

Lessons Learned in Participant Recruitment and Retention: The EXCITE Trial

Participant recruitment is considered the most difficult aspect of the research process. Despite the integral role of recruitment in randomized clinical trials, publication of data defining the recruitment effort is not routine in rehabilitation initiatives. The recruitment process for the Extremity Constraint-Induced Therapy Evaluation (EXCITE) trial illustrates obstacles to and strategies for participant accrual and retention that are inherent in rehabilitation clinical trials. The purpose of this article is to increase awareness of the multiple facets of recruitment necessary for successful clinical trials, thus supporting the continued development of evidence-based practice in physical therapy. The Recruitment Index is presented as a variable to measure recruitment efficacy. In addition, ethical aspects of recruitment are explored, including informed consent and the concept of therapeutic misconception. [Blanton S, Morris DM, Prettyman MG, et al. Lessons learned in participant recruitment and retention: the EXCITE trial. *Phys Ther*. 2006;86:1520–1533.]

Key Words: *Informed consent, Randomized clinical trials, Recruitment, Rehabilitation, Research ethics, Stroke.*

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The aim of this article is to increase awareness of the multiple facets of recruitment necessary for successful clinical trials, thus supporting the continued development of evidence-based practice in physical therapy.

The number of randomized clinical trials (RCTs) in physical rehabilitation, although having grown significantly in recent years, remains inadequate.¹ Participant recruitment is considered the most difficult aspect of the research process.²⁻⁴ Recent estimates indicate that 85% of trials do not conclude on schedule due to low participant accrual, 60% to 80% of clinical trials in the United States do not meet their temporal endpoint because of challenges in recruitment, and 30% of trial sites fail to recruit even a single participant.⁵ Despite its importance to successful research efforts, there is a dearth of literature reporting details of the recruitment process.⁶ An examination of the physical therapy literature revealed only one article that addressed multiple clinic-based research topics (including recruitment),⁷ one review article dedicated to participant recruitment concerns,⁸ and one article that described recruitment strategies for elderly people in an RCT for self-management of back pain.⁹ Even the existing recruitment literature from other medical fields (eg, public health, drug trials) fails to demonstrate a

uniform method for recording recruitment data, making evaluations or comparisons between trials difficult.⁸ For the purposes of this article, the primary focus will be recruitment and retention because these concepts relate to rehabilitation-based clinical trials.

The recruitment process is composed of several specific steps, including: (1) identifying eligible patient populations, (2) adequately explaining the study, (3) recruiting an adequate, representative sample, (4) obtaining true informed consent, (5) maintaining ethical standards,

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This study was supported by National Institute of Child Health and Human Development (NICHD) and National Institute of Neurological Disorders and Stroke (NINDS) grant RO1 HD 37606 (principal investigator: Dr Wolf). Participating EXCITE study sites were: Emory University, University of Alabama at Birmingham, University of Southern California, University of North Carolina at Chapel Hill and Wake Forest University (both collaborating as one site), Ohio State University, and the University of Florida, Gainesville. The Data Management Center was located at Washington University School of Medicine, St Louis, Mo.

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(6) retaining participants until study completion, and (7) minimizing cost-benefit ratio.⁴ Although Walson⁴ included retention as part of the recruitment process, for this article we discuss recruitment and retention separately, with recruitment including activities conducted before a participant is enrolled and retention including activities used after enrollment that are directed at keeping participants engaged. Each of the steps involved in recruitment and retention within rehabilitation clinical trials have their own unique concerns and obstacles. For example, identifying patient demographics, diagnostic categories, and length of stay in institutions available to the researcher for recruitment is essential and required by most granting agencies. Populations that may exhibit cognitive or language deficits as a result of the disablement process pose particular challenges to recruitment. For example, among patients with stroke, screening for subtle cognitive or language deficits is necessary to ensure the participant's ability to understand and fully consent to the study. Retaining participants who have multiple medical conditions in addition to the primary diagnosis of a stroke offers an enormous challenge.

Without a recruitment plan, critical problems that may jeopardize the integrity of the study can arise (eg, selection bias, disproportionate enrollment, informed consent oversights). For multi-site clinical trials, a plan must not only be present but also uniform among the sites. Rehabilitation scientists are implored to learn about recruitment from clinical trial methodology literature, treating this aspect of any clinical study as a fundamental feature of the research process and evidence-based practice.

To illustrate these unique obstacles and strategies of participant accrual and retention inherent in rehabilitation clinical trials, the recruitment process of the Extremity Constraint-Induced Therapy Evaluation (EXCITE) trial will be critically examined. At the time of initiation, the EXCITE trial was the first National Institutes of Health–funded multi-site RCT evaluation of an upper-extremity (UE) stroke rehabilitation intervention for patients 3 to 9 months poststroke in the United States. A pioneering effort in rehabilitation research, this 5-year, \$7.5 million study was funded by the National Center for Medical Rehabilitation Research within the National Institute of Child Health and Human Development and the National Institute of Neurological Diseases and Stroke. The primary purpose of the EXCITE trial was to evaluate the effects of constraint-induced (CI) therapy in patients with subacute and chronic stroke. Six sites across the United States collaborated to recruit a total of 222 (out of a goal of 240) individuals with subacute stroke and moderate to mild UE hemiparesis.

Using the EXCITE trial as a rehabilitation research model objectives of the article are: (1) to illustrate the importance of recruitment and retention in planning a clinical study, (2) to discuss obstacles to and strategies for participant recruitment and retention, (3) to review ethical aspects of recruitment and retention, and (4) to explore a method for measuring recruitment efforts. To address these objectives, the EXCITE study design, specific recruitment and retention strategies, and the results of recruitment efforts (including obstacles encountered) are presented. From these experiences, critical aspects of recruitment and retention, including project design, cultural concerns, privacy regulations, communication strategies, and ethical considerations, are then explored. Ultimately, we intend to increase awareness of the multiple facets inherent in recruitment and retention as necessary precursors for both successful clinical trials and propagation of evidence-based practice in physical therapy.

Methods

Study Design

The 6 clinical sites participating in the EXCITE study were Emory University (EU), the University of Alabama at Birmingham (UAB), the University of Southern California (USC), the University of North Carolina at Chapel Hill (UNC) and Wake Forest University (WFU) (both North Carolina universities collaborated as one site), the University of Florida at Gainesville (UF), and Ohio State University (OSU). The Data Management Center (DMC) was located at Washington University School of Medicine, St Louis, Mo. All of the EXCITE study research sites were located in or near university-based medical centers; 3 of the research laboratories were located within inpatient rehabilitation centers, and 6 research laboratories were associated closely with academic institutions having physical therapy programs. Five of the 7 participating universities were located in large metropolitan areas.

Each site had a recruitment goal of 40 participants who were 3 to 9 months poststroke. These participants had sustained a first-time clinical ischemic or hemorrhagic cerebrovascular accident and typically had completed standard poststroke rehabilitation. At randomization, each individual was categorized as either higher or lower functioning according to motor criteria described by Wolf and Binder-Macleod¹⁰ and Taub et al.¹¹ Participants who were higher functioning had to demonstrate active wrist extension of at least 20 degrees and 10 degrees of active extension of the metacarpophalangeal joints and each interphalangeal joint of all digits. The participants who were lower functioning needed active wrist extension of no less than 10 degrees and 10 degrees of abduction and extension of the thumb and at least 2

additional digits. In addition to the motor criteria, participants had to demonstrate adequate balance and safety as a precursor to restraint use during training. Specific balance criteria included: the ability to transfer to and from the toilet independently and safely and the ability to stand from a sitting position and maintain standing balance independently for at least 2 minutes with or without their own UE support. To avoid any substantial structural or biomechanical restrictions to active range of motion, passive range of motion was required to be at least 90 degrees of shoulder flexion and abduction, 45 degrees of shoulder external rotation, no less than -30 degrees of elbow extension, 45 degrees of forearm supination (from neutral), 45 degrees of forearm pronation (from neutral), wrist extension to neutral, and finger extension (all digits) such that no metacarpophalangeal joint had a contracture of greater than a 30 degrees.

To avoid the confounding effects of cognitive and medical conditions, potential participants were excluded if the medical or physical screening examination revealed a score of less than 24 on the Folstein Mini-Mental State Exam¹² (MMSE), a physician determined that major medical problems existed that would interfere with participation, they had a previous cerebrovascular accident with a clinical residual, they had excessive pain in any joint or more affected extremity that would limit participation, they had aphasia to such a degree that questions could not reliably answered, they were less than 18 years of age (adult status for informed consent), and they had insufficient endurance and stamina to participate in the intensive protocol. An upper limit of performance for participation was designated as an average score of greater than 2.5 on the Motor Activity Log (MAL)¹³ Amount of Use scale at the time of the intake screen (a score of 2.5 indicates that the participant was using his or her arm more than half as much as before the stroke). To avoid confounding effects of other intervention studies, potential participants were excluded if they were participating in other pharmacological or physical intervention studies, including prior or pending participation in any form of CI therapy, or had received injections of antispasticity drugs (eg, botulinum toxin) into the UE musculature within the past 3 months. For practical reasons and because of the 2-year follow-up with frequent assessments (every 4 months), any eligible participants who planned to move from their local areas within 2 years also were excluded. An overall sample size target of 240 participants was selected based on a power analysis of the most demanding hypothesis that requires a test of the difference in the treatment effect between the higher- and lower-functioning groups.¹⁴

Upon enrollment, participants were randomly assigned to either an “immediate treatment” (intervention) group or a “delayed treatment” (control) group by the study’s Data Management Center using an adaptive treatment assignment procedure.¹⁴ This statistical procedure sequentially assigned each new participant to a particular treatment group, taking into account predetermined baseline covariates of the participant as well as previously assigned participants. Achieving a balance of important covariates between treatment groups was important to ensure that any observed treatment effect was from the treatment itself. The participants were not notified of their assignment to condition until after the first baseline evaluation. Project coordinators and trainers were aware of participant randomization, but study investigators and evaluators were blinded to condition. The immediate treatment group received 2 weeks of CI therapy, and the delayed treatment group received usual and customary care. One year after intake, the delayed treatment participants were crossed over to receive CI therapy. Both groups received follow-up evaluations at 4, 8, 16, 20 and 24 months after baseline. Consequently, full participation required a daily attendance for 6 hours of training on weekdays for 2 weeks and a total of 9 testing visits over an approximate 2-year period.

In an attempt to systematically explore recruitment and retention challenges faced and resolved at each of the EXCITE sites, we used a *post hoc* survey with key project personnel. The survey contained both closed- and open-ended questions and was sent to project coordinators at each study site after the project was completed. Information revealed by the surveys is included in the “Results” and “Discussion” sections of this article.

Recruitment Strategies

To assist with the recruitment goals, the Study Steering Committee (principal investigators from all sites) identified a number of tools as part of the recruitment plan. A study Web site (www.excite.wustl.edu) was developed containing information about the trial goals, interventions, inclusion criteria, and contact information for each site. A “frequently asked questions” sheet was written for potential participants and those who may have questions about their continued role in the trial. A uniform study brochure was created and distributed within the community of people with stroke and for media avenues at each site locale. A variety of token gifts with the study logo were produced for use at each site, including T-shirts, pens, refrigerator magnets, coffee mugs, and post-it pads.

Although recruitment responsibilities varied according to each site’s personnel distribution, primarily project coordinators made the initial contacts with patients and performed the screens. At the beginning of the EXCITE

study, personnel from all sites gathered for 9 days of intensive training of the full study protocol, and during that time the entire staff worked together planning recruitment strategies. Through monthly coordinator conference-call meetings, additional strategies and problem-solving techniques were shared as various obstacles arose across time.

Project coordinators reported that personnel at each site conducted in-service meetings at local rehabilitation clinics to enlist other health care providers (eg, physical therapists, occupational therapists, physiatrists) to identify and refer potential clients. During the presentations, research personnel distributed packets of information containing research articles concerning CI therapy, detailed descriptions of inclusion and exclusion criteria, sheets of frequently asked questions, and contact information. Local support groups for people with stroke were identified, and presentations were given throughout each site's catchment area. Recruitment of underrepresented groups was not specifically emphasized because each site targeted a variety of facilities that collectively were regarded as representative of that site's population demographics.

Once potential participants were identified, a screening visit was scheduled for a physical evaluation to determine eligibility. These visits were offered at the training site, allowing participants to see where training would occur, meet project staff, and in some cases, meet other study participants who were training. Recruiting staff also traveled to clinical sites or to potential participants' homes to conduct screening. This personal visit allowed clinicians who assisted with recruitment to understand the inclusion criteria more clearly and facilitated recruitment of potential subjects who might be deterred by transportation and parking challenges.

Communication among members of the EXCITE team, both within individual sites and between sites, was critical to the recruitment effort. Bar graphs indicating the progress of recruitment at each site were posted on the study Web site. The display promoted "friendly" competition among the research sites. Additionally, the EXCITE study primary principal investigator (SLW) conducted regular conference calls with all site principal investigators, at which time recruitment progress was discussed. Similarly, project coordinators at all sites conducted monthly conference calls and discussed logistical issues, including recruitment efforts. When recruitment benchmarks at specific sites were not met, the study principal investigator (SLW) held meetings with the entire research site team to problem-solve and motivate personnel to try more effective recruitment strategies.

Retention Strategies

Several sites issued an EXCITE notebook to participants, which was personalized with a monthly calendar of all visits across the 24 month period of enrollment, a copy of their signed informed consent statement, contact information for study staff to address emerging questions, pockets to hold training documentation (home exercise program and home diary), and a letter of gratitude. An educational newsletter, *Stroke Savvy*, was produced early in the trial and was sent to all participants on a monthly basis. The purposes of the newsletter were to maintain frequent contact with enrollees throughout the extensive follow-up testing period and to offer general informational tips on topics such as stroke education, nutrition, and stress reduction. Principal investigators encouraged their site personnel to make monthly telephone calls to each participant to encourage adherence to visits and to monitor adverse events. Additional suggestions for retention included the regular distribution of birthday and holiday cards to build a personal relationship and maintain communication.

Results

Recruitment

The Figure presents a standard consort flow diagram of the entire recruitment, screening, randomization, and retention effort from January 2001 through January 2003. Although the process took 13 months longer than expected (the proposed recruitment goal challenged each site to enroll an average of 3–4 participants each month from January to December 2001), recruitment was ultimately successful, achieving 93% (222 participants) of the targeted goal (240 participants). Originally, 229 patients were enrolled; however, 7 participants withdrew after enrollment but prior to randomization.

Table 1 shows the recruitment process by site, listing the number of facilities contacted, total participant contacts, total screens, and total participants enrolled. A "participant contact" was operationally defined as a basic telephone screen with a patient or referring therapist to determine a patient's eligibility or a location screen occurring within a therapy setting with a therapist and a list of potential participants. The number of participants enrolled as a percentage of actual contacts ("enrollment ratio") varied across sites, ranging from 3.5% (EU) to 22% (USC), with an overall average of 6.1%. This variance among sites was due to differences in recruiting methods and recording of recruitment data. For example, because the EU site was located within the Emory Center for Rehabilitation Medicine, all stroke admissions to the center were screened for possible inclusion, substantially increasing that site's contacts. Not all sites were located within such a convenient geographical proximity to a rehabilitation center.

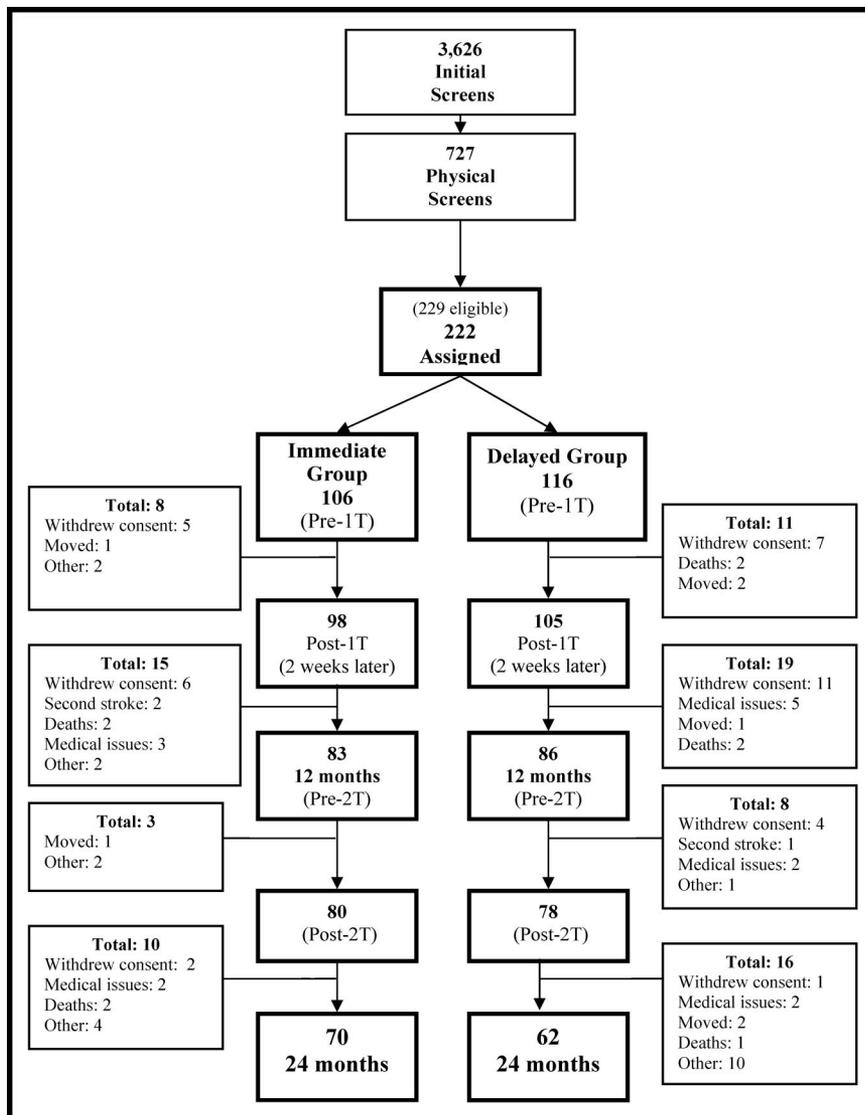


Figure. Flow diagram of Extremity Constraint-Induced Therapy Evaluation (EXCITE) trial recruitment. Pre-1T=baseline assessment, post-1T=2 weeks after baseline assessment, pre-2T=12-month assessment, post-2T=2 weeks after 12-month assessment.

Table 2 details the reasons for participant ineligibility across all of the sites. Often more than one reason could exclude a participant, but the most definitive reason was used in the calculations. The primary reasons for exclusion from the EXCITE study were: too much UE function (participants were using the more-affected arm for most of their daily activities almost as much as before their stroke, as measured by the amount portion of the MAL¹³), too limited more-affected arm function (participants did not exhibit the minimum movement criteria), and too far postinjury (stroke onset was greater than 9 months). Trends for ineligibility were generally similar across sites, but discrepancies probably arose due to differing recruitment and tracking methods.

Several factors made recruitment for this study particularly challenging. The subacute stage of recovery for eligibility was initially 3 to 6 months poststroke; however, this time frame was too narrow for all the pre-enrollment activities required for randomization and was too early for some participants to meet the minimum motor criteria. Consequently, this criterion was lengthened to 3 to 9 months, with 11 participants actually enrolled between the 9- to 12-month time period. The ischemic stroke criterion was expanded to include people with hemorrhagic stroke to increase the pool of potential participants.

Transportation emerged as an important factor and the most critical (non-medically related) recruitment concern, as participants were required to travel to and from the research site on a frequent basis. On-site attendance for 10 consecutive weekdays of training necessitated caregiver support for daily participant drop-off and pick-up or sufficient financial resources to afford local hotel accommodations. Five of the 7 participating universities also were located in large metropolitan areas where traffic congestion posed challenges for all motorists, especially older adults and people with disabilities.

Individuals with lower income or those who lived alone were less likely to resolve these challenges. Consequently, few individuals living more than 80 km (50 miles) from a research site were enrolled. In anticipation of transportation concerns, the study budget included limited funding to cover travel costs for research participants. Typically, participants were reimbursed at each visit for transportation, parking, and meals and beverages (when appropriate). Each site determined their own reimbursement scale during initial budget planning, based on area demographics and individual patient needs. These fees ranged from \$20 per visit (EU in the Atlanta area) to \$50 per visit (USC in the Los Angeles area). Flexibility in reimbursement rates helped each site tailor fees to address their specific transportation issues. For example, EU reimbursed all participants \$20 for gas and travel costs per visit, and WFU reimbursed for actual mileage. The UAB and UNC were able to offer transportation to participants who lived nearby the facility, as needed.

Table 1.Extremity Constraint-Induced Therapy Evaluation (EXCITE) Trial Participant Recruitment Efforts From January 2001 to January 2003 by Site^a

Site ^b	Total Facilities Contacted	Total Participant Contacts	Physical Screens	Participants Randomly Assigned to Groups	Participants at Baseline Visit	Sex	
						Male	Female
EU	21	1,138	182	41	40	29	11
UAB	81	469	123	41	39	27	12
UFL	40	498	170	42	39	23	16
OSU	18	619	55	30	29	18	11
USC	30	286	63	42	42	27	15
UNC/WFU	57	616	134	33	33	18	15
Total	247	3,626	727	229	222	142	80

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^b EU=Emory University, UAB=University of Alabama at Birmingham, UFL=University of Florida, OSU=Ohio State University, USC=University of Southern California, UNC=University of North Carolina, WFU=Wake Forest University. UNC and WFU collaborated as one site.

Table 2.Summary of Extremity Constraint-Induced Therapy Evaluation (EXCITE) Trial Participant Ineligibility Reasons by Site^a

Site ^b	Ineligibility Reasons ^c												Total Contacts	No. of Participants
	TH	TL	TF	AP	SS	NI	TP	HS	MS	MP	SI	OP		
EU	246	155	199	24	113	37	100	5	44	31	24	119	1,138	40
UAB	100	53	27	5	34	26	16	NA	NA	NA	NA	167	469	39
UFL	37	44	257	1	30	20	13	1	15	11	0	27	498	39
OSU	64	76	107	29	54	70	30	18	4	97	17	22	619	29
USC	10	34	129	3	10	16	1	0	3	11	5	22	286	42
UNC	56	36	103	3	84	64	52	6	21	39	2	35	520	18
WFU	20	10	22	6	2	2	6	NA	2	5	NA	6	96	15
Total	533	408	844	71	327	235	218	30	89	194	48	398	3,626	222

^a Reprinted by permission of Sage Publications Inc from: Winstein CJ, Miller JP, Blanton S, et al. Methods for a multisite randomized trial to investigate the effect of constraint-induced movement therapy in improving upper extremity function among adults recovering from a cerebrovascular stroke. *Neurorehabil Neural Repair*. 2003;17:137-152.

^b EU=Emory University, UAB=University of Alabama at Birmingham, UFL=University of Florida, OSU=Ohio State University, USC=University of Southern California, UNC=University of North Carolina, WFU=Wake Forest University. UNC and WFU collaborated as one site.

^c Ineligibility reason codes: TH=too high on Motor Activity Log Amount of Use scale score, TL=too low on minimum motor criteria, TF=too far poststroke, AP=aphasia, SS=second/multiple strokes, NI=not interested, TP=transportation problems/out-of-state inquiries, HS=hemorrhagic stroke (prior to changing criteria for inclusion), MS=mental status, MP=mental problems, SI=spasticity issues, OP=other problems (eg, patient did not show for screen or did not return calls, not true cardiovascular accident, family issues).

Project coordinators at UNC also collaborated with the General Clinical Research Center at University of North Carolina Hospital to house participants from more distant rural areas during the training phase. Despite these initiatives, the largest obstacles to recruitment were inadequate financial resources to reimburse participants (for time, effort, and inconvenience), caregiver (and participant) time away from work, and actual travel costs. In addition, sufficient time for project coordinators to attend to all necessary recruitment activities was not available.

Although the primary patient referral sources were not systematically tracked in the EXCITE study, a review of 2 sites indicates that participants primarily came from health care professional referrals and few came from self-referrals. For example, at the EU site, only 15% of

the 40 participants were self-referrals. All sites stated that the most effective recruitment strategies were presentations at physical therapy and occupational therapy clinics with regular and frequent follow-up telephone calls. Identification of a specified contact at these clinical sites was an important component to maintaining effective and consistent communication. Presentations for stroke support groups were considered useful because group members frequently "spread the word" to other people with stroke who might meet the inclusion criteria. Although most sites believed these presentations were somewhat effective, one site (UFL) conducted these talks frequently and described this strategy as very effective. Media coverage (newspaper, television, and radio) was sporadic and identified as only somewhat effective. In addition to the EXCITE Web site, 3 sites also had their own Web site. Surprisingly, this strategy was reported as

Table 3.

Characteristics of Extremity Constraint-Induced Therapy Evaluation (EXCITE) Trial Participants at Baseline and 24-Month Follow-up

	24-Month Completers (n=132)	Dropout Cases (n=90)	Total Sample (n=222)	Statistical Test of Difference
Age (y) at enrollment, $\bar{X}\pm SD$	62.0±12.1	62.4±14.4	62.2±13.0	$t=-0.18, P=.8587$
Years of education, $\bar{X}\pm SD$	14.5±3.3	13.8±3.0	14.2±3.2	$t=1.41, P=.1609$
Sex				$\chi^2=0.03, P=.8716$
Male	85 (64%)	57 (63%)	142 (64%)	
Female	47 (36%)	33 (37%)	80 (36%)	
Race				$\chi^2=0.01, P=.9159$
White	93 (70%)	64 (71%)	157 (71%)	
Nonwhite	39 (30%)	26 (29%)	65 (29%)	
Ethnicity				$\chi^2=0.39, P=.5330$
Hispanic	5 (4%)	5 (6%)	10 (5%)	
Non-Hispanic	127 (96%)	85 (94%)	212 (95%)	
Affected side				$\chi^2=0.20, P=.6511$
Left	73 (55%)	47 (52%)	120 (54%)	
Right	59 (45%)	43 (48%)	102 (46%)	
Dominant side				$\chi^2=0.02, P=.8816$
Left	11 (8%)	7 (8%)	18 (8%)	
Right	121 (92%)	83 (92%)	204 (92%)	
Stroke concordance				$\chi^2=0.03, P=.8709$
Discordant	66 (50%)	46 (51%)	112 (50%)	
Concordant	66 (50%)	44 (49%)	110 (50%)	
Stroke type				$\chi^2=0.19, P=.6593$
Ischemic	117 (89%)	78 (87%)	195 (88%)	
Hemorrhagic	15 (11%)	12 (13%)	27 (12%)	
Functional level				$\chi^2=2.62, P=.1058$
Higher	110 (83%)	67 (74%)	177 (80%)	
Lower	22 (17%)	23 (26%)	45 (20%)	
EXCITE trial condition				$\chi^2=3.64, P=.0563$
Immediate treatment	70 (53%)	36 (40%)	106 (48%)	
Delayed treatment	62 (47%)	54 (60%)	116 (52%)	
No. of comorbidities, $\bar{X}\pm SD$	3.0±1.4	2.5±1.4	2.8±1.4	$t=2.24, P=.0260$

somewhat to not very effective. Informational mailings to support groups, physical therapist and occupational therapist clinicians, and physicians occurred at varying degrees at sites, but none described these methods as very effective.

Retention

The Figure lists reasons for withdrawal at each of the following primary visits: pre-1T (baseline assessment), post-1T (after 2-week period of treatment for the immediate treatment group), pre-2T (12-month assessment), post-2T (after 2-week period of treatment for the delayed treatment group), and the final 24-month follow-up assessment. A total of 169 participants returned for the 12-month assessment, yielding a retention rate of 76%.

At 24 months, 132 participants returned, yielding a retention rate of 59% for the entire length of the study.

Table 3 describes participant characteristics at baseline, both overall and for the retained and withdrawn groups. To compare groups for continuous variables, *t* tests were used. To compare proportions for discrete variables, chi-square tests were used. Both groups were comparable. There were no demographic or baseline characteristic variables or condition-specific (immediate treatment group versus delayed treatment group) predictors for study withdrawal. Although the difference between withdrawals for the immediate treatment group and delayed treatment group approaches statistical significance (with more delayed treatment group participants dropping out), only the number of comorbidities differed significantly between groups ($t=2.24, P=.0260$). Interestingly, however, the immediate treatment group, with a better retention rate, reported more comorbidities than the delayed treatment group reported.

Project coordinators reported that the retention strategies of sending birthday and holiday cards and the *Stroke Savvy* newsletter proved to be too labor intensive after the first year of the study and were eventually dropped from the retention procedures. The monthly telephone calls were important to maintain communication and valuable to build personal relationships with participants. Unfortunately, the time

demand involved in calling so many individuals at each site caused this strategy to be inconsistently applied at regular intervals.

Discussion

Although we achieved 93% of the recruitment goal, the original estimation of the allotted recruitment time period had to be doubled. Despite extensive preliminary planning by the investigators to evaluate each site's eligible patient pool, unforeseen recruitment and retention obstacles did occur and valuable lessons can be learned by reviewing the literature on research recruitment and the EXCITE project experience. Factors influencing recruitment and retention included project design, privacy regulations, reaching under-represented

groups, and communication within and outside of the research team. Additionally, the EXCITE project experience unveiled ethical challenges that are uniquely important to rehabilitation research and measurement issues.

Recruitment

Lasagna's law on planning clinical trials suggests that scientists routinely overestimate the number of participants available for enrollment in their studies.¹⁵ Viewed realistically, the accrual of a sufficient number of research participants is a slow and laborious process. A review of recruitment data from 15 stroke prevention studies revealed that the average enrollment rate at research sites was only 0.78 participant each month.¹⁶ Although comparisons with other rehabilitation trials are difficult due to the scarcity of recruitment information in the limited number of rehabilitation RCT publications, the overall enrollment ratio (the number of participants enrolled as a percentage of actual contacts) of 6.1% for the EXCITE trial is somewhat lower than in the few studies that did report this recruitment statistic. A similar ratio of 8.8% was documented by Werner and Kessler,¹⁷ who sent 552 letters to prospective participants with subacute stroke, resulting in recruitment of 49 eligible participants. Studenski and colleagues¹⁸ screened 582 patients in a stroke registry for an RCT evaluating a therapeutic exercise program in patients with subacute stroke. Of those individuals, 100 were enrolled, revealing a 17% rate. In a study examining early and repetitive sensorimotor stimulation in people with acute stroke,¹⁹ 1,000 patients were screened to randomly assign 100 participants to study groups. These studies are clear representations of the substantial effort essential for adequate participant accrual in stroke rehabilitation RCTs, yet little is known about why recruitment rates and ratios vary among trials. Potential reasons for these differences are presented below.

Project design. Stringent inclusion and exclusion criteria challenge the number of participants who are eligible for randomization. The design of the study will dramatically influence recruitment efforts. Prolonged and arduous data collection procedures challenge both enrollment and retention. The EXCITE trial involved an intensive intervention (60 hours), multiple evaluations (9), and a prolonged follow-up period (2 years), and any of these factors may have affected individuals' willingness to participate. However, based on explanations for ineligibility (Tab. 2), "not interested" ranked as the sixth reason, whereas "too far poststroke" and not meeting the minimum movement criteria were the primary causes of exclusion (accounting for 50% of the excluded participants).

In light of recruitment demands, investigators are encouraged to limit selection criteria to those that are

scientifically meaningful and necessary yet still maximize the pool of potential research candidates.⁴ Once selection criteria are identified, these requirements should be pilot tested to investigate less obvious selection obstacles before the final inclusion and exclusion criteria are set. Screening for selection criteria that are therapeutically based, such as the minimum movement criteria in the EXCITE trial, typically involves a more complicated process than screening for clinical trials in medicine. Typically, pharmaceutical or other medical RCTs may utilize a simple chart review to identify appropriate patients. In comparison, the lack of a nationally standardized and accepted set of outcome measures in stroke rehabilitation requires individualized physical screens of each potential participant. Although most rehabilitation centers use the Functional Independence Measure,²⁰ this tool is very generalized and does not capture specific UE or lower-extremity movement limitations. Additional time and resources are consequently required because physical screens often take a minimum of 30 to 45 minutes. Even when participants can be quickly identified as ineligible, the screening clinician will still compassionately and respectfully spend time with the individual. Coordinators who are well versed in the selection criteria, who have recruitment experience, and who possess a strong clinical background as physical therapists or occupational therapists (for therapeutically based protocols) are invaluable in this process.

Recruitment rates in EXCITE trial improved with time as coordinators at each site gained experience in the process. Adequate time allocation for coordinator positions on a clinical trial is a critical component of budgeting for recruitment. Although percentage distributions varied across sites in the EXCITE trial, nearly every location provided either a full-time individual coordinator or a combination of staff (research assistant, therapist, and clerical staff) that equaled at least 100% time of a full-time recruitment/coordinator staff position. Based on experience from this trial, a minimum of one full-time position for recruitment/coordination with the addition of 25% to 50% allocated for clerical support is recommended. Professionals involved in training and evaluations in the study may assist in distribution of these responsibilities.

Participant tolerance for treatment and testing should be considered in the project design phase. Particular attention should be paid to transportation to and from the research site and other inconveniences for participants and their families. Duncan et al²¹ noted in their RCT that, upon evaluating a home-based exercise program after stroke, only 3 of the 20 participants could have participated if the investigators had not provided transportation for assessments. Incentives to compensate for the burden imposed by travel and time should be

budgeted. Unfortunately, rehabilitation-based clinical trials tend to be funded by government agencies with limited fiscal resources as compared with medical trials such as those supported by pharmaceutical companies. Consequently, less financial assistance is available for participant reimbursement in therapeutically based RCTs.

In many RCTs containing a placebo arm, an option for receiving the intervention after control data are collected is required and can reduce concerns about the randomization process. In the EXCITE trial, project coordinators noted that the ability to offer CI therapy to both groups aided in recruitment. Although the 1-year wait for the delayed treatment group caused a few individuals to withdraw, there were relatively equal numbers of participants in both groups who reached the 12-month evaluation (78% of the immediate treatment group and 74% of the delayed treatment group).

Patient privacy. While protecting privacy rights of patients and study participants is not a new ethical concept for investigators, recent efforts to control access to medical records have created multiple obstacles to participant recruitment.^{22,23} The Health Information Portability and Accessibility Act (HIPAA) legislation of 1996 was established to keep protected health information private and secure. The HIPAA regulations went into effect in April 2003 with the enactment of the Privacy Rule. Investigators can no longer approach a health care setting, obtain a list of potential participants for their study, and contact the individuals directly for recruitment purposes. Ness²⁴ stated that these regulations have had a negative effect on the pace of recruitment and have substantially slowed down the entire research process.

Although HIPAA was not enacted during the recruitment phase of the EXCITE trial, awareness of existing and impending privacy regulations was one of the explanations for limited recruitment from referral site clinicians. The EXCITE trial personnel provided detailed information to clinicians along with an ample supply of brochures that placed responsibility on patients or their families to contact the research sites, thus removing the clinician from a risk of releasing private information.

Recruiting under-represented groups. Demographic information regarding race and ethnicity is an important aspect of RCT reports and is required by the government funding agencies, such as the National Institutes of Health. The majority of the participants in the EXCITE trial were non-Hispanic and white, but these ratios were representative of the collective population pools from which they were recruited. However, substantial evidence exists that some population subgroups are typi-

cally under-represented in clinical research.^{22,25,26} Slower accrual rates have been reported for minority populations, leading to the need for longer recruitment periods. Groups vulnerable to poor recruitment include inner-city residents, ethnic and racial minorities, rural citizens, people with disabilities, people with low incomes, older adults, and people with traumatic memories of health-related events.^{26,27} These subgroups are frequently the very targets of rehabilitation research efforts. Racially influenced distrust has been proposed as one reason for reduced sampling among people of color.²⁷ Other researchers disagree with the “distrust” explanation and cite reduced access to health care research as responsible for reduced participant from minority groups.²⁸ Instead, they believe that investigators frequently bypass efforts to tailor their recruitment advertisements to appeal to their target audience in a culturally competent fashion.

Regardless of the underlying causes, the research recruitment literature strongly advocates the use of culturally and racially competent recruitment efforts to ensure a more heterogeneous participant pool. Direct strategies to reach potential participants through advertising in newspapers, radio, and television have yielded poor results for some groups, especially minority populations.²⁶ Other communication channels for under-represented populations should be considered. For example, in the African-American community, better success may be achieved by posting flyers, illustrated with African Americans, in physicians’ offices, medical clinics, churches, beauty salons, and barbershops. Only a few of the sites reported any specific attempts to reach minority populations (ie, conducted presentations at African-American churches). As such, we are uncertain about why the EXCITE trial was successful in sufficiently recruiting minority participants. One reason may be related to the fact that 4 of the 7 participating universities are located in cities with a large population of African Americans. Another site was located in a city with a large Asian and Hispanic population. Another possible explanation could be that many other rehabilitation research trials were taking place in other laboratories at each of the EXCITE trial sites. There may have been a “carryover” effect from recruitment efforts of other trials, making the EXCITE trial more visible to minority populations.

Communication. In addition to directly contacting potential research candidates, investigators frequently identify potential participants through other health care professionals in clinical settings. Lack of a clear understanding of the project’s purpose and relevant inclusion criteria may interfere with the effectiveness of these recruitment efforts. The information distributed to clinicians in the EXCITE trial was extensive, and research

personnel feared that it was occasionally overwhelming to recipients. As mentioned previously, research personnel were required to increase contact with local clinicians and strive toward a delicate balance between “reminding” and “pestering.” While juggling multiple responsibilities, clinicians are likely to forget to identify potential research participants.⁷ In light of current productivity burdens in the clinical setting, this is certainly understandable. As such, investigators need to develop clear and concise recruitment materials to educate clinicians about the recruitment efforts and provide frequent but gentle reminders to seek candidates for the study. Consistent with suggestions from Fitzgerald and Delitto,⁷ project coordinators for EXCITE trial sites advocated the practice of identifying one contact person at each clinic approached and maintaining ongoing contact. The clinic contacts were individuals who were accessible and who appeared to be enthusiastic about the project. Although this strategy appeared to be very effective, it also was time consuming. Investigators should consider these tasks in workload assignments and budget planning. Methods of recognition and appreciation for clinical site contributions also should be incorporated in this planning, as the success of steady recruitment hinges upon these relationships.

Communication among members of the research team is likewise critical. As with the EXCITE trial, recruitment benchmarks should be set and reviewed on a frequent basis. Close attention should be directed toward failure to meet these goals, including brainstorming and solution-oriented discussions for resolving obstacles identified during regularly scheduled meetings of research personnel and investigators.

Retention

Examining retention within a clinical trial is an integral part of evaluation of the study results. As part of data analysis, the characteristics of participants at baseline should be compared with those of participants who withdrew from the study to ensure valid results. In the EXCITE trial, the comparisons of both groups (Tab. 3) showed remarkably similar distributions across age, sex, race, ethnicity, side of stroke, hand dominance, and motor capabilities.

A total of 203 participants (91%) in both groups were retained initially after the 2-week training period in the EXCITE trial, with 76% and 59% retained for first and second years, respectively. This retention rate is slightly lower than data reported from a one-city trial in which Duncan et al²⁹ evaluated a 12-week therapeutic exercise program in patients with subacute stroke. These investigators experienced a successful retention rate of 92% of 100 enrolled participants immediately after training and 80% at the 6-month follow-up.¹⁸ Evaluating the effect of

repetitive sensorimotor retraining of the arm after chronic stroke, Feys and colleagues¹⁹ also had comparable retention rates of 72% of 100 enrolled participants at the 1-year follow-up and 62% at a 5-year follow-up. Similarly, in an acute stroke RCT examining UE interventions,³⁰ 69% of the participants completed the 9-month follow-up.

The relationship between study staff and participants cannot be overemphasized when examining retention strategies. The importance of staff characteristics, such as responsiveness and friendliness, that create an atmosphere of trust and empathy is essential to foster motivation and retention.³¹ Project coordinators at the EXCITE trial sites consistently reported that this factor was very important in influencing retention. Dias and colleagues³¹ described 4 components of retention strategies: (1) communication, (2) support, (3) symptom management, and (4) data collector supervision. Personnel in this pediatric study were trained to respond promptly to any study-related concerns, thus creating an environment that encouraged families to openly communicate any needs, questions, or problems. Clinic coordinators, who were the primary points of contacts for the families, “further strengthened the positive study experience of families by maintaining ongoing contact with them between visits and developing close relationships with them.”³¹ (p444) In this manner, retention strategies could be tailored to fit individual families’ needs and lifestyles. This perspective has been shared in other studies.^{32,33} However, in an effort not to jeopardize the validity of the clinical trial, any retention strategy needs to be evaluated for neutrality of effect on the study outcomes.

Ethical Considerations of Recruitment

Consent. The ethics of informed consent are fundamental to research protocols. Institutional review boards require that all staff involved in human subject research receive ethics training and successfully complete a competency examination before any work can be initiated with participants. In order to consent for research participation, 3 conditions must be met: (1) participant capacity (the participant’s understanding of the study, including risks and benefits), (2) voluntariness (freedom from undue coercion), and (3) disclosure (the participant is provided with all information necessary to make a truly informed decision).³⁴

For the EXCITE trial, consideration of these conditions existed at each research site, and the mode of assessing investigator appreciation of informed consent criteria was institutionally specific. This oversight for EXCITE trial personnel was particularly relevant because the decision-making capacity of participants with neurolog-

ical conditions, including stroke, can be complex to assess, especially when deficits in cognitive reasoning ability are not readily apparent. Language capabilities and the presence of aphasia should be evaluated by the study personnel prior to obtaining final consent. The researcher must be not only vigilant but also willing to explore any “red flags” that may indicate that the participant lacks sufficient decision-making capacity. True voluntariness on the part of the patient occurs only when there is no undue coercion (whether deliberate or unintended). The EXCITE trial inclusion criteria required a score of ≥ 24 on the Folstein MMSE.¹² This brief cognitive screen was a valuable tool for the consent process as well as ensuring reliability in data collection. Patient families were included when possible during the process of obtaining consent from participants so that adequate understanding of the study protocol was ensured and participant retention was promoted. Within the rehabilitation setting, the bond that develops between patients and their health care providers (such as physicians, nurses, and therapists) can be exceptionally strong and powerful.³⁵ Consequently, patients may be more likely to agree to participate in a research project out of a desire to please their health care team. Investigators should be cognizant of these factors as they discuss participation options with their patients to ensure that appropriate consent is obtained. Importantly, true consent is considered an ongoing process, not simply the review and signature of a form. Although a participant’s agreement to continue in a study is often implied by the adherence to study visits and protocol, consent should still be confirmed *and documented* as part of an ongoing process of interaction.

Therapeutic misconception. A deeper exploration of true informed consent involves the distinct differences that exist between the basic ethical requirements of performing research and providing treatment to patients. The principle of “personal care” describes the clinician’s allegiance to a patient’s well-being.³⁶ Although rehabilitation researchers are most often clinicians evaluating a treatment, the role of the investigator has different and competing obligations. Investigators must balance the need for valid data and accurate interpretation of results with protection of the patient’s best interests. Research is designed to generate data that may lead to improved overall patient care, not with the aim of providing the best care for individual participants in the study. Consequently, a mismatch of study intervention to specific patient needs may occur. The concept of “therapeutic misconception” occurs when the research participant fails to grasp the distinction between the imperatives of clinical research and ordinary treatment, thus inaccurately attributing the primacy of therapeutic intent seen in clinical care to research procedures.³⁷ Therapeutic misconception does not

imply the simple failure of the participant to understand the nature or purpose of the research study. Instead, participants consent because of a belief that they will receive the same or better individually focused treatment than they would receive in a nonresearch clinical setting.³⁸ Due to the therapeutic nature of rehabilitation research, therapeutic misconception is more likely in these types of clinical trials. Patients have a strong need to believe that the researcher’s primary interest is helping study participants.³⁹ Project coordinators and clinicians who may assist with recruitment must be keenly aware of this concern whenever discussing research protocols with their patients, being particularly sensitive when potential participants have exhausted resources for obtaining therapy with conventional funding.

Within the EXCITE trial experience, project coordinators were faced with the challenging role of distinguishing the research evaluation of CI therapy from a typical clinical treatment. Certainly, a frequent temptation during recruitment was to describe EXCITE trial participation as an additional opportunity for extra therapy. One may understand the frequent confusion of participants when they received a treatment administered by clinical therapists at an even more intense level (than typical treatment frequencies) and were subsequently followed on a regular basis for 2 years by study staff. The concept of therapeutic misconception is not one that has been discussed in the physical therapy literature, and the EXCITE trial recruitment experience keenly illustrates the need for heightened awareness of this construct.

As investigators review the obstacles and concerns with participant recruitment and retention, a simple summary of participant expectations may guide study design. Interaction among EXCITE trial staff and prospective research subjects was guided by the fact that study participants want: (1) a simple explanation of the study, (2) a clear understanding of what is expected of them, (3) a clear understanding of potential benefits and risks, (4) a list of who to contact if they have concerns or questions, (5) the knowledge that they can withdraw at any time, (6) the opportunity to know the results, and, most importantly, (7) a feeling of being appreciated and valued. Although the research and clinical treatment involve different goals and different participant expectations, the principle of respect-for-persons is the common ethic that bridges both worlds and that ultimately should drive all client interactions.

Prediction and Evaluation of Recruitment Activity—The Recruitment Index

Recruitment rate is typically the driving factor behind duration, cost, and feasibility of acute stroke trials.⁴⁰ Use of an evidenced-based approach to study recruitment is recommended to improve efficiency in the conduction

of RCTs.⁴¹ Direct comparison of recruitment activity within and between studies is limited due to a lack of unified measure of recruitment efficacy.^{8,42} Rojavin⁴² suggested the “Recruitment Index” (RI) as a measure of participant recruitment activity in clinical trials. This index represents the number of days required for an average site in a multicenter study to recruit one analyzable participant. The RI can be used to evaluate the efficacy of various recruitment strategies, to plan the duration of a recruitment period for a new study, or to project the number of participating sites required to supply a given number of participants within a certain time period.

The RI can be expressed as:

$$RI = (LPFV - FPFV) \times S / P$$

where LPFV is the date of last participant first visit, the end of study recruitment phase; FPFV is the date of first participant first visit, the beginning of recruitment phase; *S* is the number of participating sites; and *P* is the number of participants who successfully completed study participation.

Although the RI was not available for use in the planning stages of the EXCITE trial, applying preliminary estimates in the original grant application (12 months was estimated to recruit 240 participants across 6 sites with a 20% dropout rate), an example of the equation would be: $365 \times 6 / 192 = 11.4$. Retrospectively, the RIs from this study calculated from the actual recruitment time period of 730 days with a retention of 169 participants in year 1 and 132 participants in year 2 are: $730 \times 6 / 169 = 25.9$ for the first year and $730 \times 6 / 132 = 33.2$ for the entire 2-year study. Thus, 33.2 days were required to recruit one analyzable participant who successfully completed the entire 2-year study participation. Although this number is lower than examples quoted by Rojavin⁴² for clinical trials in patients with functional dyspepsia⁴³ (RIs ranging from 45.9 to 154.1), this length of time still represents a much larger index than would have been estimated previously and indicates the enormous burden of recruitment on study resources and personnel. Importantly, a study’s RI alone does not reflect the percentage of the original recruitment goal that was finally attained. Given the various recruitment strategies of the EXCITE trial, 730 days were needed to achieve a 93% successful recruitment. In light of current federal funding limits, reductions in rehabilitation stays and productivity demands on clinical therapists limiting research participation, one should anticipate rehabilitation trial RIs to increase.

This index value has not been used to date within the rehabilitation literature. A careful review of an investiga-

tor’s recruitment data would yield an RI that could be used in future calculations using similar study designs. Currently, in the clinical trial setting, there are no other validated predictive models that can be used to objectively estimate recruitment activity in clinical trials. Use of this index may provide important guidance as investigators of rehabilitation studies initiate project planning, especially in the budgeting and application process.

Conclusion

The success of a clinical trial is impossible without proper planning and implementation of recruitment. Visanji and Oldham^{8(p143)} stated, “Only when it is considered essential to routinely publish all recruitment information will investigators fully ensure that this is given the consideration it needs right from the initial plan.” Experience from the EXCITE trial offers valuable insights about this perspective that are relevant to the expanding area of RCTs in physical therapy. In planning rehabilitation studies, investigators should be aware of the ethical principles of informed consent and therapeutic misconception and the influence of these principles on interactions with participants. Comprehensive delineation of participant attributes and their accessibility will result in more successful and timely recruitment efforts. Future studies are encouraged to explore recruitment and retention strategies in a proactive and systematic manner, including the use of the RI tool, to ensure successful and ethical utilization of time and resources in the ongoing evolution of evidence-based practice.

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