the four RCTs, we are testing the hypothesis that a specific physical therapy intervention which enhances muscle performance and movement ability can be used to positively modify the impairment-to-disability relationship and in so doing, have a positive effect on quality of life (Wilson & Cleary, 1995).**

d. Clinical Trials Research Will Benefit from the Network Collaboration

We suggest that foundational research in movement science can have a useful and long-lasting impact on rehabilitation practice. The practice of physical rehabilitation evolved in part from practical needs (e.g., WWII injuries) and was influenced primarily by a physiological/medical perspective. Recently, however the behavioral and neurophysiological science of motor control has had an obvious influence on the practice of rehabilitation as evidenced by the introduction of such interventions as constraint-induced movement therapy for upper extremity recovery in stroke (Taub & Wolf, 1997) and body weight-assisted gait training in spinal cord injury (Harkema et al., 1997) and stroke (Barbeau et al., 1999). Both interventions developed out of research using animal models and fundamental questions about how movements are generated and controlled. Similarly, in a recent research agenda following a 1997 workshop dealing with facilitating patient learning during medical rehabilitation, Fuhrer and Keith (Fuhrer & Keith, 1998), proposed that "the effectiveness and efficiency of learning-oriented practices will likely be enhanced by well-formulated investigations grounded in available learning theory and research" (p. 560). In our case, the team of scientists including *PTClinResNet* PI (Winstein), Co-PI (Gordon), Lead Investigators, and Scientific Advisory Panel each have primary research training in a diversity of relevant disciplines (biomechanics, kinesiology/movement science, clinical psychology, health services) and with an established track record of research that provides an excellent and informed foundation for the design and testing of optimal clinical interventions proposed herein. In other words, the collaborative team of *PTClinResNet* is well suited to translate the science into clinical practice in physical therapy. The need to foster translation of the biological and physical sciences into clinical practice has been recognized for some time in medicine (Gray & Bonventre, 2002; Smith et al., 1998). Physical therapy has lagged behind medicine considerably in this regard. We highlight the contributions of the *PTClinResNet* scientific team in the next section.

*Principal Investigator:* Carolee J. Winstein, Ph.D., PT, received her BA from the University of California, Los Angeles (UCLA), her MS from the University of Southern California (USC), and her Ph.D., from the University of California, Los Angeles. Prior to receiving her Ph.D. Dr. Winstein served as Adjunct Faculty at USC, Department of Physical Therapy and Research Associate in the Department of Kinesiology at UCLA. Following doctoral training she was a postdoctoral fellow at the University of Wisconsin in the area of behavioral neuroscience. After postdoctoral training she joined the faculty of USC and was promoted to Associate Professor in 1996. Her current primary academic appointment is in the Department of Biokinesiology and Physical Therapy where she is also Chair of the Biokinesiology Program Committee, the committee that administers the M.S. and Ph.D. Programs in Biokinesiology. She also holds joint appointments in the Department of Neurology, Keck School of Medicine and the Ph.D. Program in Neuroscience, within the College of Letters, Arts and Sciences of USC.

Dr. Winstein began her research career while an undergraduate student enrolled in a combined psychology-kinesiology major at UCLA. Ironically, for her undergraduate thesis, she conducted research in the laboratory of V.R. Edgerton, Ph.D. (whose subsequent work with spinal cats contributed significantly to the body-weight supported treadmill training paradigm now being tested in humans with spinal cord injury) on the effects of exercise on rat intrafusal muscle fibers. After training to be a physical therapist, she again pursued a Master's degree part-time while working as a clinician specializing in neurological rehabilitation at Rancho Los Amigos Medical Center (now Rancho Los Amigos National Rehabilitation Center). Shortly after completing her M.S. degree she pursued doctoral work with Richard Schmidt, Ph.D. at UCLA in Kinesiology, specifically in the areas of human motor control and skill learning. Her postdoctoral fellowship at the University of Wisconsin

was in the speech and motor control laboratory of James Abbs, Ph.D. There, she initiated behavioral studies in the neural control of grasp and hand function. She has combined and continued both lines of research using human models in her laboratory at USC. Her current research has direct clinical relevance to the recovery of upper extremity function following central nervous system damage (e.g., stroke). In this regard, she recently completed an NIH funded, phase II RCT, Recovery and Rehabilitation of Arm Use Post-Stroke (Winstein et al. 2001). Since 2000, she has been the USC-Site Principal Investigator for the NIH funded, Multi-site Extremity Constraint-Induced Therapy Evaluation (EXCITE) RCT in sub-acute stroke (PI: Steven Wolf, Ph.D., P.T., FAPTA) and, as of January, 2002 she became the Co-PI for the multi-site EXCITE trial.

Dr. Winstein has taken an active leadership role in promoting clinical research training both at the program level and the policy level within the APTA. She served as chair of the research committee for the Neurology Section of APTA from 1994-1996. She served a three-year term as a member of the Postdoctoral Fellowship and Doctoral Scholarship Committee, for the Foundation for Physical Therapy from 1995-1998. She received the Research Award from the Neurology Section, APTA in 1998 and the Eugene Michels New Investigator Award in 1992. She has been a member of the Editorial Board of *Physical Therapy*, the journal of the APTA since 1997. She currently chairs the, Data Monitoring and Safety Committee for the NIH funded clinical trial, "Locomotor Therapy Trial for Spinal Cord Injury" (NIH U01 HD37439, PI: Bruce Dobkin, MD).

*Co-Principal Investigator: James E. Gordon, Ed.D., PT* joined the faculty at USC in the capacity of Associate Professor and Chair of the Department of Biokinesiology and Physical Therapy in July, 2000. Dr. Gordon has a distinguished career in research and education in Physical Therapy. Dr. Gordon received his B.S. degree from SUNY Downstate Medical Center, his MA and Ed.M. in movement science from Teachers College, Columbia, New York and his Ed.D. from the same institution. Prior to receiving his Ed.D., Dr Gordon was coordinator for the Master's degree program in motor learning for Teacher's College, Columbia. Following doctoral training he was a postdoctoral fellow at Columbia University, New York in the Center for Neurobiology and Behavior. After postdoctoral training, he assumed the position of Research Scientist, Center for Neurobiology and Behavior, College of Physicians and Surgeons, Columbia University, and NYS Psychiatric Institute. Following this and for four years he was Assistant Professor, Program in Physical Therapy, College of Physicians and Surgeons, Columbia University, New York. Prior to his arrival at USC and for five years, he was Professor of Practice and Program Director, Program in Physical Therapy, Graduate School of Health Sciences, New York Medical College, Valhalla, NY.

Dr. Gordon's research contributions are numerous and significant (see Biosketch). While at Columbia University and working with Dr. Claude Ghez, he was the lead investigator in three major research projects that each made significant contributions to our understanding of motor control. The aspect of Dr. Gordon's expertise that has particular significance for this training proposal is his interest in helping students and clinicians to make connections between research and clinical practice. His appreciation for the need to bridge the gap between the laboratory and the clinic in biokinesiology-rehabilitation science is captured in several review articles and textbook chapters. We highlight two of these publications. First, in 1987, he published an article called "Assumptions underlying physical therapy intervention: Theoretical and historical perspectives" in a textbook called *Movement Science*. This article has often been cited in the rehabilitation literature and it is widely used in physical therapy educational programs. It proposes a theoretical basis for evaluating therapeutic approaches to neurological rehabilitation. He recently updated the article for the 2<sup>nd</sup> edition (Assumptions underlying physical therapy intervention: Theoretical and historical perspectives. In J.H. Carr & R.B. Shepherd, Eds., *Movement science: Foundations for physical therapy in rehabilitation*, 2<sup>nd</sup> edition. 2000, Aspen Publishers, Rockville, MD.)

Second, since he gave three of the motor systems lectures in Columbia medical school's Neural Science course from 1984 to 1995, he was asked by Kandel, Schwartz, and Jessell to write two chapters in the third edition (1991) of *Principles of Neural Science*, covering muscle receptors and spinal reflexes. This textbook is highly regarded and widely used in neural science courses; the editors are members of the faculty at Columbia. Indeed, Eric Kandel won the Nobel Prize in Physiology or Medicine last year for his fundamental work in the cellular and molecular basis of learning and memory. Dr. Gordon recently revised these two chapters with Keir Pearson, Ph.D. The new chapters appear in the fourth edition of the textbook, published two years ago (Kandel et al., 2000).

*Lead Investigator: David Brown, Ph.D., PT (NWU) will lead the phase III multi-site RCT, *Strength-Training Effectiveness Post-Stroke* (STEPS) to determine the optimal strength training program for recovery of locomotor function post-stroke using a combination of body-weight-assisted treadmill training and one of four forms of resistance training. Dr. Brown's previous research dealing with the effect of increased workloads to enhance force output during pedaling exercise in persons with poststroke hemiplegia (e.g., Brown & Kautz, 1998) provides an excellent foundation for this project. His Co-PI's include Katherine Sullivan, Ph.D., P.T., (USC, Sullivan et al., in press), and Sara Mulroy, Ph.D., P.T. (RLANRC, Mulroy et al., 2002), each with relevant publications and a prior research record to inform this project.*

*Lead Investigator: Eileen Fowler, Ph.D., PT (UCLA) will lead the phase I RCT, *Pediatric Endurance Development and Limb Strengthening* (PEDALS) to determine if a 12-week program of stationary cycling can enhance function in children with cerebral palsy (CP). Dr. Fowler's previous research dealing with the biomechanics of cycling (Gregor & Fowler, 1996) and the effects of strengthening on spasticity in CP (Fowler et al., 2001) provides an excellent foundation for this project. Her Co-PI's include Loretta Knutson, Ph.D., P.T. PCS (SMSU, Knutson et al., 1999) and Sharon DeMuth, DPT (USC, Watts & DeMuth, 1998), each with relevant publications and prior experience to inform this project.*

*Lead Investigator: Kornelia Kulig, Ph.D., PT (USC) will lead the phase I RCT, *Muscle-Specific Strength Training Effectiveness Post Lumbar Microdiscectomy* (MUSSEL) to assess the immediate and long-term effects of trunk-specific resistance exercises on decreasing pain and improving function in people status-post lumbar microdiscectomy. Dr. Kulig's primary training in biomechanics, her previous research experience dealing with muscle activation as determined from MRI (Kulig et al., 2001) and her recently funded project, "The effects of single intervention session on pain response and lumbar segmental mobility in persons with low back pain: A comparison of spine mobilization and active extension using dynamic MRI." (Foundation for Physical Therapy, PI, Powers, Co-PI, Kulig) provides an excellent foundation for this project. Her Co-PI on this project is Christopher Powers, Ph.D., PT (USC).*

*Lead Investigator: Bryan Kemp, Ph.D. (RLANRC) will lead the phase I RCT, *Strengthening and optimal movements for painful shoulders* in chronic spinal cord injury (STOMPS) to investigate the effectiveness of a combined shoulder exercise and optimization of performance technique program on pain reduction, performance, and health-related as well as overall quality of life in patients with chronic spinal cord injury (paraplegia). Dr. Kemp's long history of research dealing with the effects of aging with a disability (Kemp & Adkins, 2001) and quality of life while living and aging with a spinal cord injury and other impairments (Kemp & Ettlson, 2001) provides an excellent foundation for this project. His Project Manager, Lilli Thompson, B.S., P.T. (RLANRC) whose recent clinical research (Thompson & Yakura, 2001) and experience dealing with aging-related functional changes in SCI, provides a strong foundation for this phase I RCT*

In addition to the PI, Co-PI, Lead Investigators, and Project Co-PIs, we have appointed a Scientific Advisory Panel (SAP). The role of the SAP is to grow collaborations and provide expertise in design, outcome measures, and analyses across the projects. The SAP, including our valued consultants (Jette and Lewthwaite), makes an important contribution, by adding depth and breadth to the scientific and organizational aims of *PTClinResNet*. SAP members and consultants are listed here with special areas of expertise in parentheses: Bryan Kemp, Ph.D. (Subjective QOL assessment; Research center design and training; also Lead Investigator for STOMPS), George Salem, Ph.D. (Resistance exercise, muscle physiology, periodicity; also advisor to STOMPS), Stan Azen, Ph.D. (Director, Statistical Consultation and Research Center [SCRC], biostatistics, design, study power for clinical trials research), Sara Mulroy, Ph.D., PT (clinical biomechanics; research experience relevant to STOMPS project, clinical research design; also Rancho site PI for STEPS), Mark Rogers, Ph.D., PT (balance and postural control in geriatric and neurologic populations; Co-I for STEPS project), Denise Globe, Ph.D. (HRQL assessment), Rebecca Lewthwaite, Ph.D. (psychosocial aspects of exercise adherence, motivation, evidence-based practice; Editor-in-Chief of *Infusions: Research into Practice*) and Allan Jette, Ph.D., PT (health services research and management, health outcomes research).

#### e. Coordinating Center-Institutional History

The Department of Biokinesiology and Physical Therapy is one of three departments (including Nursing and Occupational Therapy and Science) that are unified in the Division of Independent Health Professions (IHP) on the Health Sciences Campus of the University of Southern California. The Vice President for Health Affairs, Dr. Joseph P. Van Der Meulen, a noted leader in the field of neurology is the Director of the Division of IHP. BKN & PT at the University of Southern California (USC) has been in the business of training physical therapy practitioners for over 50 years. USC is considered one of the great private research institutions in the country. It is renowned for many of its graduate and professional programs including: music and performing arts; social work; communications; public administration; medicine; engineering; pharmacy; law; and dentistry. BKN & PT mirrors the excellence of USC as one of the premier programs (Ranked # 2 in the Nation, U.S. News & World Report, 2002) offering graduate and professional degrees in biokinesiology and physical therapy, respectively. BKN & PT (then called Physical Therapy) was established in 1944. For those wishing to enter the profession, the department offers the Doctor of Physical Therapy (DPT) degree, a three-year, post-baccalaureate entry-level professional program in physical therapy. For persons who are already practicing physical therapists, the department offers a Master of Science (MS) program (also open to qualified, non-physical therapists). In addition, the department offers an academic research Ph.D. degree program in Biokinesiology. All degree programs are administered through the Graduate School of USC. In 1991, the department changed its name from *Physical Therapy* to *Biokinesiology and Physical Therapy* to reflect the distinction between the research degree programs (i.e., M.S./Ph.D.) in biokinesiology, the study of the biological basis of movement, and the professional degree programs in physical therapy (i.e., DPT, Post-professional DPT). The Ph.D. program in biokinesiology awarded its first Ph.D. in 1984 to Marybeth Brown, Ph.D., P.T., who has gone on in her academic career to make significant contributions in the area of age and exercise effects on skeletal muscle (e.g., Brown & Hasser, 1996). Since then, the Ph.D. program has trained 17 scientists, many of whom have careers in academic settings and are promoters/supporters of clinical research in physical therapy (e.g., Christopher Powers, Ph.D., Katherine Sullivan, Ph.D., both at USC and Co-Is for *PTClinResNet* projects).

In addition to the academic programs, the Department maintains a fully functioning physical therapy practice to serve as an extension of the department to further its mission of educating

Physical Therapists. The mission of USC Physical Therapy Associates is to establish levels of excellence in all aspects of clinical practice. USC Physical Therapy Associates is a group of Physical Therapy practices, which is staffed and operated by the faculty members from the Department of BKN & PT. The primary goal of USC PT Associates is to provide excellent clinical sites for the students of the Department's Physical Therapy program. There are currently three practices, which fall under the PT Associates umbrella: 1) Faculty Practice—HRA Building Marrengo (USC site for proposed STEPS project and current EXCITE clinical trial); 2) Student Health Center/PM PT University Park Campus; and 3) Women's Health (Comprehensive Continence Center).

Advanced clinical training is provided through two different post-professional residency programs; one program in orthopedics and a newly established residency in adult neurology. The Orthopedic Physical Therapy Residency is a one-year program that provides exceptional post-graduate clinical education for two residents per year. The primary mentoring environment is the Faculty Practice (USC PT Associates). The residents are mentored, in a well-grounded evidence-based environment, by doctorally prepared physical therapists and surgeons. The residents are learning in the rich academic and clinical environment, by studying and teaching in the company of medical residents and Ph.D. students. Furthermore, the residents are engaged in teaching in the entry-level doctoral physical therapy program. The mission of the Residency builds on the mission of the University and the Department. In particular, the mission of the Orthopedic Physical Therapy Residency Program at USC BKN & PT is to graduate advanced practitioners of orthopedic physical therapy who will express their education through excellence in the practice and teaching of clinical skills, who will continue to expand the body of knowledge in their specialty by conducting and publishing clinical research, and who will make a lasting contribution to their local and professional community. It is possible that the Orthopedic residents will have some involvement with *PTClinResNet* and the MUSSEL project; the nature of that involvement has not been worked out at the time of this writing.

The University of Southern California/Rancho Los Amigos National Rehabilitation Center (USC/RLANRC) Post-Professional Residency Program in Adult Neurology anticipates enrolling its first two residents in August of 2002. This unique residency program in neurological physical therapy is designed to produce effective evidence-based practitioners who will serve as agents to advance neurologic physical therapy practice. This program is expected to further strengthen the partnership between the University of Southern California and Rancho Los Amigos National Rehabilitation Center and will expose residents and clinical staff at RLANRC to the cutting-edge interventions in physical therapy represented by the work of *PTClinResNet* participants. Several members of *PTClinResNet* (Drs. Sullivan, Lewthwaite, Mulroy, and Winstein) are key members of the leadership or faculty for this residency program, which may well serve as an additional springboard toward clinical research careers for some of the residents.

### **B3. Infrastructure Creation for Clinical Trials Research in Physical Therapy (Specific Aim # 2)**

The second specific aim of *PTClinResNet* is to create the infrastructure needed to develop and sustain clinical research in physical therapy in the long-term. One of the major obstacles to clinical research in physical therapy is the lack of an appropriate infrastructure to support it. The APTA has only recently acknowledged this problem and mechanisms including the development of the Clinical Research Agenda (*Physical Therapy*, 2000) and FPT-CRN call for proposals represent the first steps to organize larger scale efforts to fill the void in clinical research. Medicine recognized this problem over forty years ago. Indeed, and authorized by Congress in 1959, the General Clinical Research Center (GCRC) program at the NIH now encompasses 78 GCRCs located at major medical institutions throughout the United States (one at USC and NWU). These GCRCs, supported by the

National Center for Research Resources (NCRR) Clinical Research Area, are a national network of centers that provide optimal settings for medical investigators to conduct safe, state-of-the art, in-patient and out-patient studies of both children and adults. GCRC's also provide infrastructure and resources that support several career development and training opportunities.

*PTClinResNet* could use the GCRC model as a guide in its development of the infrastructure and resources necessary to support clinical trials research in physical therapy for the future. At our Retreat held in early March (and funded by the \$5000 planning grant from the Foundation), the *PTClinResNet* scientific team (PI, Co-PI, Lead Investigators, Co-Leads, SAP, and consultants), identified **eight major challenges to the clinical research process that have factored into the current infrastructure for *PTClinResNet*** (see Appendix A, planning Retreat minutes). We describe them below. This list represents our current framework and one that we expect to evolve over the course of the 3-year funding period.

*PTClinResNet* will provide a test-bed for determining and providing solutions to the identified challenges surrounding the design and implementation of high quality, definitive and clinically relevant research in physical therapy. During our planning process, we identified eight primary challenges to clinical trials research in physical therapy: 1) clear, precise and logical formulation of a focused and tractable clinical problem that is, can, or could be addressed by physical therapy (see clinical research agenda, 2000); particularly problems that foster the translation of science into clinical practice; 2) choice of the appropriate study design—feasibility, case report, pre-clinical trial, phase 1, RCT, etc.; 3) choice of appropriate outcome measures (primary and secondary) and stratification variables that allow the development of theory (i.e., impairment/ disability) and hypothesis testing of the pathogenesis of disablement/enablement (Jette, 1995); 4) determining a budget to carry out the study and finding an appropriate funding source(s); 5) characterization and standardization of the physical therapy intervention for systematic investigation; 6) determination of the appropriate sample size and data analysis (Hulley et al., 2001; Ottenbacher, 1995); 7) study implementation including: randomization, realistic determination of subject recruitment and retention, personnel training and standardization; single-blind considerations, and coordination within and across sites, if multi-site design; and 8) dissemination of findings; determination of the next step in the scientific development process.

How will/has *PTClinResNet* address(ed) these challenges? First, and most importantly, the *PTClinResNet* administrative and investigative team has the experience and track record that is critical to the design and successful implementation of clinical research in physical therapy. *PTClinResNet* comprises a breadth of research skills that will allow successful management, completion, and preparation of future multi-dimensional clinical research proposals. This will be important for our ability to secure future funding, an important and critical long-range plan for *PTClinResNet*. The Foundation funding is just the start (see section B5 Limitations below). Our team is highly likely to leverage this support into more based on our past experience and track record. Indeed, for future multi-site efforts, we are establishing the foundation for large scale phase II and III trials. More specifically, the CRN will address these challenges by: 1) providing collaborative and expert oversight for the process (see Governance below). 2) partnering with the Statistical Consultation and Research Center (SCRC) at USC for consultation on issues related to a) study design (e.g., choice of research design and setting, determination of sample size, and analytic plan), b) study conduct (e.g., participation in developing the Manual of Procedures, design of database system, recruitment, randomization and tracking follow-up of participants, regulatory compliance), and c) statistical analyses and reporting of results. 3) testing several different clinical research designs and settings (phase I, phase III) in four projects that span the breadth of physical therapy practice, and 3) training junior investigators in this process (DPT, Ph.D., and junior faculty).

For data management, we have established a coordinating data management center (DMC) directed by Stanley Azen, Ph.D. at USC. The DMC will organize all subject enrollment, randomization, tracking, data entry and analysis for each of the four projects and across the projects. The DMC will be established under the current, SCRC-an organized research unit at the Coordinating Center's Institution (see Appendix B). Having a central data management unit will foster systematic and common practices across the satellites for implementation of the manuals of procedures (MOPs), subject enrollment, randomization, tracking, data entry, and regulatory operations (i.e., IRB, adverse events). The DMC will also work with the investigative team to develop a data dictionary for standardized definitions of study variables across the satellites. A common website for *PTClinResNet* will allow rapid communication of study recruitment, changes in procedures and new information across the sites and projects. The website will have both public and restricted areas to allow education of the public about the benefits of physical therapy, and at the same time the restricted (password protected) access will allow systematic subject enrollment (with inclusion criteria checks), randomization (to assist in the single-blinding process), data entry for primary outcome measures (using common instruments), and reporting of any adverse events required by our regulatory agencies and IRBs.

a. Collaboration Through Data Sharing and Cross-Study Analysis

The similar designs, common disablement dimensions (impairment, function, HRQL), and, in some cases, common outcome measures (i.e., SF-36; Peds QL) across the four studies should allow an examination of conclusions about the efficacy of resistance exercise across the disabilities. We can determine a preliminary Effect size (ES) for each RCT, compare these ES for each disability group and determine a pooled ES for a preliminary estimate of the overall efficacy across the studies. Normally, these kind of meta-analyses require larger sample sizes, thus with our relatively small sample size, only an estimate of the overall efficacy will be possible. However, this estimate, if it is in the expected direction, can provide a strong rationale for future directions (e.g., phase II RCT) in the process.

b. Governance, Committee Structure and Future Direction

We established a steering committee made up of the PI, Co-PI and the four Lead Investigators. Up until the time of submission of our proposal, the PI has been responsible for all major decisions with recommendations from the Co-PI and Lead Investigators. After funding begins (presuming our proposal is successful), we will establish several additional committees. The Lead Investigators will be responsible for guiding the development of all Manuals of Procedures (MOP); the PI will oversee the process and coordinate the electronic conversion of all MOPs with the DMC. The Scientific Advisory Panel will become active in the review of the Manuals of Procedures as they are developed. The Steering committee will begin seeking sources of supplemental funds to support the research, education and training mission of *PTClinResNet* and in planning for future funding at the end of the FPT 3-yr funding period. We will explore the possibility of a partnership with existing clinical research networks (e.g., GCRC, C-BREK-see Appendix C). We will appoint a Publications Committee to begin formulating a "design" paper that describes the Clinical Research Network in Physical Therapy (pros and cons). The recently appointed Data Safety and Monitoring Board (Byl, Kailes, Watts) will elect a Chair and establish communication with the DMC (Azen).

Longer-term objective for *PTClinResNet*: One, as yet unexplored, possibility is that the infrastructure (scientific and administrative) that we build will provide the appropriate environment (with additional funding) for the establishment of a Center for Clinical Trials Research in Physical Therapy (see GCRC model). This could take the form of an Organized Research Unit (ORU) that

would be self-sustaining through external funding and could solicit and support proposals for pre-clinical or feasibility studies in Physical Therapy. Its primary mission, however, would be to organize the administration of safe, state-of-the-art, definitive, clinical trials in physical therapy to address the clinical research agenda of the profession.

#### **B4. Education and Training Opportunities (Specific Aim # 3)**

The need for well-trained clinical researchers in physical therapy has never been greater than in this time of health care cost containment when effective decisions require the best evidence. Less than seven years ago and in response to a published review of research reports in *Physical Therapy* (3), Michels pointed to the "lack of theory required to direct research efforts....." (4). The clinical research training opportunities outlined as the third aim of *PTClinResNet* is based on the proposition that there is a special need for clinical research scientists who are capable of developing and testing theory through clinical trials research in physical therapy.

The training of research scientists in the field of rehabilitation was identified as one of seven cross-cutting priority areas for the National Center for Medical Rehabilitation Research (NCMRR, <http://www.nichd.nih.gov/publications/pubs/ncmrr/plan/plan.htm>) in its 1993 Research Plan (1). In 1997, the Institute of Medicine, in its report, "Enabling America: Assessing the Role of Rehabilitation Science and Engineering," pointed to the critical need for more and better trained rehabilitation scientists and recommended "interdisciplinary training in rehabilitation science and engineering"(2). The third aim of *PTClinResNet* outlined in this proposal is for predoctoral (pre-DPT and Ph.D.) and postdoctoral training (Ph.D.) opportunities that will begin to meet the critical need for clinical research scientists whose work will ultimately lead to better methods for rehabilitation of individuals with physical disabilities. We outline four mechanisms for this below:

1. Provide a summer internship experience in clinical research within *PTClinResNet* to predoctoral DPT, postgraduate, and/or academic faculty. We will seek candidates for our clinical research training program in support of clinical research trials that are ongoing within the network or to be developed. The purpose of the training program is to provide an opportunity for physical therapists to participate in the design, implementation, and publication of scientific investigations. In this program, students will work side by side with the Lead and/or Co-Lead Investigators of one of the four RCTs proposed herein. Summer internships generally last from eight to ten weeks, beginning in late May and ending in mid- to late August. We will, however allow some flexibility to accommodate student needs. Physical Therapy program Academic clinical coordinators of education should contact the *PTClinResNet* PI for information on participation in this summer internship experience.
2. Mentor potential junior clinician-researchers using the collaborative evidence-based literature review approach of *Infusions: Research into Practice*. One purpose of the *Infusions* mechanism is to build a bridge between academic and clinical worlds in which substantive scholarly work is encouraged for future leaders who are research-oriented and capable of high-level professional contributions. Top students about to enter the last year of their entry-level preparation will be recruited to work as authors with the Editor-in-Chief and/or other faculty researchers (including the researchers of *PTClinResNet*) and a select set of research-oriented and evidence-based community clinicians. Evidence-based reviews of the literature underlying the *PTClinResNet* projects will form the basis for four to six issues of *Infusions*. (see Appendix D for examples)  
*Infusions* is a publication, previously produced through the Center for Research in Clinical Biokinesiology at Rancho Los Amigos National Rehabilitation Center, that has been in publication

hiatus for several years (due to clinical downsizing and re-engineering) and is in the process of being resurrected as a web-based e-publication with the same Editor-in-Chief, via the sponsorship assistance of the Department of BKN & PT at USC. *Infusions* has a history of clinician authors who have gone on to Ph.D. level training, postdoctoral fellowships, and research positions, supporting the value of a bridge mechanism for promising professional leaders into further critical research training. The Editor-in-Chief, Rebecca Lewthwaite, Ph.D., is the Director of Research and Education in the Physical Therapy Department at Rancho Los Amigos National Rehabilitation Center and an Instructor in the Evidence-based Practice courses in the USC entry-level DPT curriculum. *PTClinResNet* PI, Dr. Winstein and Lead Investigator, Dr. Kulig (MUSSEL) are Senior Editors of *Infusions* and USC faculty members, and Project Manager (STOMPS) Thompson (a former *Infusions* author) also sits on the Editorial Board. Lilli Thompson, P.T. is Education Director of the Rehabilitation and Research Training Center for Aging with a Spinal Cord Injury located on the campus of Rancho Los Amigos National Rehabilitation Center.

3. Submit a proposal to the 2004 Combined Sections Meeting of the APTA for an organized workshop in the systematic conduct of clinical trials research in physical therapy, using *PTClinResNet* as a template. A draft outline of proposed topics follows:
  - A. Generation of the clinical research question (efficacy vs effectiveness, Clinical Research Agenda, 2000)
  - B. Clinical Research design considerations (e.g., pre-clinical; phase I)
  - C. Randomization and blinding—How essential are they?
  - D. Choice of Outcome Measures (e.g., framework using disablement model; psychometric properties)
  - E. How many subjects? Sample size determination
  - F. Participant recruitment, follow-up, retention strategies (e.g., importance of follow-up)
  - G. Patient safety and Regulatory issues (IRB, DMSB, adverse events)
  - H. Funding; strategies for optimization of funds (e.g., fee for service structure for blinded evaluator)
  - I. Protected time, project coordination, tracking and reporting
  - J. Specific examples with different diagnostic groups and clinical settings
    - i. Orthopedic/out-patient
    - ii. Sub-acute/chronic neurological/rehabilitation
    - iii. Pediatric/out-patient
  - K. Importance of Academic-Clinical partnerships in clinical research

The other education and training opportunities that are embedded into *PTClinResNet* are with the individual research assistants (RA) selected by the Lead Investigators across the four RCTs. The Lead Investigators will provide mentoring in the clinical research process with the RA who may be a graduate student (e.g., M.S., or Ph.D.), or junior faculty. For example, and in the case of Dr. Knutson at SMSU, the RA to be considered is a junior faculty at SMSU (Jeanne Cook). Jeanne is working on her Ph.D. at the U. of Nebraska and has a background in neurological physical therapy. At NWU, Dr. Brown will provide mentoring in the clinical research process for the clinician who will provide the intervention at NWU in the STEPS project. This RA will attend regular laboratory meetings with the Lead-PI and be involved in reviewing the literature relevant to the STEPS project. Also, Dr. Brown participates in several NIH T32 Training Grants that give him access to postdoctoral fellows in the area of Neuroscience and Rehabilitation Sciences. Interested Fellows will be invited to train with the STEPS project. Finally, at UCLA, Dr. Fowler in her capacity as faculty of the University Center of

Excellence—Targan Center for Developmental Disabilities (funded by the Federal Government - Administration on Developmental Disabilities) is responsible for advanced training of physical therapists. Targan trainees will have the opportunity to participate in this research project. Research Assistants involved in the PEDALS project will have an opportunity to receive additional training through this program in the area of Developmental Disabilities. In addition, Dr. Fowler has arranged for students from the UCLA Undergraduate Research Program (SRP) to participate in the PEDALS project. These students work between 8-10 hours per week under the guidance of UCLA faculty and receive course credit for their participation in this program. Many of the students who seek to work with Dr. Fowler subsequently pursue a degree in physical therapy. Students will receive training about cerebral palsy and appropriate verbal communication with persons with disability (e.g. person first language). For PEDALS, they will be responsible for monitoring the subject calendars that are returned to Dr. Fowler and for contacting the subjects to facilitate compliance with the return of calendars.

### **B5. Limitations**

No proposal would be complete without an acknowledgement of its limitations. First, our primary funding limitation (within the constraints of four projects and seven sites) has prompted us to look to the future for additional funding before we have even begun. For example, one of our projects (MUSSEL) is designed around an innovative collaboration of the mechanistic (biomechanical and physiological) and the therapeutic (resistance exercise) aspects of musculoskeletal rehabilitation medicine. However, without the integration of methods, it regresses from the 'innovative' to the 'standard' category of clinical trials research. Our budget could not afford the nearly \$50,000 in MRI costs for this project. The plan is for Dr. Kulig to apply to the American Academy of Orthopedic Surgeons (application deadline, August 1, 2002) for supplemental funding for the MRI portion of the MUSSEL proposal within *PTClinResNet*. It is well known that clinical trials research is expensive and as such, we have projected a budget that relies on significant institutional support (average 19% of the requested amount) to carry out our proposed work (see budget summary and institutional contribution).

Second, we plan only one phase III RCT and depending on how you define it (the definition for therapeutic interventions must be modified from the FDA definition for pharmaceutical trials), STEPS might be considered a phase II RCT. This is however, the stage of scientific development for this particular intervention in the stroke population and it would not be wise nor advisable to attempt a more advanced stage of work before sufficient groundwork has been established.

Third, we have a somewhat limited education and training plan. We had planned to fund a postdoctoral fellowship for two years in *PTClinResNet*. Applicants were to be a physical therapist with an academic doctoral degree (Ph.D or Ed.D) interested in a mentored clinical scientist training experience through *PTClinResNet*. The fellowship was to be designed similar to the Mentored Patient-Oriented Research Career Development Award (K23) from NIH. This mechanism provides support for a period of supervised study and research for clinically trained professionals who have the potential to develop into productive clinical investigators focusing on patient-oriented research. The objective is to encourage research-oriented clinicians to develop independent clinical research skills and gain experience in advanced methods and experimental approaches that will allow them to conduct patient-oriented clinical trials research, and to capitalize on the discoveries of movement science research and translate them to clinical settings. Candidates would identify a member of the *PTClinResNet* faculty with extensive research experience to be the primary mentor and must be willing to spend a minimum of 75% of full-time professional effort in research career development and clinical research activities within *PTClinResNet*. Support under this award could extend to 3 years.

This post-doctoral fellowship was to provide \$48,000 per year of salary support and including benefits. The *PTClinResNet* mentored career development award recipient would be invited to attend the annual CRN investigator's meeting at the APTA. Unfortunately, our budget was not able to keep this postdoctoral fellowship in the final proposal and stay within the \$500,000/yr limit. We are investigating other funding sources for this worthwhile education and training mechanism.

Finally, we have no established partnership with other Clinical Research Networks. This means there is considerable inertia to overcome in a relatively short period of time in the establishment of *PTClinResNet*. However, the process of overcoming the initial inertia should provide considerable motivation to capitalize on what we develop for the future. We would like to see *PTClinResNet* live well beyond the 3-yr Foundation funding period. Indeed, this long-sighted motivation factors into most of our decisions including the current work plan proposed herein.