

UCLA

UCLA Previously Published Works

Title

The Promise of mHealth

Permalink

<https://escholarship.org/uc/item/8g11k4sq>

Journal

Neurorehabilitation and Neural Repair, 25(9)

ISSN

0888-4390

Authors

Dobkin, Bruce H

Dorsch, Andrew

Publication Date

2011-11-01

DOI

10.1177/1545968311425908

Peer reviewed

The Promise of mHealth: Daily Activity Monitoring and Outcome Assessments by Wearable Sensors

Neurorehabilitation and
Neural Repair
25(9) 788–798
© The Author(s) 2011
Reprints and permission: <http://www.sagepub.com/journalsPermissions.nav>
DOI: 10.1177/1545968311425908
<http://nnr.sagepub.com>


Bruce H. Dobkin, MD¹, and Andrew Dorsch, MD¹

Abstract

Mobile health tools that enable clinicians and researchers to monitor the type, quantity, and quality of everyday activities of patients and trial participants have long been needed to improve daily care, design more clinically meaningful randomized trials of interventions, and establish cost-effective, evidence-based practices. Inexpensive, unobtrusive wireless sensors, including accelerometers, gyroscopes, and pressure-sensitive textiles, combined with Internet-based communications and machine-learning algorithms trained to recognize upper- and lower-extremity movements, have begun to fulfill this need. Continuous data from ankle triaxial accelerometers, for example, can be transmitted from the home and community via WiFi or a smartphone to a remote data analysis server. Reports can include the walking speed and duration of every bout of ambulation, spatiotemporal symmetries between the legs, and the type, duration, and energy used during exercise. For daily care, this readily accessible flow of real-world information allows clinicians to monitor the amount and quality of exercise for risk factor management and compliance in the practice of skills. Feedback may motivate better self-management as well as serve home-based rehabilitation efforts. Monitoring patients with chronic diseases and after hospitalization or the start of new medications for a decline in daily activity may help detect medical complications before rehospitalization becomes necessary. For clinical trials, repeated laboratory-quality assessments of key activities in the community, rather than by clinic testing, self-report, and ordinal scales, may reduce the cost and burden of travel, improve recruitment and retention, and capture more reliable, valid, and responsive ratio-scaled outcome measures that are not mere surrogates for changes in daily impairment, disability, and functioning.

Keywords

mobile health, wireless sensors, clinical trials, outcome assessments, compliance, stroke rehabilitation, Parkinson disease, multiple sclerosis, telemedicine

A white paper from the National Institute of Child Health and Human Development's Diagnostics and Therapeutics Vision Workshop¹ examined issues that are vital for progress in daily clinical care and clinical trials in neurological diseases and neurorehabilitation. One of the common themes was "the need for novel and accurate diagnostics, and for more precise, low-cost, and practical methods for tracking intervention outcomes . . . for an individual illness episode and for tracking disease in impaired populations across the lifespan." The white paper suggested, "New, low-cost, portable sensors may ultimately replace prevailing clinical instruments used for outcome assessments. Existing clinical assessment instruments lack reliability and sensitivity, and their relationship to mechanisms of recovery needs to be established. Advanced technology/sensors must be developed to establish better tracking of compliance and clinical outcomes, at several ICF [International

Classification of Functioning, Disability, and Health²] levels."

Referred to as mobile health (mHealth) or wireless health, the notion of portable internal and wearable sensors to monitor health is quickly becoming a reality. Sensors can transmit biochemical (glucose, chemistries) and physiological (electroencephalogram, blood pressure, heart rate, electrocardiogram, cardiac output, and weight) information from the home to remote sites. Wearable mHealth sensors are beginning to be able to measure the type, quantity, and

¹Geffen UCLA School of Medicine, Los Angeles, CA, USA

Corresponding Author:

Bruce H. Dobkin, MD, Department of Neurology, Geffen UCLA School of Medicine, Los Angeles, CA, USA
Email: BDobkin@mednet.ucla.edu

quality of daily activity, movement and balance (<http://www.wirelesshealth.ucla.edu>)³⁻⁸ This issue of *Neurorehabilitation and Neural Repair* includes an example of an accelerometry device that monitors people with Parkinson disease at home.⁹ Potential mHealth devices include (1) accelerometers to measure accelerations/decelerations, velocity, and displacement of the body segments to which they are attached; (2) gyroscopes that sense angular velocity, which are often joined with accelerometers to measure rotation of the body or a limb during actions; (3) vector magnetometers to reveal spatial orientation; (4) goniometers attached to joints to measure range of motion; (5) piezoelectrode and textile pressure sensors in a thin glove to report grasp and pinch forces or in insoles to record foot contact time and pressure distribution; (6) electromyography to reveal the amount and timing of muscle activation; (7) tilt/bend sensors across a joint such as the wrist to report flexion or extension angle change; and (8) global positioning satellite (GPS) signals to indicate geographic location and calculate walking distance and velocity for continuous gait. These and other combinations of sensor arrays are becoming so small and flexible that they may become ubiquitous, either woven into clothing¹⁰ or laminated onto ultrathin skin interfaces and placed anywhere on the body.¹¹

By processing data from multiple, unobtrusive sensors using algorithms trained to recognize movement patterns of the legs, upper extremities, and trunk, clinicians and researchers may solve many of the problems that continue to limit the quality of daily care and clinical trials. Inexpensive sensors will communicate via Bluetooth, ZigBee, or another transmission source to a cell phone or Wifi connection, then over the Internet to an automated analytic system. Certain types of data will be analyzed on chips in the sensors. These platforms will provide rapid feedback to users or clinicians, enable access to expert care from the home, give clinicians real-world data to better monitor their patients, increase compliance with a medical or rehabilitation regimen, and support telerehabilitation efforts. For clinical trials, sensing platforms may provide low-cost, remote recruitment and management of participants, increase retention by reducing visits to clinic sites, and enable continuous monitoring and outcome assessments that make manifest the clinical meaningfulness of the interventions being tested.

The Problem

Daily Care

Some of the frequent problems faced by clinicians who care for patients with chronic diseases such as stroke, Parkinson disease, and multiple sclerosis include measuring gains and losses of daily functioning over time, assessing the effects of the timing and dose of a medication on target symptoms

related to physical functioning, being allowed to order enough physical therapy to maintain or improve daily activities, assessing compliance with instructions for exercise and skills practice, providing adequate feedback about performance of that practice, and being able to update instructions more frequently than only at the time of an office visit.

Access to rehabilitation services. Examples of daily care confounders can be found for any neurological disease as well as in the chronic pain, cardiovascular, pulmonary, and cancer literature. Stroke will serve as an exemplar. After inpatient stroke rehabilitation, outpatient training is needed by most patients. A 2005 Centers for Disease Control survey found that only 31% of stroke survivors received outpatient rehabilitation,¹² significantly fewer than expected if clinical guidelines were followed.^{13,14} Even when offered, these services are often unstructured, difficult to obtain, and not driven by progressive goals to enable independent walking in the community and functional use of an affected upper extremity or to lessen deconditioning.^{15,16} Not only in the United States, but around the world, access to rehabilitation is very uneven, and expertise in solving problems related to sensorimotor impairments and disabilities seems limited. Some efforts are under way to develop affordable inpatient and outpatient systems that can reach more patients,¹⁷⁻¹⁹ but new strategies for less expensive and more relevant home-based care are urgently needed to reduce disability after stroke as well as for most other neurological diseases.

Availability of home-based therapies. Home-based therapies after stroke usually lack coordination and a focus on higher levels of functioning. During a home-based therapeutic program directed by verbal instruction, physicians and therapists are unable to weigh a patient's progress in terms of actual time and effort spent on prescribed activities, such as the number of repetitions and the quality of practiced movements. The ability of patients to self-monitor rehabilitation practice is probably even less reliable when more technical information is given about practice parameters, such as advice about ways to reduce gait deviations that impede balance. Counseling alone about the benefits of practice and physical activity has not been effective.²⁰ For neurological diseases such as stroke, "the best and most cost effective way of increasing physical activity has not been found."^{21,22} On the other hand, the efficacy of highly supervised and rather intensive training to improve balance, walking speed, fitness, or use of the affected upper extremity after stroke is evident.^{16,23,24} Indeed, a progressive, home-exercise program managed by therapists in the Locomotor Experience Applied Post-Stroke (LEAPS) clinical trial revealed walking-related gains that were equivalent to a much more walking-intensive physical therapy provided at clinics.¹⁶ The problem is how to inexpensively make direct supervision available. In addition, although exercise for fitness and more functional mobility^{25,26} may reduce

falls, moderate the cardiovascular risk profile, and enable greater participation in usual roles,²⁷⁻³¹ outpatient therapy for these goals is usually not covered by medical insurance.^{15,32,33} Wireless health strategies that enable monitoring and feedback by professionals from their offices as patients practice skills, walking, strengthening, and fitness in the home may be an efficient and effective alternative strategy for the delivery of needed care.

Complications of impairment and disability. Many motor-related errors of omission and commission can add to morbidity after stroke, such as contractures, pain, decubitus ulcers, nonuse of an upper extremity, and falls. For example, in the first year after stroke, 60% of disabled people suffer falls,³⁴ and half have multiple falls¹⁶ with frequent injuries and bone fractures.³⁵ Fear of falling leads to a decline in physical activity followed by greater risk for cardiovascular morbidity and further loss of quality of life. Clearly, better recognition of mechanisms underlying imbalance and falls and more effective interventions are needed.³⁶ Falls, of course, are common among older people and most of those with neurological diseases that cause ataxia or paresis.³⁷⁻⁴⁰ Measurements by wearable sensors of balance during real-world activities and at the time of a fall may offer a more promising mechanistic approach to prevention.

Spasticity has many treatments, but their effect on impairment and disability in actual use of the hand, arm, or leg is unclear and not revealed by existing measures of outpatient activities.⁴¹⁻⁴⁷ Indeed, some studies question the clinical meaning of measures of spasticity, especially the Ashworth Scale.⁴⁸ Measures for the upper extremity usually do not assess changes in voluntary movement.^{49,50} Could assessment of the quantity and quality of purposeful everyday use of the affected arm or leg add a reliable measure of the efficacy of interventions?

Clinical Trials

Some of the confounders that limit interpretation of the results of randomized clinical trials include the use of highly selected patient samples that may not represent the disease population at large; slow recruitment and failure to retain participants; the inability to monitor the fidelity of a physical intervention within subjects and across sites; uncertainty in accounting for what participants may or may not be practicing outside of the research interventions; the acquisition of outcomes that are only surrogates for changes in daily impairment, disability, and functioning; and use of outcome measurements that are not recognized by community clinicians or patients to be meaningful, so that the results of a positive trial may not be accepted into practice and disseminated.

Limitations of assessment tools. Clinical researchers have been limited to performing assessments in the clinic or laboratory. Laboratory measures in most clinical trials

indirectly assess the outcomes that are most meaningful to the investigators and perhaps to the participants. Indeed, the extent to which the limitations of existing rating scales are to blame for the failure of clinical trials to deliver better treatments, while unknown, is a source of discomfort for all trialists.⁵¹ Researchers have long sought direct, ecologically valid measures of upper- and lower-extremity activities. Inexpensive interval and ratio measures of real-world functioning could offer higher face validity for valued outcomes than ordinal, self-reported scales or timed laboratory tasks. Optimal activity-based outcome measures would also be agnostic, in the sense that they would not be disease centric. Rather, the tools would help integrate the domains of sensorimotor impairment, disability, activity, and participation, regardless of pathology.

Walking. Everyday sensing measures may offer greater validity and accuracy about outcomes of interventions than laboratory-based tests, which must be supplemented by questionnaires of self-reported daily activity to discern real-world behavior. For example, short-distance (6-15 m) walking speed on a flat indoor surface is the primary outcome measure of most clinical trials of interventions to improve walking after stroke, multiple sclerosis, Parkinson disease, and spinal cord injury and for neuropsychiatry.^{16,52-63} Walking capacity, that is, the distance walked in 3 to 6 minutes, is a common secondary outcome and may serve as an indicator of overall health, at least in older people.⁶⁴ These walking tasks under ideal conditions cannot, however, reveal how much, how fast, and how well people ordinarily walk in the home and community when faced with the constraints of their environments and impairments. Pedometers can count the number of steps, but no more. On the other hand, wireless sensor data about the range of walking speeds used in the home and community, distances walked in each bout, actual leg exercise time and energy expended on a stationary bicycle, and alterations in spatiotemporal parameters of gait under varying demands could complement laboratory tests and ordinal scales of walking, disability, and activity-related quality of life.

Functional use of the upper extremity. Ordinal scales of upper-extremity impairment and disability are commonly used but are limited by floor and ceiling effects, examiner expertise and bias, interrater reliability across trial sites, and uncertain face validity.⁵¹ Timed tasks such as the Wolf Motor Function Test (WMFT) are often used as the primary outcome in clinical trials of rehabilitation interventions such as constraint-induced movement therapy, bimanual therapy, and brain stimulation.^{24,65-75} The WMFT and complementary ordinal scales are the de facto outcomes for most robotic, functional neuromuscular stimulation, and neurostimulation trials as well.⁷⁶⁻⁸⁴ Interpretation of the WMFT improves when combined with a structured interview, such as the Motor Activity Log, about the amount of

upper-extremity activity.⁸⁵ Like all self-report tools, the Motor Activity Log has some inherent weaknesses, including recall bias, subjectivity, demand characteristics, and experimenter bias. Thus, available tools do not give an investigator a direct measure of the variety and quantity of purposeful movements performed in everyday reaching, self-care, skills practice, and exercise.

The Solutions

mHealth

mHealth is a rapidly growing field, increasingly supported by the computer and communications industry, the National Institutes of Health (<http://commonfund.nih.gov/strategicplanning/>), the National Science Foundation, and charitable foundations. Wireless mHealth requires a range of engineering and computer science development (<http://sensornets.org/>). These include types of sensors, sensor networking software and architectures, hardware (eg, technology standards, design, fabrication, packaging, reliability, electronic noise, power management and energy efficiency, connectivity and communications, and interoperability of platforms), signal processing (eg, routing techniques, statistical and adaptive processing, multimedia, coding and compression of data, data fusion, neural networks, fault detection, and data mining), cloud computing, security, infrastructure, research funding, economic viability, and other issues. For neurology and rehabilitation, the most important recent technological advancement is in the systematic and flexible merging of sensor data and transmission hardware with software programs for ease of use by participants and researchers. In addition, algorithms are becoming available to remotely recognize the type, quantity, and aspects of quality of purposeful movements.

Sensors. Single biaxial accelerometers have been commercially available (Actigraph, RT3, and Omron) to count movements of the arm or leg during reaching or stepping.^{55,86,87} Several types of biaxial and triaxial accelerometers have also been used in laboratory-based research.⁸⁶ A triaxial piezoresistant accelerometer, fastened over the L3 spinous process (DynaPort MiniMod, McRoberts) can define gait stance and swing times as well as walking speeds >0.5 m/s.⁸⁸ A system of 5 wired biaxial accelerometers (IDEAA, Minisun) placed over the thigh, sole, and sternum can quantify spatiotemporal aspects of gait and discriminate between specific activities, such as walking versus stair climbing, but the algorithms do not detect walking speeds <0.4 m/s.^{89,90} The intraclass correlation coefficient for repeatability and reliability of acceleration-based gait analysis, however, is very high for detecting cadence, speed, step length, and asymmetry in stance and swing times along with irregularities associated with turns and changes in speed in healthy participants and hemiparetic patients after

stroke.⁹¹ A central problem for the deployment of commercial devices by rehabilitation researchers is that they use proprietary data analysis systems to detect a small repertoire of movements, mostly in healthy individuals. In addition, they are too expensive to be distributed widely among outpatients for trials, with prices ranging from \$1000 (Bio-Sensics) per accelerometer to \$4000 (MiniSun) for a set.

Research groups are beginning to publish reports of sensor-based algorithms that better identify purposeful upper-extremity and walking movements for highly impaired reaching and walking.^{7,8,92} Other pilot studies found that wearable accelerometers can substitute for traditional force-plate measures to reveal postural sway and anticipatory postural adjustments.⁹³⁻⁹⁵ Chest and waist triaxial accelerometers, using threshold-based algorithms, can discriminate between a fall and daily activities.^{94,96,97} In general, these devices have only been put to use in a laboratory setting.

The Wireless Health Institute at the University of California Los Angeles developed and tested a complete architecture for activity pattern recognition, called the Medical Daily Activity Wireless Network (MDAWN).^{5,98,99} The MDAWN includes components for automated sensor data collection, transport to a remote and secure repository, individualized subject modeling, and activity state classification based on multiple sensor, data-fusion methods.⁹⁹ Data obtained from triaxial accelerometers (Gulf Coast Data Concepts, \$230 per set) placed just above each lateral malleolus are uploaded to a computer by USB port or to a smartphone by Bluetooth, then sent opportunistically via WiFi or cell connection to the MDAWN server. Analyzed data are automatically sent to a clinical trial database or to a participant for feedback.

Machine-learning algorithms in MDAWN primarily use Bayesian sensor fusion to generate an individual activity template based on the movements of interest made by each participant.⁹⁹⁻¹⁰¹ About 10 repetitions of a movement or 2 timed walks of 10 m at more than 1 speed fulfill the requirements for pattern recognition to identify walking or calculate walking or exercise parameters.^{5,102} The template is a set of statistically unique features derived from frequencies, amplitudes, waveforms, time average of acceleration, and derivatives of these across all 3 gravity-sensitive axes from both ankles. The training data take into account the peculiarities of each person's movements and motor control. Once a person's template has been defined, further data collections during everyday activities are evaluated by the MDAWN system for periods of activity with features that match it.^{5,103,104}

Sensor-derived algorithms can potentially be trained to recognize most real-world daily activity patterns, such as reaching, eating, washing, exercising with equipment, standing up, walking at any speed, and climbing stairs. The optimal placement of the accelerometers depends on the activities to be captured. By merging the activity data with

GPS, voice notation, or on-demand photo/video using a tiny camera hanging from the neck, the environs of the participant or the object/task being managed can be distinguished. In addition, for less than \$15, torque sensors and Bluetooth can be integrated into inexpensive exercise equipment such as elastic resistance bands and cycling apparatus to add the capability of recording and transmitting the actual forces or repetitions exerted by participants. An important next step is to test existing sensors in real-world settings across neurological diseases to demonstrate their reliability, validity, and responsiveness to measure purposeful activities at several ICF levels.

Data analyses. The use of Bayesian fusion to combine data from multiple body sites and different types of sensors provides the opportunity to implement a wide range of analytic techniques to compare community-based activities with laboratory- or clinic-based testing. For example, the coefficient of variation of stride-to-stride fluctuations can be assessed with an accelerometer on each ankle.⁹⁰ Other promising methods for modeling fluctuations in spatiotemporal and foot pressure measurements during stance and gait,^{105,106} such as high stride and swing time variances, may help predict falls across neurological diseases as well as freezing of gait in Parkinson disease.¹⁰⁷ mHealth technology also offers repeated measures that are easy to acquire, enabling researchers to use time-series methodology to single-participant and group data. Additional analytic tools such as trend estimation, structural modeling, and bioinformatics will also lend themselves to the large clinical and sensor data sets obtained in trials.

Daily Clinical Care

For wireless health, translation is the process of converting scientific knowledge into practitioner-friendly products that can be implemented to improve health care and research.¹⁰⁸ This stage of progress has been anticipated by the NIH (<http://commonfund.nih.gov/InnovationBrainstorm/post/Innovative-Mobile-and-Wireless-Technologies-%28mHealth%29-to-Improve-Health-Research-and-Health-Outcomes.aspx>) and by industry (<http://www.wirelesshealth2011.org>) but not yet demonstrated convincingly for dissemination.

Sensors offer potential solutions to the problems described earlier regarding daily care. Remote monitoring enables access by patients to a therapist for instruction about exercise and motor skills anywhere within reach of the Internet. Compliance with practice and exercise can be assessed daily and the information of interest made immediately available to a therapist or physician. Feedback about performance from accumulated sensor data collected over weeks can be provided by graphs and text over anyone's cell smartphone or computer. Indeed, real-time interactions using a camera built into a cell phone, electronic tablet, or

computer for face-to-face contact or as an inexpensive way to watch a patient perform a task may emerge as another tool for better care and feedback. The therapist can make corrections, then monitor home-based practice through sensors. Thus, sensor platforms will likely better enable and complement telerehabilitation strategies.¹⁰⁹⁻¹¹¹

Sensor platforms also provide an opportunity to assess the longitudinal impact of health care. For example, to comply with recent Center for Medicare Services rules for reimbursement coverage for hospitals, one strategy may be to monitor the amount and quality of mobility for the 30-day transition from hospital or inpatient rehabilitation to home. Remote monitoring of daily activity may serve as a physiological measure of wellness or decline in health.⁶⁴ A toxic-metabolic complication, fear of falling, and other confounders may be recognizable by abrupt alterations in the usual amount, type, or quality of walking, balance, exercise, and everyday activities.

Generic data about daily activity will lead to age and gender norms in healthy persons and perhaps serve to segment the neurological disease population into levels of activity-related severity that can be compared with the norms. With an electronic medical record that receives a summary of daily sensor data, data mining across disease populations may allow rigorous retrospective analysis of patient response to treatments. By this means, each patient, if agreeable, also becomes a research participant, which will maximize data mining. Indeed, bioinformatic techniques will be needed to create individual prediction models, so that sensor data can guide tailored prevention and therapeutic interventions. For Medicare and other large insurers, all these individual data may also help predict the need for rehospitalization or discern between valued and adverse effects of drugs by their impact on daily activity.

Clinical Trials

Remote sensing may enable researchers to recruit and follow patients without transporting them to a research setting. This advantage should increase geographical access to potential participants and improve retention in trials by lessening burdens on patients who are disenfranchised by their disability, geography, or social and economic disadvantages.¹¹² In turn, study samples may be more representative, the quantity and quality of community-based follow-up data may increase, and duration and costs may be reduced.

Remote sensing could monitor the fidelity of a physical intervention across trial sites as well as inform researchers about how much or how little participants are practicing on their own. Informal practice or exercise may augment or reduce the effects of an assigned randomized controlled trial (RCT) intervention and confound the results. Researchers also cannot readily assess what participants practice from the time the experimental intervention stops

until final outcome measures are performed, often 3 to 6 months later. This variation in participant activity and intensity of informal practice may confound the interpretation of gains attributed to the type and dose of the intervention itself. Sensing can provide this critical information. Indeed, a RCT is in progress—the Stroke Inpatient Rehabilitation Reinforcement of ACTivity (SIRRACT; ClinTrials.gov #NCT01246882)—that monitors daily formal and informal lower-extremity activities via wireless ankle accelerometers and the MDAWN platform during inpatient therapy, at 16 international sites. One arm receives feedback 3 times a week about the daily range of walking speeds and distances achieved, duration of exercises, and time spent in formal therapy and informal practice. The other arm only gets feedback about average daily walking speed. The RCT's hypothesis is that enhanced feedback about performance will lead to more activity and practice and, thus, improve walking-related outcomes at the time of discharge.^{113,114} The goal is to detect what has never been feasible: that is, the type, quantity, and quality of all lower-extremity activity using technology that can be used in the community within the context of daily care.

Measurement of the actual dose of exercise and daily mobility will be essential to future trials that aim to assess, for example, the effects of exercise on cognition after stroke^{115,116} or for aging and dementia.¹¹⁷ Real-world measures of impairment and functional use enabled by sensors could also lead to better brain-behavior correlations in studies of neuroplasticity^{118,119} as well as reveal the effects of fatigability on bouts of daily activity.¹²⁰⁻¹²² In addition, reliable, serial ratio-scale measurements should improve the ability of investigators to discern the dose-response and effects over time of therapeutic augmentation of skills by pharmacological,^{123,124} neural-stimulation,^{125,126} and neural-repair¹²⁷⁻¹²⁹ interventions for neurorehabilitation.

With ratio-scale monitoring and outcome mHealth tools, pilot studies of new interventions may be able to develop more exact dose-response data to optimize the intensity of a therapy prior to conducting a RCT.^{130,131} For example, the trajectory of gains over time can be assessed immediately before, during, and after a day's intervention and as often as desired throughout the course of treatment and follow-up. For studies of patients with chronic impairments and disabilities, multiple baseline measurements of activities of interest can be quantified to assess their stability prior to the start of a RCT,¹³² or the stability of these baseline tests can be perturbed by providing a brief task-related therapy to see if that alters the baseline level of activity. This strategy may reduce the number of outliers who respond to a control or experimental therapy simply because the participants have latent function that any form of motivation or practice can rapidly restore. Baseline differences in activities of interest to investigators, serving as a measure of the severity of disease symptoms or disability, could also be used to stratify

participants prior to randomization.¹³³ The capacity to collect repeated measures for weeks at a time at almost no cost to a trial also allows the option of obtaining longitudinal outcomes well beyond the formal end of a trial. These convenient repeated assessments may also improve our understanding of the trajectories of motor learning, compensation, and recovery following an injury or rehabilitation.^{134,135}

The development of standardized sensor measures should promote common monitoring and outcome tools and methodologies across trials. By using reliable, clinically meaningful generic measurements of arm or leg activity across relevant RCTs, the use of meta-analysis for evidence-based practices will become more valid. Common measurements will also improve and encourage data sharing. Ratio-scaled data may also improve the conceptual basis for what is considered to be a meaningful change in function—that is, give greater substance to notions such as the minimal detectable change and the minimal clinically important difference for walking speed or functional use of the upper extremity.¹³⁶⁻¹³⁹ In addition, sensor data can contribute to more novel clinical trial designs, especially to help overcome the relative constraints of small participant sample sizes. The availability of repeated measurements, for example, is well suited to adaptive or Bayesian designs.¹⁴⁰

Conclusion

The rapid evolution of low-cost, energy-efficient wireless sensing and processing platforms is a long-awaited opportunity for health care services, clinical practice, and research. The integration of wireless technologies requires a foundation of evidence about reliability, validity, and responsiveness for each application across the range of disease- and injury-related impairments and disabilities. To gather evidence quickly, sensors could be added to applicable clinical trials funded by the NIH, so that rapid comparisons can be made between sensing data and conventional tools for monitoring and outcome measurements. Researchers could work with Medicare, large insurers or group practices, and health maintenance organizations to test the utility of community-acquired sensor data about daily activity levels as a predictor of health status in patients with chronic diseases that are associated with repeated hospitalizations. As these trials proceed, attention must also focus on ways to make devices more user-friendly and acceptable to patients and clinicians.

Collaboration between clinicians, engineers, and the wireless industry is essential for the design and optimization of inexpensive wireless systems that are based on clinical needs. Funding organizations need to create strategic ways to bridge the present gap in making grants that involve both engineering design and clinical application. Growth of the field and new applications will be spurred by joint training of young engineers and clinicians who want to contribute to national and global health care. The great promise of

mHealth is to enable evidence-based practices to wirelessly reach into the homes and communities of people who cannot readily or affordably access health care.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors thank the Richard Merkin Foundation for Neural Regeneration at UCLA for funding. Wireless Health Institute colleagues William Kaiser, PhD, Maxim Batalin, PhD, Greg Pottier, PhD and Celia Xu provided intellectual and materials support.

References

1. Barkovich A, Szeffler S, Olson E, Rymer W. *White Paper: Scientific Vision Workshop on Diagnostics and Therapeutics*. Bethesda, MD: NICHHD.
2. Bernabeu M, Laxe S, Lopez R, et al. Developing core sets for persons with traumatic brain injury based on the international classification of functioning, disability, and health. *Neurorehabil Neural Repair*. 2009;23:464-467.
3. Morris Bamberg S, Benbasat A, Krebs D, Paradiso J. Gait analysis using a shoe-integrated sensor system. *IEEE Trans Inf Technol Biomed*. 2008;12:413-423.
4. Jovanov E, Hanish N, Courson V, et al. Avatar: a multisensory system for real time body position monitoring. *Conf Proc IEEE Eng Med Biol Soc*. 2009;2009:2462-2465.
5. Dobkin B, Xu X, Batalin M, Thomas S, Kaiser W. Reliability and validity of bilateral ankle accelerometer algorithms for activity recognition and walking speed after stroke. *Stroke*. 2011;42:2246-2250.
6. Prajapati S, Gage W, Brooks D, Black SE, McIlroy W. A novel approach to ambulatory monitoring: investigation into the quantity and control of everyday walking in patients with subacute stroke. *Neurorehabil Neural Repair*. 2011;25:6-14.
7. Patel S, Chen B, Buckley T, et al. Home monitoring of patients with Parkinson's disease via wearable technology and a web-based application. *Conf Proc IEEE Eng Med Biol Soc*. 2010;2010:4411-4414.
8. Patel S, Hughes R, Hester T, et al. Tracking motor recovery in stroke survivors undergoing rehabilitation using wearable technology. *Conf Proc IEEE Eng Med Biol Soc*. 2010;2010:6858-6861.
9. Weiss A, Sharifi S, Plotnik M, van Vugt J, Giladi N, Hausdorff J. Towards automated, at-home assessment of mobility among patients with Parkinson's disease using a body-worn accelerometer. *Neurorehabil Neural Repair*. In press.
10. Lymberis A, Paradiso R. Smart fabrics and interactive textile enabling wearable personal applications: R&D state of the art and future challenges. *Conf Proc IEEE Eng Med Biol Soc*. 2008;2008:5270-5273.
11. Kim D-H, Lu N, Ma R, et al. Epidermal electronics. *Science*. 2011;333:838-843.
12. Centers for Disease Control. Outpatient rehabilitation among stroke survivors: 21 states and the District of Columbia, 2005. *MMWR Morb Mortal Wkly Rep*. 2007;56:504-507.
13. Duncan PW, Zorowitz R, Bates B, et al. Management of adult stroke rehabilitation care: a clinical practice guideline. *Stroke*. 2005;36:E100-E143.
14. Duncan P, Horner R, Reker D, Samsa G, Hoenig H. Adherence to postacute rehabilitation guidelines is associated with functional recovery in stroke. *Stroke*. 2002;33:167-178.
15. Management of Stroke Rehabilitation Working Group. VA/DoD clinical practice guidelines for the management of stroke rehabilitation. <http://www.rehab.research.va.gov/jour/10/479/pdf/VADODclinicalGuidelines479.pdf>. Accessed September 20, 2011.
16. Duncan P, Sullivan K, Behrman A, et al. Body-weight-supported treadmill rehabilitation program after stroke. *N Engl J Med*. 2011;364:2026-2036.
17. Weinrich M, Stuart M. Coverage policy for neurorehabilitation: an international perspective. *Neurorehabil Neural Repair*. 2011;25:531-539.
18. Miyai I, Sonoda S, Nagai S, et al. Results of new policies for inpatient rehabilitation coverage in Japan. *Neurorehabil Neural Repair*. 2011;25:540-547.
19. Stuart M, Benvenuti F, Macko R, et al. Community-based adaptive physical activity program for chronic stroke: feasibility, safety, and efficacy of the Empoli Model. *Neurorehabil Neural Repair*. 2009;23:726-734.
20. Eden KB, Orleans C, Mulrow C, Pender N, Teutsch S. Does counseling by clinicians improve physical activity? A summary of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2002;137:208-215.
21. Boysen G, Krarup LH, Zeng X, et al. ExStroke pilot trial of the effect of repeated instructions to improve physical activity after ischaemic stroke: a multinational randomised controlled clinical trial. *BMJ*. 2009;339:b2810.
22. Langhorne P, Taylor G, Murray G, et al. Early supported discharge services for stroke patients: a meta-analysis of individual patients' data. *Lancet*. 2005;365:501-506.
23. Duncan P, Studenski S, Richards L, et al. Randomized clinical trial of therapeutic exercise in subacute stroke. *Stroke*. 2003;34:2173-2180.
24. Wolf SL, Winstein CJ, Miller JP, et al. Effect of constraint-induced movement therapy on upper extremity function 3 to 9 months after stroke: the EXCITE randomized clinical trial. *JAMA*. 2006;296:2095-2104.
25. Ridgel A, Vitek J, Alberts J. Forced, not voluntary exercise improves motor function in Parkinson's disease patients. *Neurorehabil Neural Repair*. 2009;23:600-608.
26. Tang A, Sibley KM, Thomas SG, et al. Effects of an aerobic exercise program on aerobic capacity, spatiotemporal gait parameters, and functional capacity in subacute stroke. *Neurorehabil Neural Repair*. 2009;23:398-406.

27. Reisman D, Rudolph K, Farquhar W. Influence of speed on walking economy poststroke. *Neurorehabil Neural Repair*. 2009;23:529-434.
28. van Hedel H. Gait speed in relation to categories of functional ambulation after spinal cord injury. *Neurorehabil Neural Repair*. 2009;23:343-350.
29. Bowden MG, Balasubramanian CK, Behrman AL, Kautz SA. Validation of a speed-based classification system using quantitative measures of walking performance poststroke. *Neurorehabil Neural Repair*. 2008;22:672-675.
30. Huang Y, Wu C, Hsieh Y, Lin K. Predictors of change in quality of life after distributed constraint-induced therapy in patients with chronic stroke. *Neurorehabil Neural Repair*. 2010;24:559-566.
31. Rudhe C, van Hedel H. Upper extremity function in persons with tetraplegia: relationships between strength, capacity, and the Spinal Cord Independence Measure. *Neurorehabil Neural Repair*. 2009;23:413-421.
32. Mackintosh SFH, Hill K, Dodd KJ, Goldie P, Culham E. Falls and injury prevention should be part of every stroke rehabilitation plan. *Clin Rehabil*. 2005;19:441-451.
33. Ferrarello F, Baccini M, Rinaldi LA, et al. Efficacy of physiotherapy interventions late after stroke: a meta-analysis. *J Neurol Neurosurg Psychiatry*. 2011;82:136-143.
34. Weerdesteijn V, de Niet M, van Duijnhoven HJR, Geurts ACH. Falls in individuals with stroke. *J Rehabil Res Dev*. 2008;45:1195-1213.
35. Pouwels S, Lalmohamed A, Leufkens B, et al. Risk of hip/femur fracture after stroke: a population-based case-control study. *Stroke*. 2009;40:3281-3285.
36. Hollands K, Hollands M, Zietz D, Wing A, Wright C, van Vliet P. Kinematics of turning 180 [degrees] during the-timed up and go in stroke survivors with and without falls history. *Neurorehabil Neural Repair*. 2010;24:358-367.
37. Wirz M, Müller R, Bastiaenen C. Falls in persons with spinal cord injury: validity and reliability of the Berg Balance Scale. *Neurorehabil Neural Repair*. 2010;24:70-77.
38. Corsinovi L, Bo M, Aimonino NR, et al. Predictors of falls and hospitalization outcomes in elderly patients admitted to an acute geriatric unit. *Arch Gerontol Geriatr*. 2009;49:142-145.
39. Nilsagard Y, Lundholm C, Denison E, Gunnarsson L-G. Predicting accidental falls in people with multiple sclerosis: a longitudinal study. *Clin Rehabil*. 2009;23:259-269.
40. Wong WL, Masters RS, Maxwell JP, Abernethy AB. Reinvestment and falls in community-dwelling older adults. *Neurorehabil Neural Repair*. 2008;22:410-414.
41. Elbasiouny V S, Moroz D, Bakr M, Mushahwar V. Management of spasticity after spinal cord injury: current techniques and future directions. *Neurorehabil Neural Repair*. 2010;24:23-33.
42. Bensmail D, Robertson J, Fermanian C, Roby-Brami A. Botulinum toxin to treat upper-limb spasticity in hemiparetic patients: grasp strategies and kinematics of reach-to-grasp movements. *Neurorehabil Neural Repair*. 2010;24:141-151.
43. Bensmail D, Ward A, Wissel J, et al. Cost-effectiveness modeling of intrathecal baclofen therapy versus other interventions for disabling spasticity. *Neurorehabil Neural Repair*. 2009;23:546-552.
44. Rameckers E, Speth L, Duysens J, Vles J, Smits-Engelsman B. Botulinum toxin-A in children with congenital spastic hemiplegia does not improve upper extremity motor-related function over rehabilitation alone: a randomized controlled trial. *Neurorehabil Neural Repair*. 2009;23:218-225.
45. Kofler M, Quirbach E, Schauer R, Singer M, Saltuari L. Limitations of intrathecal baclofen for spastic hemiparesis following stroke. *Neurorehabil Neural Repair*. 2009;23:26-31.
46. Hutin E, Pradon D, Barbier F, Gracies J, Bussel B, Nicolas Roche N. Lower limb coordination in hemiparetic subjects: impact of botulinum toxin injections into rectus femoris. *Neurorehabil Neural Repair*. 2010;24:442-449.
47. Sun S, Hsu C, Sun H, Hwang C, Yang C, Wang J. Combined botulinum toxin type A with modified constraint-induced movement therapy for chronic stroke patients with upper extremity spasticity: a randomized controlled study. *Neurorehabil Neural Repair*. 2010;24:34-41.
48. Fleuren J, Voerman G, Erren-Wolters C, et al. Stop using the Ashworth Scale for the assessment of spasticity. *J Neurol Neurosurg Psychiatry*. 2010;81:46-52.
49. Francis H, Wade D, Turner-Stokes L, Kingswell R, Dott C, Coxon E. Does reducing spasticity translate into functional benefit? An exploratory meta-analysis. *J Neurol Neurosurg Psychiatry*. 2004;75:1547-1551.
50. Simpson D, Gracies J, Yablon S, Barbano R, Brashear A. Botulinum neurotoxin versus tizanidine in upper limb spasticity: a placebo-controlled study. *J Neurol Neurosurg Psychiatry*. 2009;80:380-385.
51. Hobart J, Cano S, Zajicek J, Thompson A. Rating scales as outcome measures for clinical trials in neurology: problems, solutions, and recommendations. *Lancet Neurol*. 2007;6:1094-1105.
52. Ada L, Dean C, Morris M, Simpson J, Katrak P. Randomized trial of treadmill walking with body weight support to establish walking in subacute stroke: the MOBILISE trial. *Stroke*. 2010;41:1237-1242.
53. Dobkin BH. Short-distance walking speed and timed walking distance: redundant measures for clinical trials? *Neurology*. 2006;66:584-586.
54. Duncan P, Studenski S, Richards L, et al. Randomized clinical trial of therapeutic exercise in subacute stroke. *Stroke*. 2003;34:2173-2180.
55. Duncan PW, Sullivan KJ, Behrman AL, et al. Protocol for the locomotor experience applied post-stroke (LEAPS) trial: a randomized controlled trial. *BMC Neurol*. 2007;7:39.
56. Hesse SA, Jahnke MT, Bertelt CM, Schreiner C, Lucke D, Mauritz KH. Gait outcome in ambulatory hemiparetic

- patients after a 4-week comprehensive rehabilitation program and prognostic factors. *Stroke*. 1994;25:1999-2004.
57. Hidler J, Nichols D, Pelliccino M, et al. Multi-center randomized clinical trial evaluating the effectiveness of the Lokomat in sub-acute stroke. *Neurorehabil Neural Repair*. 2009;23:5-13.
 58. Goodman A, Brown T, Krupp L, et al. Sustained-release oral fampridine in multiple sclerosis. *Lancet*. 2009;373:732-738.
 59. Wevers L, van de Port I, Vermue M, Mead G, Kwakkel G. Effects of task-oriented circuit class training on walking competency after stroke: a systematic review. *Stroke*. 2009;40:2450-2459.
 60. Widener G, Allen D, Gibson-Horn C. Randomized clinical trial of balance-based torso weighting for improving upright mobility in people with multiple sclerosis. *Neurorehabil Neural Repair*. 2009;23:784-791.
 61. Lam J, Globas C, Cerny J, et al. Predictors of response to treadmill exercise in stroke survivors. *Neurorehabil Neural Repair*. 2010;24:567-574.
 62. de Groot J, Takken T, van Brussel M, et al. Randomized controlled study of home-based treadmill training for ambulatory children with spina bifida. *Neurorehabil Neural Repair*. 2011;25:597-606.
 63. Jonsdottir J, Cattaneo D, Recalcati M, et al. Task-oriented biofeedback to improve gait in individuals with chronic stroke: motor learning approach. *Neurorehabil Neural Repair*. 2010;24:478-485.
 64. Studenski S, Perera S, Patel K, et al. Gait speed and survival in older adults. *JAMA*. 2011;305:50-58.
 65. Wolf SL, Thompson PA, Morris DM, et al. The EXCITE Trial: attributes of the Wolf Motor Function Test in patients with subacute stroke. *Neurorehabil Neural Repair*. 2005;19:194-205.
 66. Lin K, Chen Y, Chen C, Wu C, Chang Y. The effects of bilateral arm training on motor control and functional performance in chronic stroke: a randomized controlled study. *Neurorehabil Neural Repair*. 2010;24:42-51.
 67. Lin K, Huang Y, Hsieh Y, Wu C. Potential predictors of motor and functional outcomes after distributed constraint-induced therapy for patients with stroke. *Neurorehabil Neural Repair*. 2009;23:336-342.
 68. Lin K-C, Wu C, Liu J, Chen Y, Hsu C-J. Constraint-induced therapy versus dose-matched control intervention to improve motor ability, basic/extended daily functions, and quality of life in stroke. *Neurorehabil Neural Repair*. 2009;23:160-165.
 69. Platz T, Kaick S, Mehrholz J, Leidner O, Eickhof C, Pohl M. Best conventional therapy versus modular impairment-oriented training for arm paresis after stroke: A single-blind, multicenter randomized controlled trial. *Neurorehabil Neural Repair*. 2009;23:706-716.
 70. Cacchio A, De Blasis E, De Blasis V, Santilli V, Spacca G. Mirror therapy in complex regional pain syndrome type 1 of the upper limb in stroke patients. *Neurorehabil Neural Repair*. 2009;23:792-799.
 71. Aarts P, Jongerius P, Geerdink Y, van Limbeek J, Geurts A. Effectiveness of modified constraint-induced movement therapy in children with unilateral spastic cerebral palsy: a randomized controlled trial. *Neurorehabil Neural Repair*. 2010;24:509-518.
 72. Stoykov M, Lewis G, Corcos D. Comparison of bilateral and unilateral training for upper extremity hemiparesis in stroke. *Neurorehabil Neural Repair*. 2009;23:945-953.
 73. Donaldson C, Tallis R, Miller S, Sunderland A, Lemon R, Pomeroy V. Effects of conventional physical therapy and functional strength training on upper limb motor recovery after stroke: a randomized phase II study. *Neurorehabil Neural Repair*. 2009;23:389-397.
 74. Timmermans A, Spooren A, Kingma H, Seelen H. Influence of task-oriented training content on skilled arm-hand performance in stroke: a systematic review. *Neurorehabil Neural Repair*. 2010;24:858-870.
 75. Conforto A, Ferreiro K, Tomasi C, et al. Effects of somatosensory stimulation on motor function after subacute stroke. *Neurorehabil Neural Repair*. 2010;24:263-272.
 76. Housman S, Scott K, Reinkensmeyer D. A randomized controlled trial of gravity-supported, computer-enhanced arm exercise for individuals with severe hemiparesis. *Neurorehabil Neural Repair*. 2009;23:505-514.
 77. Mehrholz J, Platz T, Kugler J, Pohl M. Electromechanical and robot-assisted arm training for improving arm function and activities of daily living after stroke. *Cochrane Database Syst Rev*. 2008;(4):CD006876d.
 78. Kwakkel G, Kollen BJ, Krebs HI. Effects of robot-assisted therapy on upper limb recovery after stroke: a systematic review. *Neurorehabil Neural Repair*. 2008;22:111-121.
 79. Lo A, Guarino P, Krebs H, et al. Multicenter randomized trial of robot-assisted rehabilitation for chronic stroke: methods and entry characteristics for VA ROBOTICS. *Neurorehabil Neural Repair*. 2009;23:775-783.
 80. Lo A, Guarino P, Richards L, et al. Robot-assisted therapy for long-term upper-limb impairment after stroke. *N Engl J Med*. 2010;362:1772-1783.
 81. Hughes A, Freeman C, Burridge J, Chappell P, Lewin P, Rogers E. Feasibility of iterative learning control mediated by functional electrical stimulation for reaching after stroke. *Neurorehabil Neural Repair*. 2009;23:559-568.
 82. Chae J, Harley M, Hisel T, et al. Intramuscular electrical stimulation for upper limb recovery in chronic hemiparesis: an exploratory randomized clinical trial. *Neurorehabil Neural Repair*. 2009;23:569-578.
 83. Nowak D, Grefkes C, Ameli M, Fink G. Interhemispheric competition after stroke: brain stimulation to enhance recovery of function of the affected hand. *Neurorehabil Neural Repair*. 2009;23:641-656.
 84. Harvey R, Winstein C. Design for the Everest randomized trial of cortical stimulation and rehabilitation for arm

- function following stroke. *Neurorehabil Neural Repair*. 2009;23:32-44.
85. Park SW, Wolf SL, Blanton S, Winstein C, Nichols-Larsen DS. The EXCITE trial: predicting a clinically meaningful Motor Activity Log outcome. *Neurorehabil Neural Repair*. 2008;22:486-493.
 86. Manns P, Baldwin E. Ambulatory activity of stroke survivors: measurement options for dose, intensity, and variability of activity. *Stroke*. 2009;40:864-867.
 87. Rand D, Eng JJ, Tang PF, Jeng JS, Hung CY. How active are people with stroke? Use of accelerometers to assess physical activity. *Stroke*. 2009;40:163-168.
 88. Hartmann A, Murer K, de Bie R, de Bruin E. Reproducibility of spatio-temporal gait parameters under different conditions in older adults using a trunk tri-axial accelerometer system. *Gait Posture*. 2009;30:351-355.
 89. Regnaud JP, Saremi K, Marehbian J, Bussel B, Dobkin BH. An accelerometry-based comparison of 2 robotic assistive devices for treadmill training of gait. *Neurorehabil Neural Repair*. 2008;22:348-354.
 90. Saremi K, Marehbian J, Regnaud J, et al. Reliability and validity of bilateral thigh and foot accelerometry measures of walking in healthy and hemiparetic subjects. *Neurorehabil Neural Repair*. 2006;20:297-305.
 91. Henriksen M, Lund H, Moe-Nilssen R, Bliddal H, Danneskiold-Samsøe B. Test-retest reliability of trunk accelerometric gait analysis. *Gait Posture*. 2004;19:288-297.
 92. Roy S, Cheng M, Chang S-S, et al. A combined sEMG and accelerometer system for monitoring functional activity in stroke. *IEEE Trans Neural Syst Rehabil Eng*. 2009;17:585-594.
 93. Scanail C, Garrattini C, Greene B, McGrath M. Technology innovation enabling falls risk assessment in a community setting. *Ageing Int*. 2011;36:217-231.
 94. Narayanan MR, Redmond SJ, Scalzi ME, Lord SR, Celler BG, Lovell Ast NH. Longitudinal falls-risk estimation using triaxial accelerometry. *IEEE Trans Biomed Eng*. 2010;57:534-541.
 95. Noshadi H, Dabiri F, Ahmadian S, Amini N, Sarrafzadeh M. HERMES: mobile system for instability analysis and balance assessment. *ACM Trans Embedd Comput Syst*. In press.
 96. Bourke A, O'Brien J, Lyons G. Evaluation of a threshold-based tri-axial accelerometer fall detection algorithm. *Gait Posture*. 2007;26:194-199.
 97. Boyle J, Karunanithi M. Simulated fall detection via accelerometers. *Conf Proc IEEE Eng Med Biol Soc*. 2008;2008:1274-1277.
 98. Au LK, Wu W, Batalin M, McIntire D, Kaiser WJ. Micro-LEAP: energy-aware wireless sensor platform for biomedical sensing applications. *IEEE Biomed Circuits Syst Conf*. 2007:158-162.
 99. Wu W, Bui AA, Batalin M, Au LK, Binney J, Kaiser WJ. MEDIC: Medical Embedded Device for Individualized Care. *Artif Intell Med*. 2008;42:137-152.
 100. Domingos P, Pazzani M. On the optimality of the simple Bayesian classifier under zero-one loss. *Mach Learn*. 1997;29:103-130.
 101. Wu W, Bui AA, Batalin M, Liu D, Kaiser WJ. Incremental diagnosis method for intelligent wearable sensor systems. *IEEE Trans Inf Tech Biomed*. 2007;11:553-562.
 102. Xu X, Batalin M, Kaiser W, Dobkin B. Robust hierarchical system for classification of complex human mobility characteristics in the presence of neurological disorders. *Int Conf Body Sens Netw*. 2011;2011:65-70.
 103. Wu W, Batalin M, Au LK, Bui AA, Kaiser WJ. Context-aware sensing of physiological signals. *Conf Proc IEEE Eng Med Biol Soc*. 2007;2007:5271-5275.
 104. Preece S, Goulermas J, Laurence P, Howard D. A comparison of feature extraction methods for the classification of dynamic activities from accelerometer data. *IEE Trans Biomed Eng*. 2009;56:871-879.
 105. Hausdorff JM. Gait variability: methods, modeling and meaning. *J Neuroeng Rehabil*. 2005;2:19.
 106. Hausdorff JM. Gait dynamics, fractals and falls: finding meaning in the stride-to-stride fluctuations of human walking. *Hum Mov Sci*. 2007;26:555-589.
 107. Hausdorff J, Rios D, Edelberg H. Gait variability and fall risk in community-living older adults: a 1-year prospective study. *Arch Phys Med Rehabil*. 2005;82:1050-1056.
 108. Wandersman A, Duffy J, Flaspohler P, Noonan R, Lubell K, Stillman L. Bridging the gap between prevention research and practice: the interactive systems framework for dissemination and implementation. *Am J Community Psychol*. 2008;41:171-181.
 109. Brown S, Lewis C, McCarthy J, Doyle S, Hurvitz E. The effects of internet-based home training on upper limb function in adults with cerebral palsy. *Neurorehabil Neural Repair*. 2010;24:575-583.
 110. Carey JR, Durfee WK, Bhatt E, et al. Comparison of finger tracking versus simple movement training via telerehabilitation to alter hand function and cortical reorganization after stroke. *Neurorehabil Neural Repair*. 2007;21:216-232.
 111. Conklyn D, Stough D, Novak E, Paczak S, Chemali K, Bethoux F. A home-based walking program using rhythmic auditory stimulation improves gait performance in patients with multiple sclerosis. *Neurorehabil Neural Repair*. 2010;24:835-842.
 112. Jette A, Tao W, Norweg A, Haley S. Interpreting rehabilitation outcome measures. *J Rehabil Med*. 2007;39:585-590.
 113. Subramanian S, Massie C, Malcolm M, Levin M. Does provision of extrinsic feedback result in improved motor learning in the upper limb poststroke? A systematic review of the evidence. *Neurorehabil Neural Repair*. 2010;24:113-124.
 114. Dobkin B, Plummer-D'Amato P, Elashoff R, Lee J, Group S. International randomized clinical trial, Stroke Inpatient Rehabilitation With Reinforcement of Walking Speed (SIRROWS) improves outcomes. *Neurorehabil Neural Repair*. 2010;24:235-242.

115. Quaney BM, Boyd LA, McDowd J, He J, Mayo M, Macko R. Exercise improves cognition and motor function post-stroke. *Neurorehabil Neural Repair*. 2009;23:879-885.
116. Rand D, Eng J, Liu-Ambrose T, Tawashy A. Feasibility of a 6-month exercise and recreation program to improve executive functioning and memory in individuals with chronic stroke. *Neurorehabil Neural Repair*. 2010;24:722-729.
117. Hillman CH, Erickson KI, Kramer AF. Be smart, exercise your heart: exercise effects on brain and cognition. *Nat Rev Neurosci*. 2008;9:58-65.
118. Askim T, Indredavik B, Vangberg T, Haberg A. Motor network changes associated with successful motor skill relearning after acute ischemic stroke: a longitudinal fMRI study. *Neurorehabil Neural Repair*. 2009;23:295-304.
119. Cramer S, Sur M, Dobkin B, et al. Harnessing neuroplasticity for clinical applications. *Brain*. 2011;134:1591-1609.
120. Hornby T, Lewek M, Thompson C, Heitz R. Repeated maximal volitional effort contractions in human spinal cord injury: initial torque increases and reduced fatigue. *Neurorehabil Neural Repair*. 2009;23:928-938.
121. Dobkin BH. Fatigue versus activity-dependent fatigability in patients with central or peripheral motor impairments. *Neurorehabil Neural Repair*. 2008;22:105-110.
122. Steens A, de Vries A, Hemmen J, et al. Fatigue perceived by multiple sclerosis patients is associated with muscle fatigue [published online ahead of print August 19, 2011]. *Neurorehabil Neural Repair*. doi:10.1177/1545968311416991.
123. Cramer S, Dobkin BH, Noser E, Rodriguez R, Enney L. Randomized, placebo-controlled, double-blind study of ropinirole in chronic stroke. *Stroke*. 2009;40:3034-3038.
124. Chollet F, Tardy J, Albucher J, et al. Fluoxetine for motor recovery after acute ischemic stroke (FLAME): a randomised placebo-controlled trial. *Lancet Neurol*. 2011;10:123-130.
125. Castel-Lacanal E, Marque P, Tardy J, et al. Induction of cortical plastic changes in wrist muscles by paired associative stimulation in stroke patients. *Neurorehabil Neural Repair*. 2009;23:366-372.
126. Lindenberg R, Renga V, Zhu L, Nair D, Schlaug G. Bihemispheric brain stimulation facilitates motor recovery in chronic stroke patients. *Neurology*. 2010;75:2176-2184.
127. Lima C, Escada P, Pratas-Vital J, et al. Olfactory mucosal autografts and rehabilitation for chronic traumatic spinal cord injury. *Neurorehabil Neural Repair*. 2010;24:10-22.
128. Janssen H, Bernhardt J, Collier J, et al. An enriched environment improves sensorimotor function post-ischemic stroke. *Neurorehabil Neural Repair*. 2010;24:802-813.
129. Dobrossy M, Busse M, Piroth T, Rosser A, Dunnett S, Nikkhah G. Neurorehabilitation with neurotransplantation. *Neurorehabil Neural Repair*. 2010;24:692-701.
130. Dobkin BH. Rehabilitation and functional neuroimaging dose-response trajectories for clinical trials. *Neurorehabil Neural Repair*. 2005;19:276-282.
131. Birkenmeier R, Prager E, Lang C. Translating animal doses of task-specific training to people with chronic stroke in 1-hour therapy sessions: a proof-of-concept study. *Neurorehabil Neural Repair*. 2010;24:620-635.
132. Dobkin BH. Progressive staging of pilot studies to improve phase III trials for motor interventions. *Neurorehabil Neural Repair*. 2009;23:197-206.
133. Sosnoff J, Goldman M, Motl R. Real-life walking impairment in multiple sclerosis: preliminary comparison of four methods for processing accelerometry data. *Mult Scler*. 2010;16:868-877.
134. Piron L, Turolla A, Agostini M, et al. Motor learning principles for rehabilitation: a pilot randomized controlled study in poststroke patients. *Neurorehabil Neural Repair*. 2010;24:501-508.
135. Levin M, Kleim J, Wolf S. What do motor "recovery" and "compensation" mean in patients following stroke? *Neurorehabil Neural Repair*. 2009;23:313-319.
136. Chen H, Chen C, Hsueh I, Huang S, Hsieh C. Test-retest reproducibility and smallest real difference of 5 hand function tests in patients with stroke. *Neurorehabil Neural Repair*. 2009;23:435-440.
137. Fritz S, Blanton S, Uswatte G, Taub E, Wolf S. Minimal detectable change scores for the Wolf Motor Function Test. *Neurorehabil Neural Repair*. 2009;23:662-667.
138. Tilson J, Sullivan K, Cen S, et al. Meaningful gait speed improvement during the first 60 days poststroke: minimal clinically important difference. *Phys Ther*. 2010;90:196-208.
139. Lin K, Fu T, Wu C, et al. Minimal detectable change and clinically important difference of the Stroke Impact Scale in stroke patients. *Neurorehabil Neural Repair*. 2010;24:486-492.
140. Schmidli H, Bretz F, Racine-Poon A. Bayesian predictive power for interim adaptation in seamless phase II/III trials where the endpoint is survival up to some specified timepoint. *Stat Med*. 2007;26:4925-4938.