

Physical Activity and Exercise Recommendations for Stroke Survivors: A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

Sandra A. Billinger, Ross Arena, Julie Bernhardt, Janice J. Eng, Barry A. Franklin, Cheryl Mortag Johnson, Marilyn MacKay-Lyons, Richard F. Macko, Gillian E. Mead, Elliot J. Roth, Marianne Shaughnessy and Ada Tang
on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Lifestyle and Cardiometabolic Health, Council on Epidemiology and Prevention, and Council on Clinical Cardiology

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Physical Activity and Exercise Recommendations for Stroke Survivors

A Statement for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists.

Sandra A. Billinger, PT, PhD, FAHA, Chair; Ross Arena, PT, PhD, FAHA, Co-Chair;
Julie Bernhardt, PT, PhD; Janice J. Eng, BSc, PT/OT, PhD; Barry A. Franklin, PhD, FAHA;
Cheryl Mortag Johnson, OTR; Marilyn MacKay-Lyons, BSc, MScPT, PhD;
Richard F. Macko, MD; Gillian E. Mead, MD, MA, FRCP; Elliot J. Roth, MD, FAHA;
Marianne Shaughnessy, PhD, RN, CRNP; Ada Tang, PT, PhD; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Lifestyle and Cardiometabolic Health, Council on Epidemiology and Prevention, and Council on Clinical Cardiology

Purpose—This scientific statement provides an overview of the evidence on physical activity and exercise recommendations for stroke survivors. Evidence suggests that stroke survivors experience physical deconditioning and lead sedentary lifestyles. Therefore, this updated scientific statement serves as an overall guide for practitioners to gain a better understanding of the benefits of physical activity and recommendations for prescribing exercise for stroke survivors across all stages of recovery.

Methods—Members of the writing group were appointed by the American Heart Association Stroke Council's Scientific Statement Oversight Committee and the American Heart Association's Manuscript Oversight Committee. The writers used systematic literature reviews, references to published clinical and epidemiology studies, morbidity and mortality reports, clinical and public health guidelines, authoritative statements, personal files, and expert opinion to summarize existing evidence and indicate gaps in current knowledge.

Results—Physical inactivity after stroke is highly prevalent. The assessed body of evidence clearly supports the use of exercise training (both aerobic and strength training) for stroke survivors. Exercise training improves functional capacity, the ability to perform activities of daily living, and quality of life, and it reduces the risk for subsequent cardiovascular events. Physical activity goals and exercise prescription for stroke survivors need to be customized for the individual to maximize long-term adherence.

Conclusions—The recommendation from this writing group is that physical activity and exercise prescription should be incorporated into the management of stroke survivors. The promotion of physical activity in stroke survivors should emphasize low- to moderate-intensity aerobic activity, muscle-strengthening activity, reduction of sedentary behavior, and risk management for secondary prevention of stroke. (*Stroke*. 2014;45:2532-2553.)

Key Words: AHA Scientific Statements ■ aerobic exercise ■ exercise, physical ■ physical activity ■ rehabilitation ■ strength training

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Annually, 795 000 people in the United States experience a stroke; or ≈ 1 person every 40 seconds, and nearly one quarter of these strokes are recurrent.¹ An estimated 7 million American adults are living with a stroke,¹ and it is projected that an additional 4 million will have a stroke by 2030, which is almost a 25% increase in prevalence from 2010.² Data from the Framingham Study revealed a lifetime stroke risk of 1 in 5 for women and 1 in 6 for men among those 55 to 75 years of age.³ Moreover, the incidence of stroke is likely to continue to escalate because of an expanding population of elderly Americans⁴ and the apparent epidemic in the general population regarding modifiable cardiovascular risk factors, including diabetes mellitus, obesity, and physical inactivity. American adults with disability are more likely to be obese, to smoke, and to be physically inactive,⁵ which leads to an increased cardiovascular risk in an already functionally compromised population. When considered independently from other cardiovascular diseases (CVDs), stroke continues to be the fourth-leading cause of death in the United States.¹

Unfortunately, stroke remains a leading cause of long-term disability in the United States.¹ Consequently, stroke survivors are often deconditioned and predisposed to a sedentary lifestyle that adversely impacts performance of activities of daily living, increases the risk for falls, and may contribute to a heightened risk for recurrent stroke and other CVDs. The majority of studies have investigated ischemic stroke, although stroke is often considered a broader term for a transient ischemic attack (TIA), ischemic stroke, or intracerebral hemorrhage. All 3 of these categories pose an increased risk for a future vascular event^{6,7}; however, this risk is further elevated in patients with cerebrovascular disease and comorbid CVD.^{6,7} Although stroke survivors vary in their level of participation in physical activity, hospital- and community-based studies have consistently found low levels of activity.^{8,9} On a population basis, the physical activity of community-living stroke survivors is lower than that of older adults with other chronic health conditions of the musculoskeletal or cardiovascular system.¹⁰

Physical activity and exercise have the potential to positively influence multiple physical and psychosocial domains after stroke. We define *physical activity* as “any bodily movement produced by skeletal muscles that results in energy expenditure,” whereas *exercise* is “a subset of physical activity that is planned, structured, and repetitive and has as a final or an intermediate objective the improvement or maintenance of physical fitness.”¹¹ There is strong evidence that exercise after stroke can improve cardiovascular fitness,¹² walking ability,¹³ and upper-extremity muscle strength.¹⁴ There are less consistent reports of lower-extremity muscle strength gains.¹⁵ Although exercise has been shown to reduce falls in older adults,¹⁶ this finding has not been confirmed in stroke,¹⁷ likely a consequence of too few studies with relatively small sample sizes. Although exercise has primarily been used to improve physical function after stroke, emerging research suggests that exercise may improve depressive symptoms,¹⁸ some aspects of executive functioning and memory,^{19–21} and health-related quality of life²² after stroke and poststroke fatigue.²³

Therefore, stroke survivors can benefit from counseling on increasing participation in physical activity,²⁴ as well as the

appropriate prescription for exercise training. However, most healthcare professionals have limited experience and guidance in exercise programming for this diverse and escalating patient population. The present scientific statement is intended to help bridge the current knowledge gap in physical activity and exercise recommendations in the stroke population.

Methods

Writing group members were nominated by the committee chair on the basis of their previous work in relevant topic areas and were approved by the American Heart Association (AHA) Stroke Council’s Scientific Statement Oversight Committee and the AHA’s Manuscript Oversight Committee. The writers used systematic literature reviews, references to published clinical and epidemiology studies, morbidity and mortality reports, clinical and public health guidelines, authoritative statements, personal files, and expert opinion to summarize existing evidence and indicate gaps in current knowledge. All members of the writing group had the opportunity to comment and approved the final version of this document. The document underwent extensive AHA internal peer review, Stroke Council Leadership review, and Scientific Statements Oversight Committee review before consideration and approval by the AHA Science Advisory and Coordinating Committee.

Results

Prestroke Disability, Poststroke Sequelae, and Comorbid Conditions

The World Health Organization’s *International Classification of Functioning, Disability, and Health* organizes the effects of conditions such as stroke into problems of “body functions and structure” (impairments), “activity,” and “participation” dimensions.²⁵ The majority of stroke survivors have residual impairments caused by the stroke, such as hemiparesis, spasticity, cognitive dysfunction, and aphasia. Full recovery is achieved in only a small proportion of stroke survivors. Activity limitations are manifested by reduced ability to perform daily tasks, and at 6 months after stroke, 40% of stroke survivors have difficulties with basic self-care (eg, dressing, feeding).²⁶ More than 30% of stroke survivors report participation restrictions (eg, difficulty with autonomy, engagement, or fulfilling societal roles) even at 4 years after stroke.²⁷

One of the major consequences of these impairments, activity limitations, and participation restrictions is a chronic sedentary lifestyle.²⁸ What is particularly disconcerting is that many of these stroke survivors have the ability to undertake higher levels of physical activity but choose not to do so.²⁹ Likely reasons for limited exercise participation by people with stroke include a lack of (1) awareness that exercise is feasible or desirable, (2) access to resources to support exercise, and (3) structured exercise sessions whereby exercises could be demonstrated by a rehabilitation specialist or exercise leader.³⁰ These sedentary behaviors cause further declines in cardiorespiratory fitness, which compounds the deleterious impact on functional capacity after a stroke. After 6 to 12 months after stroke, stroke survivors with ambulatory ability have substantially diminished cardiorespiratory fitness, measured by peak oxygen consumption ($\dot{V}O_2$).^{31,32}

In addition to being far below age- and sex-predicted normative levels, these values fall below or scarcely surpass the minimal peak $\dot{V}O_2$ values (≈ 15 to $18 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) necessary for independent living.³³ The concomitant presence of other CVDs in the majority of stroke survivors is a major explanatory factor of poor cardiorespiratory fitness; however, there are other physiological consequences from the stroke that also contribute to compromised function. In terms of skeletal muscle on the stroke-affected side, there is severe muscle wasting, increased intramuscular fat, a shift from slow-twitch toward fast-twitch “fatigable” muscle fiber characteristics, greater expression of inflammatory cytokines involved in muscle atrophy, and reduction of capillaries per muscle fiber.³⁴ Other biological changes that may negatively affect cardiorespiratory health after stroke are elevated systemic levels of proinflammatory markers, abnormal glucose and insulin metabolism, impaired autonomic control, and respiratory dysfunction.³⁴

Elevated energy costs of movement after stroke also contribute to a sedentary lifestyle, especially in physically deconditioned older patients. The oxygen cost of walking (ie, $\dot{V}O_2$ per distance walked) is 2-fold higher than values reported for able-bodied subjects.³⁵ Poststroke fatigue is common, with a prevalence rate from 35% to 92%,³⁶ and may also contribute to and be aggravated by a sedentary lifestyle. Fatigue may have different constructs in which exertional fatigue is related to cardiorespiratory and skeletal muscle fitness, whereas chronic fatigue is related to depression.³⁷ Appropriate screening and treatment of fatigue and depression are paramount to the initiation of exercise and long-term compliance in this population.

Although impairments may limit daily activities to some extent, they reduce participation to a lesser extent.^{38,39} For example, participation in physical activity may be influenced by a wide range of individual factors, such as stroke severity, preexisting and comorbid conditions, motivation, fatigue, depression, adaptability and coping skill, cognition, and learning ability. In addition, societal and environmental influences such as program costs, means of transportation, accessibility, family support, social policies, and social stigmas can have a substantial influence on physical activity participation.⁴⁰

Stroke does not usually occur in isolation. Patients with stroke have a high prevalence of associated medical problems. These conditions may predate the stroke (“preexisting conditions”), occur for the first time after stroke (“poststroke sequelae”), or present as manifestations of preexisting medical conditions after stroke (eg, poststroke angina in patients with a history of coronary artery disease [CAD]). Other preexisting CVDs are present in the majority of poststroke individuals: high rates of CAD, chronic hypertension, atrial fibrillation, hyperlipidemia, metabolic syndrome, and diabetes mellitus.^{41,42} Although traditionally, stroke has not been considered a CVD, vascular health appears to have important implications for recovery from stroke, with low aortic stiffness being a biomarker of vascular integrity that is associated with favorable neurological outcomes at hospital discharge.⁴³

There is strong evidence for a clear inverse relation between physical activity and cardiovascular health.⁴⁴ There have been reports that 20% of patients admitted for stroke already

have moderate to severe disability⁴⁵ and 10% have dementia⁴⁶ before the stroke event. Poorer preexisting function measured by greater disability⁴⁵ or low physical activity⁴⁷ has been associated with greater stroke severity and poorer long-term outcomes. Obese patients with stroke who are referred to rehabilitation demonstrate less improvement in motor recovery and functional outcomes^{48,49} but may have decreased mortality rates compared with those who are underweight.⁵⁰

Collectively, the above-mentioned variables can create a vicious circle of decreased activity and greater exercise intolerance, which leads to secondary complications such as reduced cardiorespiratory fitness, increased fatigability, muscle atrophy/weakness, osteoporosis, and impaired circulation to the lower extremities in stroke survivors. In addition, diminished self-efficacy, greater dependence on others for activities of daily living, and reduced ability for normal societal interactions can have a profound negative psychological impact. This situation has several important implications for individuals with stroke and the professionals who counsel them. Coexisting cardiovascular conditions, whether they develop before or after stroke, can delay or inhibit participation in an exercise program, complicate the rehabilitation and long-term course of care, and limit the ability of the patient to perform functional activities independently.⁵¹ In fact, poststroke patients with CAD have 3 times as many cardiac complications during rehabilitation.⁵² A study characterizing patients at the time of recurrent stroke found that 75% had hypertension, 37% had ischemic heart disease, 56% had hyperlipidemia, 29% had atrial fibrillation, and 24% had diabetes mellitus.⁵³ Given the heightened risk of secondary cardiac complications and recurrent stroke, the poststroke period is a particularly important time to implement stroke secondary prevention interventions (eg, a post-stroke exercise program).⁴¹

Importance of Comprehensive Stroke Care and CVD Risk Reduction

The primary objectives of comprehensive care are stroke are to (1) reverse the deficits caused by the stroke and minimize their impact; (2) prevent, recognize, and manage secondary medical conditions, including recurrent stroke; (3) maximize independence in ability to perform activities of daily living; (4) facilitate psychological and social adaptation and coping by the patient and family; (5) optimize the resumption of prior life roles and reintegration into the community; and (6) enhance quality of life.⁵⁴ Although maximizing functional recovery and facilitating physical independence are often the defining goals of formal rehabilitation and long-term care, they are not the only focus areas of the poststroke care process. Preventing secondary conditions such as subsequent stroke and other cardiovascular events also constitutes an important function for stroke care professionals. This is particularly compelling in view of the fact that stroke is the fourth-leading cause of death and the leading cause of severe disability in the United States.¹

Overall, $\approx 30\%$ of stroke survivors will have recurrent stroke within their lifetimes, 18% of which will be fatal. Rates of recurrence are thought to differ between the sexes; within 5 years of a stroke, 24% of women and 42% of men can be

expected to experience a secondary stroke.^{55,56} Even young adults (aged <50 years) have a >10% recurrence rate of stroke within 5 years after a first-ever ischemic stroke, with atherothrombotic, cardioembolic, or lacunar subtypes having the highest risk.⁵⁷ Recurrent strokes have higher rates of mortality and are usually associated with increased severity of disability because of the reduced resilience of the remaining injured brain. Additionally, recurrent stroke is not the only concern; 5% will have a myocardial infarction within the first year after stroke, and 3% per year thereafter.⁵⁸ Manifestations of peripheral artery disease comprise additional complications, such as intermittent claudication, and other signs of leg ischemia may also occur. After stroke, healthcare professionals and stroke survivors tend to focus most of their rehabilitation on recovery, but the **prevention of a subsequent stroke, as well as CAD and peripheral artery disease, is also an important task.**

Understanding the epidemiology of ischemic stroke and its risk factors can facilitate the implementation of evidence-based measures to prevent subsequent strokes and other CVDs. Risk factors for ischemic stroke can be classified into 3 major groups: (1) nonmodifiable risk factors (including age, race, sex, and family history); (2) medically modifiable risk factors that can be altered by medical interventions such as pharmacological therapy or surgical procedures as indicated (including previous TIA, carotid artery disease, atrial fibrillation, CAD, other types of cardiac disease, hypertension, cigarette smoking, hyperlipidemia, hypercoagulability, diabetes mellitus, hormone replacement, inflammatory processes, and sickle cell disease); and (3) behaviorally modified risk factors that may be modulated by changes in lifestyle (including physical inactivity, obesity, alcohol abuse, drug abuse, oral contraceptive use, diabetes mellitus, cigarette smoking, hyperlipidemia, and hypertension).^{41,59,60} Because both CAD and ischemic stroke share links to many of the same predisposing, potentially modifiable risk factors (ie, hypertension, abnormal blood lipids and lipoproteins, cigarette smoking, physical inactivity, obesity, and diabetes mellitus), it is clear that lifestyle choices play a prominent role in the origin of stroke and CVD.⁵⁹ Modification of risk factors through a combination of comprehensive lifestyle interventions and appropriate pharmacological therapy is now recognized as the cornerstone of initiatives aimed at the prevention of recurrent stroke and acute cardiac events in stroke survivors.⁶¹

Physical activity is particularly important for the prevention of secondary complications related to recurrent stroke and other CVDs. There is emerging evidence (albeit from small controlled trials) of the beneficial impact of regular physical activity and exercise in stroke survivors on CVD risk factors, including hypertension,⁶² arterial function,⁶³ and insulin response.⁶⁴ Whether such benefits translate into a reduced risk for recurrent stroke and cardiac events is unknown; however, there is compelling evidence from large prospective cohorts that physical activity has a protective effect on CAD or first stroke, with a dose-response relationship.⁶⁵ **After stroke, exercise integrated into a comprehensive plan of care that includes diet modification and use of cholesterol-lowering medications, antihypertensive medications, and aspirin could lower the risk of a second stroke by 80%.⁶¹**

Furthermore, in formal recommendations of measures designed to prevent stroke and other CVDs, the promotion of increased physical activity and the implementation of physical exercise training are prominent as key components of a comprehensive stroke risk-reduction program.⁴¹ **This recommendation is not only important in primary stroke prevention but is also valuable for people who have sustained a prior stroke.** A formal recommendation was developed in a prior AHA statement⁴¹ that suggested that after an ischemic stroke or TIA, these individuals should engage in moderate-intensity physical activity on a regular basis. The effective dose and timing of physical activity are described in subsequent sections of the present statement. Proposed mechanisms by which exercise might lead to risk reduction are through its effects on lowering blood pressure and weight, increasing glucose tolerance, improving lipid levels, and reducing arterial inflammation. Aerobic exercise has been shown to improve glucose tolerance in people with stroke.⁶⁴ Reductions in blood pressure^{66,67} and improvements in total cholesterol⁶⁶ have been reported after moderate-intensity aerobic exercise in stroke survivors. The use of a comprehensive exercise and lifestyle program modeled after cardiac rehabilitation in people after a TIA and mild stroke was shown to yield improvements in total cholesterol, body composition, blood pressure, and behavior change toward nonsmoking.⁶⁸

Physical activity can be effective only if it is done consistently. Unfortunately, although physical activity is clearly established and widely recognized as a means to reduce the risk of stroke and other CVDs in virtually all individuals, **sedentary behaviors remain a persistent and significant problem for the general population, and even more so for chronic disease populations, including those with stroke.^{8,9}** Therefore, healthcare professionals should consider ways to educate stroke survivors and caregivers on the importance of cardiovascular risk reduction and help set goals for their continued participation in physical activity and exercise.

Goals of Prescribed Physical Activity and Exercise

After a stroke, the physical activity goals and exercise prescription for the patient need to be customized to the tolerance of the patient, stage of recovery, environment, available social support, physical activity preferences, and their specific impairments, activity limitations, and participation restrictions. **Immediately after an acute stroke, the first goals during poststroke rehabilitation relevant to physical activity and exercise are aimed at preventing complications of prolonged inactivity, regaining voluntary movement, and recovering basic activities of daily living.** Detrimental effects of bed rest include diuresis with significant losses of sodium and potassium, decreased volume of blood plasma, reduced cardiac output, depressed immune function, increased resting heart rate (0.5 bpm for each bed rest day), loss of muscle strength (eg, 25% loss of plantar flexor muscle strength over 5 weeks), reduced peak $\dot{V}O_2$ (0.8% daily loss), orthostatic intolerance, and increased risk of joint contractures and deep venous thromboembolism.⁶⁹ **Thus, during acute and inpatient rehabilitation, minimization of bed rest is critical, and simple**

exposure to orthostatic or gravitational stress (ie, intermittent sitting or standing) has been shown to obviate much of the deterioration in exercise tolerance that normally follows an acute hospital stay. Early mobilization (within 24 hours after stroke, and at regular intervals afterward) has been shown to result in earlier walking and improved functional recovery.⁷⁰


Once the patient is medically stable, the next goal is to initiate an exercise training regimen designed to **regain (or exceed) prestroke levels of activity as early and as much as possible.** Such activities typically occur within inpatient rehabilitation units or supervised community or home settings. Physical and occupational therapy is initiated to improve motor recovery (ie, gait, upper extremity function, balance, and muscle strength), motor skills, efficiency in self-care, and occupational and leisure-time activities. Emphasis is on progressive task difficulty, repetition, and functional practice.⁷¹ **It is recommended that interventions for motor recovery include cardiovascular and strengthening exercises.**⁷¹ Consequently, rehabilitation exercise programs designed to optimize functional motor performance in stroke survivors increasingly have incorporated aerobic exercise training that uses a variety of modalities (eg, treadmill, cycle ergometer, recumbent stepper, chest-deep water, functional exercises) to improve cardiorespiratory fitness, muscle strength, and functional mobility.¹⁵ Improving cardiorespiratory fitness increases submaximal exercise tolerance and endurance and consequently the ability to execute activities of daily living. **Aerobic treadmill exercise has been shown to increase peak $\dot{V}O_2$ while lowering the energy cost of walking after stroke.**⁷² Recent research studies have shown that early aerobic exercise is feasible (studies commencing within 6 days to 6 months after stroke)⁷³ and results in improvements in peak $\dot{V}O_2$ and walking distance.⁷³ It is in this supportive environment that patients (with their families and caregivers) can also learn to self-monitor their exertion and track physical activity in hospital, home, or community settings. It is critical for the patient to develop the skills and confidence for eventual self-management of physical activity and an exercise training program.

The third set of goals after stroke rehabilitation is designed to facilitate the stroke survivor to develop and maintain an active lifestyle that meets recommended physical activity and exercise guidelines for prevention of recurrent stroke and cardiac events, as well as to maintain or improve physical function. **Physical activities must consider the individual's functional limitations and comorbidities, as well as the individual's personal preferences, environment, and resources, and could range from an exercise program at home to an appropriate community or sport program.** Partnerships with healthcare professionals and community support groups may facilitate health promotion and long-term adherence to physical activity. The use of education or personalized, tailored counseling interventions has demonstrated mixed results on improving adherence to an exercise program and increasing physical activity after stroke. A physical activity counseling intervention (2 predischARGE individual sessions and 4 phone follow-up sessions) resulted in greater physical activity 9 and 52 weeks after the event in a sample of rehabilitation patients, of whom 20% were stroke patients.²⁴ In contrast, a similar

program facilitated stroke survivors to choose suitable types of physical activity (1 predischARGE session, 5 individual sessions, and 5 phone calls) but did not demonstrate any effect on physical activity over a 24-month period.⁷⁴ As well, 8 weekly 2-hour facilitated group meetings on self-management and secondary stroke prevention did not increase walking activity after 3 months.⁷⁵ The critical elements (number of sessions, mode of delivery, type of follow-up, and monitoring) of a successful physical activity counseling intervention have not been identified definitively. A system that requires the patient to be accountable for their health behavior appears to be promising. This integrated care model includes discussion of stroke prevention guidelines, predischARGE education on modifiable risk factors, 4 telephone interviews to determine health behavior profile, 5 prescheduled visits to the healthcare provider along with faxing of health profiles before each visit, and follow-up phone calls after each visit to review recommendations. The results of this integrated care model resulted in lower systolic blood pressure, lower body mass index, and a greater number of walks after 12 months.⁷⁶ **Regular physical activity and exercise can improve mobility¹⁵ and may help maintain bone density in individuals with chronic stroke.³² Low bone density, impaired balance, and frequent falls all contribute to the 2- to 7-fold increase in fracture risk within the first year of stroke.^{77,78}** Whether initiation of exercise early after stroke can prevent the loss of bone mineral density and deterioration of bone structure commonly seen after stroke or reduce fracture risk is currently unknown.⁷⁹

Cardiorespiratory exercise training in individuals many years after stroke can result in improvements in aerobic capacity and sensorimotor function.⁸⁰ Furthermore, there is a strong association between physical activity and risk of first stroke.⁸¹ An aerobic exercise program after stroke has been shown to enhance glucose regulation,⁶⁴ improve blood pressure,⁶⁶ and improve arterial function.⁶³ These findings are consistent with the growing body of evidence that interventions that promote plaque stability, favorable changes in vascular wall function, or both have important implications for the management of patients after a stroke or other vascular events.⁸² Although extrapolation of these data to the prevention of secondary strokes is unproven, mounting evidence suggests it is likely that improving cardiorespiratory fitness and engaging in regular physical activity or exercise after stroke has broad health benefits.

Preexercise Evaluation

 Exercise is a normal human function that can be undertaken with a high level of safety by most people, including those with stroke. However, exercise is not without risks, and although adverse events are not reported systematically in the literature, the recommendation that individuals with stroke participate in an exercise program is based on the premise that the **benefits outweigh these risks.** As is the case for the general population, the major potential health hazards of exercise for stroke survivors are also likely to include musculoskeletal injury and, in rare cases, sudden cardiac death. Perhaps more pertinent to the stroke population is an increased fall risk with mobility. **Falls may occur with exercise training, and when reported, they occurred in 13%³² to 25%⁸³ of intervention-group participants**

with stroke. Although habitual physical activity is associated with an overall reduction in the risk of sudden cardiac death in the general adult population, and the likelihood of experiencing a fatal cardiac event during exercise training is extremely small, it is well established that exercise can precipitate malignant ventricular arrhythmias.^{84–86} Moreover, several studies have now shown that the transiently increased risk of cardiac arrest that occurs during exercise results primarily from the presence of preexisting CAD, especially in habitually sedentary adults.^{87,88} Because up to 75% of stroke survivors have coexisting cardiac disease, and 20% to 40% of cases present with silent cardiac ischemia,^{89–91} the foremost priority in formulating the exercise prescription is to minimize the potential adverse effects of exercise via appropriate screening, program design, monitoring, and education.

Before embarking on a physical conditioning regimen after stroke, all participants should undergo a complete medical history, usually the most important part of the preexercise evaluation, and a physical examination aimed at the identification of neurological complications and medical comorbidities that require special consideration or constitute a contraindication to exercise. These may include assessment of neurological complications or other medical comorbidities and conditions and stroke-specific issues such as weakness or balance impairment, cognitive or behavioral issues, and communication issues.

It is recommended that individuals with stroke undergo graded exercise testing with ECG monitoring as part of a medical evaluation before beginning an exercise program.^{86,92} If the physician overseeing the patient's care determines an exercise test is not indicated or such an assessment in a given facility is not possible, the initiation of an exercise training program, individually tailored to a patient's physical capabilities, should not be delayed. Although there are limited data on the safety of graded exercise testing after a stroke,⁹¹ available evidence suggests that graded exercise testing is likely to be associated with an acceptably low risk of serious cardiovascular complications in stroke survivors.^{91,93} Such testing helps determine participants' exercise capacity and identify associated adverse signs or symptoms that may affect the safety of an exercise program.

Generally, graded exercise testing after stroke should be conducted in accordance with contemporary guidelines as detailed elsewhere.^{92,94} Briefly, the exercise test modality/protocol for stroke survivors is selected to optimally assess functional capacity and the cardiovascular response to exercise. The test should evaluate the heart rate, rhythm, and ECG response to exercise, as well as the systolic and diastolic blood pressure response. Careful assessment of the subjective response (especially cardiac symptoms) should be performed. Ratings of perceived exertion should be collected. The testing mode should be selected or adapted to the needs of the individual. A standard treadmill walking protocol can be used, with the aid of handrails if needed. The progressive workload of the Bruce protocol (3-minute stages commencing from stage 1, 1.7 mph at 10% incline, to stage 7, 6.0 mph at 22% incline) or its modified version (starting at a lower intensity of 1.7 mph at 0% incline) is appropriate for some participants, with a progressive workload achieved by increasing the speed and grade of the treadmill.⁹⁵ For those with limited walking

ability, however, other modalities and special protocols are needed that consider stroke-related issues such as hemiparesis and balance impairment and use small increments of workload increases to maintain reasonable test duration.^{96,97} Upright and semirecumbent cycle ergometry may be more applicable to a greater subset of the stroke survivor population, because these offer the advantage of seated support for individuals with impaired postural control, permit the feet to be affixed to the pedals to accommodate lower-limb dysfunction,⁹⁷ and increase safety for those with cognitive or behavioral issues.

Clinically relevant abnormalities indicative of elevated risk for acute cardiac events and mortality, such as ST-segment depression, angina pectoris, ventricular arrhythmias, ventricular tachycardia, or bundle-branch block, have been observed in $\approx 11\%$ of exercise tests in stroke survivors, although despite these abnormalities, the frequency of serious adverse events remains low, and thus, such testing provides important information for establishing safe and individualized exercise prescriptions.⁹³ There are, however, limitations to graded maximal exercise testing after stroke that should be considered. Firstly, unlike the standard care pathway for individuals attending cardiac rehabilitation programs, there is limited availability and access to cardiopulmonary exercise testing in most stroke clinical and community settings. Furthermore, tests performed on cycle ergometry are often subject to termination from localized muscle fatigue rather than from attainment of maximal aerobic capacity, and peak $\dot{V}O_2$ values are typically 5% to 10% lower than those achieved via treadmill testing.⁹⁸ Whether individuals with stroke achieve "true" maximal $\dot{V}O_2$ during graded exercise tests is not clear. After stroke, exercise tests are often terminated for noncardiopulmonary reasons,⁹⁷ and the ability to achieve maximal effort is associated with greater cognitive and motor impairment.⁹⁹ Total-body recumbent steppers that engage both the upper and lower limbs appear to be a possible alternative to traditional ergometers, and stroke survivors have been found to achieve higher peak $\dot{V}O_2$ and heart rate values using this modality.¹⁰⁰

In lieu of graded maximal exercise tests, submaximal tests may be considered for stroke survivors. Walk tests, such as the commonly used 6-minute walk test (6MWT), have been designed and used as surrogate measures of cardiorespiratory fitness in other populations, but associations between distance walked and peak $\dot{V}O_2$ are low to moderate.^{101–104} Given the presence of neuromotor and walking limitations after stroke that may confound test performance, results should be interpreted with caution. Predictive submaximal tests have also been studied after stroke, but clear recommendations regarding specific protocols are not yet available. Although a modest correlation with maximal tests has been reported, there were also nonsignificant associations with hemodynamic responses (heart rate, rate pressure product).¹⁰² Studies using cycle ergometry after stroke have been unable to demonstrate accurate predictive equations of peak $\dot{V}O_2$ based on exercise test performance,^{105,106} but a recent study that used total-body recumbent steppers found strong associations between actual and predicted peak $\dot{V}O_2$.¹⁰⁷

No studies have specifically addressed the issue of how soon after a stroke graded exercise testing can be performed safely. Until such data become available, good clinical

judgment should be foremost in deciding the timing of graded exercise testing after stroke and whether to use a submaximal or symptom-limited maximal test protocol. In the absence of definitive evidence, it may be prudent to follow guidelines similar to those recommended for individuals after myocardial infarction and use submaximal protocols (with a predetermined end point, often defined as a peak heart rate of 120 bpm, or 70% of the age-predicted maximum heart rate, or a peak metabolic equivalent [MET] level of 5).⁹² In the absence of definitive evidence, it also appears prudent to consider a systolic blood pressure >250 mmHg or diastolic blood pressure >115 mmHg an absolute (rather than relative) indication to terminate a graded exercise test after stroke.⁹² As is recommended for those with CAD, the upper limit of the target heart rate range for subsequent exercise training should generally be at least 10 bpm below the heart rate associated with blood pressure responses of this magnitude.⁸⁶

From a practical standpoint, it may not be possible, for a variety of reasons, for many stroke survivors to perform an exercise test before they begin an exercise program. For those with significant impairments or activity limitations that preclude exercise testing, pharmacological stress testing may be considered.⁹¹ For those for whom an exercise ECG is recommended but not performed, lower-intensity exercise should be prescribed. The reduced exercise intensity may be compensated for by increasing the training frequency, duration, or both. Depending on the severity of disability and other coexisting medical conditions, certain people may need to participate in a medically supervised exercise program.

In summary, evaluation of the stroke survivor for an exercise program is multidimensional and includes a careful medical history and physical examination. If flexibility and adaptability are used in the selection of testing protocols, most stroke survivors who are deemed stable for physical activity can undergo exercise testing. Consideration regarding the individual's medical and functional status should be given when the testing protocol and modality are being selected. Results from submaximal exercise tests may need to be interpreted with caution. If the evaluation is conducted with the aforementioned considerations, an exercise program can be highly beneficial and safe for stroke survivors.

Early Physical Activity and Rationale for Exercise-Based Rehabilitation

Given its detrimental impact on many body systems, prolonged bed rest, as advocated before the 1950s, is no longer recommended in the care of uncomplicated and clinically stable patients with acute coronary and other CVD events.¹⁰⁸ Nearly 3 decades ago, researchers measured peak $\dot{V}O_2$ in healthy subjects before and after 14 days of bed rest using daily treatments with a reverse-gradient garment that simulated the effects of standing. Aerobic capacity remained essentially unchanged in subjects who received treatment with reverse-gradient garments, whereas there was a significant decrease (14%) in nontreated (control) subjects.¹⁰⁹ Accordingly, simple exposure to orthostatic or gravitational stress appears to obviate a significant portion of the deterioration in functional capacity that normally follows an acute coronary or vascular event.¹¹⁰

In practice, early physical (out of bed) activity prescription is dependent on a range of factors that include patient stability (although what constitutes stability is not well defined), level of impairment, staff attitudes, and hospital protocols and processes. In the first 24 to 48 hours of stroke, simply getting out of bed has been shown to significantly increase heart rate, blood pressure, and oxygen saturation and improve conscious state.¹¹¹ However, not all acute stroke survivors can tolerate activity this early. Current clinical trials in this early time point should help refine safety criteria for early commencement and protocols for exercise in the first weeks after stroke.^{108,112}

When Should Physical Activity Begin After Stroke?

The consensus view throughout the world is that physical activity should begin early after stroke; however, how early remains controversial,¹¹³ and there are no specific protocols to guide the frequency, intensity, time, or type of physical activity in this early time frame. Recent small clinical trials have tested protocols promoting physical activity that commence within 24 to 72 hours of stroke onset, but results have been inconclusive.^{70,112,114–116} These data have important implications for inpatients and early post-hospital discharge activity recommendations, yet many studies have demonstrated low levels of physical activity among individuals in the early post-stroke phase.^{94,117–120}

Rationale for Physical Activity/Structured Exercise

In 2008, the US Department of Health and Human Services published physical activity guidelines for all Americans¹²¹ based, in part, on the Physical Activity Guidelines Advisory Committee Report,⁴⁴ which included a section on the relationship between physical activity and cerebrovascular disease and stroke. The research review concluded that “physically active men and women generally have a lower risk of stroke incidence or mortality than the least active, with more active people demonstrating a 25% to 30% lower risk for all strokes.” Moreover, the benefits appear to be derived from a variety of activity types, including activity during leisure time, occupational activity, and structured exercise (eg, walking).

Several clinical guidelines now recommend increased lifestyle physical activity and a structured exercise program after stroke.^{122–124} These recommendations are based on several lines of clinical evidence, including the extrapolation of data from other nonstroke populations. One study reported that 40% of stroke survivors believed that fatigue was either their worst symptom or one of their most debilitating symptoms, impairing their performance of activities of daily living and negatively affecting psychological functioning and quality of life.¹²⁵ It has been suggested that fatigue after stroke may be triggered by physical deconditioning, which precipitates a vicious, self-perpetuating cycle of fatigue, avoidance of moderate to vigorous physical activity, decreased aerobic reserves, further deconditioning, and more fatigue.³⁶ Indeed, a recent systematic review of relevant studies found that measured peak $\dot{V}O_2$ among selected samples of stroke survivors ranged from 8 to 22 mL·kg⁻¹·min⁻¹, which was 26% to 87% (≈53% overall) lower than that of age- and sex-matched healthy control subjects.⁸⁰ Time since stroke ranged from 10 days to >7

years, which indicates that a reduced level of cardiorespiratory fitness may well persist years after stroke.

On the basis of the available evidence, it is recommended that stroke survivors undertake regular aerobic exercise to increase aerobic capacity and improve gait efficiency, thereby reducing fall risk and enhancing functional independence, as well as reducing the risk of recurrent cardiovascular events.¹²⁶ In addition, resistance (strength) training is advocated to increase independence in activities of daily living, flexibility training to increase range of movement and prevent deformities, and neuromuscular training to enhance balance and coordination.¹²⁴

The prescription of exercise for the stroke survivor is comparable in many ways to the prescription of medications; that is, one recommends a safe and effective dosage (ie, frequency, intensity, time, type) according to individual functional capacity and limitations, while simultaneously attempting to avoid underdosing or overdosing.¹²⁷ Stroke survivors who may be at risk for exertion-related cardiovascular events should be considered for peak or symptom-limited exercise testing¹²⁴ before they begin a vigorous exercise training program (ie, 60%–89% of heart rate reserve or $\dot{V}O_2$ reserve or ≥ 6.0 METs, where $\dot{V}O_2$ reserve = percent intensity \times [peak $\dot{V}O_2$ – resting $\dot{V}O_2$] + resting $\dot{V}O_2$).¹²⁸ On the other hand, empirical experience and previous studies have demonstrated the safety and effectiveness of early outpatient, medically supervised exercise rehabilitation using adjunctive intensity modulators (ie, rating of perceived exertion [11–12 on the 6–20 scale] or the patient's resting heart rate plus 20 bpm) and continuous ECG monitoring, without a preliminary peak exercise test.¹²⁹ Joo et al¹³⁰ reported that on average, this methodology corresponded to $\approx 42\%$ $\dot{V}O_2$ reserve among patients entering a phase 2 cardiac rehabilitation program, an intensity that approximates the minimum or threshold intensity for improving cardiorespiratory fitness in this patient subset.¹³¹ Such reduced exercise intensities may be compensated for in part by increasing the training frequency, duration, or both.

Aerobic training modes for stroke survivors may include leg, arm, or combined arm-leg ergometry at the appropriate intensity, as described previously.¹²⁷ Because symptomatic or silent myocardial ischemia may be highly arrhythmogenic,¹³² the target heart rate for endurance exercise should be set safely below (≥ 10 bpm) the ischemic ECG or anginal threshold.¹³³ The recommended frequency of training is ≥ 3 days per week, with a duration of 20 to 60 minutes per session depending on the patient's functional capacity. However, for many stroke survivors, multiple short bouts of moderate-intensity physical exercise (eg, three 10- or 15 minute exercise bouts), repeated throughout the day, may be better tolerated (eg, interval training, a work-rest approach) than a single long session. Structured exercise interventions should be complemented by an increase in daily lifestyle activities (eg, walking breaks at work, gardening, household chores) to improve fitness and move patients out of the least fit, least active high-risk cohort.¹³⁴

Treadmill walking appears to offer 3 distinct advantages in the exercise rehabilitation of stroke survivors.¹²⁴ First, it requires the performance of a task required for everyday living, namely, walking, which should enhance the generalizability of training effects. Second, the use of handrail

support and unweighting devices such as harnesses that lift patients, effectively decreasing their weight, allows patients who might otherwise be unable to exercise to walk on a treadmill. Finally, in patients with residual gait and balance limitations that preclude walking at faster speeds, exercise intensity can be augmented by increasing the treadmill grade. Because most stroke survivors may prefer to walk at moderate intensities, it is helpful to recognize that walking on level ground at 2 or 3 mph corresponds to ≈ 2 and 3 METs, respectively.¹³⁵ At a 2-mph walking speed, each 3.5% increase in treadmill grade adds ≈ 1 MET to the gross energy cost. For patients who can negotiate a 3-mph walking speed, each 2.5% increase in treadmill grade adds ≈ 1 MET to gross energy expenditure.¹³⁵

To maximize the specificity of training adaptations to daily activities, adjunctive muscular strength and endurance exercises are also advocated for clinically stable stroke survivors, by use of resistance-training programs.^{124,127} Because the hemodynamic response to resistance exercise is largely proportional to the percentage of maximal voluntary contraction,¹³⁶ increased muscle strength results in an attenuated heart rate and blood pressure response to any given load, because the load now represents a lower percentage of maximal voluntary contraction.¹³⁷ Thus, resistance training can decrease cardiac demands during daily activities such as carrying groceries or lifting moderate-weight to heavy objects.¹³⁸ Although there are no research-based guidelines for determining when and how to initiate resistance training after ischemic or hemorrhagic stroke, it may be prudent to prescribe 10 to 15 repetitions for each set of exercises (eg, higher repetitions with reduced loads), similar to that recommended for patients after myocardial infarction.^{124,127} Such regimens should be performed 2 to 3 days per week and include a minimum of 1 set of 8 to 10 different exercises that involve the major muscle groups of the torso, as well as the upper and lower extremities. Adjunctive flexibility and neuromuscular training, including yoga¹³⁹ and tai chi,¹⁴⁰ have also been reported to be beneficial in improving balance, quality of life, and mental health while reducing the fear of falling.

Few data are available regarding the effectiveness of suitably modified exercise programs for patients who are unable to walk after stroke and those with difficulties in communicating, because these patients have been underrepresented in previous trials.¹⁴¹ The role of complex interventions, such as interactive computer and active-play video games,^{142,143} should be evaluated in stroke survivors. Laver et al¹⁴³ reviewed the role of virtual reality and interactive video gaming as new treatment approaches in stroke rehabilitation. Although there was insufficient evidence regarding the impact of these potential therapies on gait speed, some studies suggested that these may be beneficial in improving arm function and in the performance of activities of daily living. Active-play video games require both upper- and lower-limb movement, which has the potential to allow players to reach moderate to vigorous levels of physical activity.¹⁴⁴ One study in healthy adults that used an open-circuit indirect metabolic chamber reported a wide range of energy expenditures (1.3 to 5.6 METs) during Wii Sports and Wii Fit Plus game activities.¹⁴⁵ Exercise programming recommendations for stroke survivors are summarized

in the Table. Structured treadmill or cycle ergometer exercise regimens should be complemented by muscular strength/endurance and flexibility training, as well as increased daily lifestyle activities (eg, walking breaks at work, gardening, self-care, and household chores).¹⁴⁶ Additional neuromuscular activities that may be beneficial for stroke survivors include tai chi, yoga, modified recreational activities with paddles/balloons or sport balls, and active-play video/computer gaming.

Cardiovascular, Cognitive, and Functional Outcome Measures

A recent review that summarized the reported outcomes of numerous randomized controlled trials of structured aerobic exercise and muscle resistance training after stroke concluded that cycle ergometry and intensive treadmill training can increase aerobic capacity and improve walking performance.¹⁴⁷ Resistance training enhanced muscular strength but had only modest or no transfer in bettering gait performance. A structured aerobic exercise intervention has been found to be beneficial for enhancing the vascular health of people with subacute

stroke, as assessed by preconditioning versus postconditioning improvements in brachial artery vasomotor reactivity (flow-mediated dilation) and physical performance on a 6MWT.⁶⁷

Physical activity reduces the risk of cognitive impairment, mainly vascular dementia, in older people living independently.¹⁴⁸ There is also evidence that exercise has positive effects on depression¹⁴⁹ and cognition¹⁵⁰ in adults without stroke, and there are preliminary findings that exercise may confer similar effects after stroke.^{18,21} Although few studies have investigated the impact of fitness training on cognition and mood after stroke, a recent report^{21,151} using combined aerobic and resistance training noted improvements in overall cognition and in the subdomains of attention/concentration and visuospatial/executive function. Moreover, there was a 44.5% reduction in the proportion of patients meeting the threshold criteria for mild cognitive impairment at posttraining compared with baseline assessments. **Collectively, these data and other recent comprehensive reviews¹⁵ suggest that structured aerobic exercise, including walking, is beneficial for stroke survivors, improving ambulatory ability and the performance of daily**

Table. Summary of Exercise/Physical Activity Recommendations for Stroke Survivors

Setting/Mode of Exercise	Goals/Objectives	Prescriptive Guidelines: Frequency/Intensity/Time
Hospitalization and early convalescence (acute phase)	<ul style="list-style-type: none"> Prevent deconditioning, hypostatic pneumonia, orthostatic intolerance, and depression Evaluate cognitive and motor deficits Stimulate balance and coordination 	<ul style="list-style-type: none"> ≈10- to 20-bpm increases in resting HR; RPE ≤11 (6–20 scale); frequency and duration as tolerated, using an interval or work-rest approach
Inpatient and outpatient exercise therapy or “rehabilitation”		
Aerobic	<ul style="list-style-type: none"> Increase walking speed and efficiency Improve exercise tolerance (functional capacity) Increase independence in ADLs Reduce motor impairment and improve cognition Improve vascular health and induce other cardioprotective benefits (eg, vasomotor reactivity, decrease risk factor) 	<ul style="list-style-type: none"> 40%–70% $\dot{V}O_2$ reserve or HR reserve; 55%–80% HR max; RPE 11–14 (6–20 scale) 3–5 d/wk 20–60 min/session (or multiple 10-min sessions) 5–10 min of warm-up and cool-down activities Complement with pedometers to increase lifestyle physical activity
Muscular strength/endurance	<ul style="list-style-type: none"> Increase muscle strength and endurance Increase ability to perform leisure-time and occupational activities and ADLs Reduce cardiac demands (ie, RPP) during lifting or carrying objects by increasing muscular strength, thereby decreasing the % MVC that a given load now represents 	<ul style="list-style-type: none"> 1–3 sets of 10–15 repetitions of 8–10 exercises involving the major muscle groups at 50%–80% of 1RM 2–3 d/wk Resistance gradually increased over time as tolerance permits
Flexibility	<ul style="list-style-type: none"> Increase ROM of involved segments Prevent contractures Decrease risk of injury Increase ADLs 	<ul style="list-style-type: none"> Static stretches: hold for 10–30 s 2–3 d/wk (before or after aerobic or strength training)
Neuromuscular	<ul style="list-style-type: none"> Improve balance, skill reacquisition, quality of life, and mobility Decrease fear of falling Improve level of safety during ADLs 	<ul style="list-style-type: none"> Use as a complement to aerobic, muscular strength/endurance training, and stretching activities 2–3 d/wk

1RM indicates 1 repetition maximum; ADLs, activities of daily living; HR, heart rate; MVC, maximal voluntary contraction; ROM, range of motion; RPE, rating of perceived exertion (6–20 category scale); RPP, rate-pressure product; U/L, upper/lower; and $\dot{V}O_2$, oxygen uptake.

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activities. This is highly relevant given that the prevalence of depression among stroke survivors is $\geq 30\%$ ¹⁵² whereas a stroke doubles an individual's risk for dementia (including Alzheimer disease).¹⁵³ Well-designed trials are needed to clarify optimal exercise programming and long-term outcomes of physical conditioning in this patient population, including morbidity, mortality, dependence, and disability.

Exercise Across the Continuum of Stroke Care

Cardiorespiratory Response to Acute Exercise in Stroke Survivors

The cardiac response to acute exercise (primarily during exercise testing) among stroke survivors has been documented in a small number of studies.^{154–156} Stroke survivors have been shown to achieve significantly lower maximal workloads, heart rate, and blood pressure responses than control subjects during progressive exercise testing to volitional fatigue.^{157,158} Other earlier studies, which used various adapted ergometry devices or exercise protocols with smaller sample sizes, yielded similar findings.^{159–162} In general, $\dot{V}O_2$ at a given submaximal workload in stroke survivors is greater than in healthy subjects, possibly because of reduced mechanical efficiency, the effects of spasticity, or both. In contrast, peak $\dot{V}O_2$ is reduced in these stroke survivors. However, a recent study demonstrated that stroke survivors can exercise at or above target minutes and the intensity necessary for cardiac rehabilitation.⁹³ To improve the cardiorespiratory response and acquire health benefits from exercise, more research is needed regarding stroke-adapted cardiac rehabilitation models.

Acute Phase of Stroke Recovery

Little to no information is available for aerobic exercise during the acute stage of stroke recovery; however, evidence is starting to emerge that supports early physical activity with a focus on mobility, often termed *early mobilization*. A pilot study (A Very Early Rehabilitation Trial for Stroke [AVERT]) assessing the feasibility and safety of a frequent mobilization program commencing within 24 hours after stroke was performed.¹¹⁴ Seventy-one patients during the first 24 hours after stroke were randomized to either receive standard of care or very early mobilization. Those in the early mobilization group started out-of-bed or upright activity, including standing and walking, at frequent intervals within 24 hours of stroke onset. There was no significant difference in the number of deaths between the 2 groups. Furthermore, secondary safety measurements were similar between the standard-of-care group and the very early mobilization group. Therefore, starting physical activity within the first 24 hours of stroke symptoms was observed to be safe and feasible. This trial⁷⁰ suggests that early and frequent mobilization starting within 24 hours of first onset of stroke symptoms is independently associated with improved functional outcomes as measured by the Barthel Index and the Rivermead Motor Assessment at 3 months after stroke and may improve the rate of walking recovery. Confirmation of these preliminary findings is necessary in a larger randomized controlled trial (under way).¹⁵¹ Furthermore, there remains a great need for additional experimental studies to be performed during the acute stages of

stroke recovery to establish whether the use of higher doses of physical activity commenced early after stroke slows or prevents loss of cardiorespiratory fitness and to develop detailed recommendations for frequency, intensity, time, and type of exercise to be prescribed to this population.

Subacute Phase of Stroke Recovery

Evidence continues to support exercise training for improvement of cardiorespiratory fitness during subacute stroke.^{12,73,163} Individuals in the subacute stage of recovery demonstrate low cardiorespiratory fitness levels similar to those findings in chronic stroke.^{67,164–166} Routine physical therapy appears to provide a mean of only 3 minutes of low-intensity aerobic training ($\geq 40\%$ of heart rate reserve) per session, which defines a gap in exercise provision across the subacute stroke phase.¹⁶⁴ Few randomized studies are available to guide exercise recommendations across the subacute recovery period.

Cycle ergometers have been used in several studies to examine the effect of aerobic exercise interventions on functional capacity, such as the 6MWT and stair climbing in stroke survivors.^{167,168} A supervised home-based exercise program using a cycle ergometer demonstrated improvements in peak $\dot{V}O_2$ and walking speed (using the Timed Up and Go test) and endurance (using the 6MWT).¹⁶⁹ Tang et al¹⁶⁸ assigned stroke survivors to either an exercise group using a cycle ergometer plus standard stroke rehabilitation or standard rehabilitation alone. Both groups improved from baseline measures during an average length of stay of only 9 days, but the exercise intervention group demonstrated greater improvements in peak $\dot{V}O_2$ and 6MWT distance.

Treadmill training is another option for participating in aerobic exercise. A randomized controlled trial compared standard of care in rehabilitation to a group receiving standard of care plus body weight–supported treadmill training.¹⁷⁰ A more recent study used a novel method for a walking exercise intervention. The authors tested whether robot-assisted gait training may be a potential avenue to facilitate improvements in cardiorespiratory function early after stroke. Chang et al¹⁶⁵ performed a study in which participants assigned to the intervention group received 40 minutes of gait training along with 60 minutes of standard physical therapy every day for 2 weeks. Control patients received 100 minutes of standard physical therapy for the 2-week period. The robot-assisted gait-training group demonstrated a 12.8% improvement in peak $\dot{V}O_2$ compared with the control group. Furthermore, patients who received the robot-assisted gait training increased their lower-extremity Fugl-Meyer assessment score and strength compared with control subjects. Hence, robot-assisted gait training may offer new inroads toward improving functional motor and cardiorespiratory health in subacute stroke, in conjunction with conventional physical therapy. Treadmill training can be used to increase cardiovascular fitness and improve walking in subacute stroke survivors. For balance and safety concerns, a body-weight support system can be used in conjunction with the treadmill.

An 8-week aerobic exercise intervention reported positive findings on cardiorespiratory health and physical function of patients in the subacute phase after stroke.⁶⁷ During an 8-week aerobic exercise intervention, 9 participants exercised at 50% to 59% of heart rate reserve for 4 weeks followed by

60% to 69% of heart rate reserve for the remaining 4 weeks. However, at 50% to 59% of heart rate reserve, only 70% of the exercise time was spent in the prescribed range. Only 63% of the exercise time was spent in the higher-intensity range (60%–69% of heart rate reserve). Baseline and postintervention assessments included the 6MWT, a peak exercise test, and flow-mediated dilation of the brachial artery for vascular health. At baseline, there were between-limb differences in brachial artery vasomotor reactivity through flow-mediated dilation, and participants had low peak $\dot{V}O_2$. After the intervention, improvements were noted in resting systolic blood pressure, flow-mediated dilation in bilateral brachial arteries, 6MWT distance, and peak $\dot{V}O_2$. Aerobic exercise in subacute stroke survivors facilitated improvements in cardiorespiratory and vascular health and improved the risk factor profile. Although this is 1 study, more research is needed to examine exercise prescription parameters (frequency, intensity, time) in the subacute stage of stroke recovery, for example, shorter bouts versus longer bouts of exercise time and exercise intensity (high intensity versus moderate intensity).

On the basis of the available literature, aerobic exercise in the subacute stages of stroke recovery has beneficial effects on cardiorespiratory health, functional outcomes, and cardiac risk reduction.^{67,73,169}

Chronic Phase of Stroke Recovery

It has been well established that aerobic exercise initiated during the chronic stage of stroke recovery has beneficial effects on cardiorespiratory health. Seminal aerobic exercise training studies in chronic stroke survivors demonstrated cardiovascular improvements (blood pressure response), reduced energy expenditure at submaximal efforts, and increased peak $\dot{V}O_2$.^{12,72,171} These data suggest that aerobic exercise training and improved cardiovascular fitness might enable activities of daily living to be performed at a lower percentage of aerobic capacity.

Lennon and colleagues¹⁷² implemented a 10-week program either consisting of standard of care or standard of care plus cycle ergometry sessions and 2 stress management sessions. Those who participated in aerobic exercise in the form of cycle ergometry exhibited significantly greater improvements in peak $\dot{V}O_2$ and cardiac risk at follow-up than those who only received standard of care. These findings suggest that aerobic exercise implemented during the chronic stages of stroke facilitates improvements in cardiorespiratory parameters.

Although most studies have used traditional exercise prescription parameters, recent studies have begun to examine high-intensity training. Two randomized controlled studies using high-intensity training at 60% to 80% of heart rate reserve reported improved peak $\dot{V}O_2$ at the end of the training intervention compared with the control group. Globas and colleagues¹⁷³ compared a 3-month progressive, high-intensity aerobic treadmill exercise intervention (n=18) with a conventional care physical therapy group (n=18). Results suggested that high-intensity treadmill training facilitates greater improvements in peak $\dot{V}O_2$, with the experimental group improving whereas control subjects did not. Furthermore,

the intensity of training directly correlated with the degree of improvements observed in peak $\dot{V}O_2$. After 1 year, peak $\dot{V}O_2$ continued to be significantly higher than baseline measures in the treadmill training group.

A recent single-cohort study examined high-intensity (85%–95% of peak heart rate from an exercise test) uphill treadmill walking in four 4-minute work periods, with a 3-minute active recovery between each bout.¹⁷⁴ Primary outcome measures were peak $\dot{V}O_2$ and walking economy. Despite a small sample size (n=8), significant gains in peak $\dot{V}O_2$ were found that were maintained at a 1-year follow up. However, the improvement in walking economy immediately after the intervention was not maintained at the 1-year follow-up.

Strength training also has been found to have beneficial effects in stroke survivors. Several observational studies have shown strong associations between paretic knee-extension torque and locomotion ability and between both hip flexor and ankle plantar flexor strength of the paretic limb and walking speed after stroke.^{175–177}

Results from prospective trials suggest benefit may be accrued through poststroke resistance-training programs. A 12-week, twice per week, progressive resistance-training program demonstrated positive improvements in muscle strength, gait, and balance in stroke subjects.¹⁷⁸ Lower-limb strength increased 68% on the affected side and less so on the intact side. Transfer time, motor performance, and static and dynamic balance also showed improvements. These results confirmed those of a previous study that showed benefits of strength training of the hemiparetic knee.¹⁷⁹ More recently, a pre-post study design tested whether strength training the lower extremities at 85% to 95% of 1 repetition for a maximum of 3 days per week would improve muscle strength, walking, and peak $\dot{V}O_2$. The authors reported that lower-extremity strength significantly improved, as did walking (6MWT distance and Timed Up and Go test), but not peak $\dot{V}O_2$.¹⁸⁰

There are few studies that have examined the long-term benefits of exercise after stroke. A recent study reported on a 4-year follow-up after a 10-week randomized, controlled resistance exercise training program using 80% of 1 repetition a maximum of twice weekly. Four years after intervention, the resistance-training group continued to demonstrate significant differences in muscle strength compared with the control group; however, no between-group differences were found for walking performance on the Timed Up and Go test or 6-MWT.¹⁸¹

Collectively, these findings support the use of regular exercise to improve overall health after stroke, which is consistent with consensus statements on exercise for able-bodied individuals.¹²¹ Because increased levels of physical activity are associated with a reduced risk for stroke and CAD and enhanced physical and psychosocial performance, such interventions performed in a stroke rehabilitation program and in the community may have a favorable effect on the prevention of recurrent stroke and cardiovascular events. Accordingly, professionals who design and conduct stroke rehabilitation programs should consider allocating more time to aerobic exercise training and muscle strengthening to optimize patient outcomes.

Motivators and Barriers to Physical Activity and Exercise Training

Most of the current evidence concerning the benefits of physical activity and exercise after stroke is from trials that recruited ambulatory stroke survivors. Implementation of this evidence, even for ambulatory stroke survivors, is not straightforward, because simple advice in and of itself does not increase physical activity after stroke.⁷⁴ By understanding the barriers and motivators to physical activity after stroke, we may be better able to advise stroke survivors to participate in physical activity.¹⁴¹ The promotion of physical activity in more disabled stroke survivors is likely to be even more challenging.

There are several reasons why exercise might not be performed with adequate frequencies or intensities to facilitate risk reduction,^{83,182–184} including patient-related factors (eg, depression, fatigue, lack of interest or motivation, lack of perceived self-efficacy, negative belief systems concerning exercise, and fear [of falling, subsequent stroke, and other adverse events]), practical reasons (eg, lack of family or other social supports, lack of availability of fitness resources, lack of transportation, lack of awareness of the availability of fitness services amongst health professionals), and cost. A systematic review of 6 articles reported on perceived barriers and motivators to exercise in 174 stroke survivors, most of whom were already taking part in physical activity research.¹⁸⁵ The most commonly reported barriers were environmental (access, transport, cost), health problems, stroke-related impairments, embarrassment, and fear of recurrent strokes.^{40,62,186–188} Lack of knowledge about how and where to exercise and about the potential benefits of exercise⁴⁰ and lack of motivation were also found to be barriers.^{40,186}

The most commonly reported motivator was the possibility of meeting other stroke survivors, thus providing psychological and social support,^{62,186–188} and the benefit of professional support in guiding and facilitating physical activity.^{62,187,188} Other motivators included (1) the use of group exercise classes, because participants did not want to let class members down by not attending^{186,188}; (2) the desire to carry out normal daily tasks^{186–188}; and (3) for male participants, the self-reported functional benefit, including a resumption of driving.¹⁸⁸ A subsequent study suggested that fitness instructors working in the community should be properly trained to deliver exercise to stroke survivors. These barriers and motivators appear to be different in older people; a large European survey found that the 3 most frequently cited barriers with advanced age were poor health (57.7%), lack of capacity (43.0%), and lack of interest (36.7%).¹⁸⁹

Since this systematic review by Carroll et al,¹⁸⁵ several relevant studies have been published. In a quantitative study of 14 stroke survivors, the most common motivating factors were to improve overall health, improve functional capacity, enhance confidence and reduce musculoskeletal issues, whereas lack of motivation, musculoskeletal issues, and fatigue were the most commonly reported barriers.¹⁹⁰ In a qualitative study with 11 community-dwelling stroke survivors, good balance and qualified personnel to deliver the intervention were important.¹⁸² In a survey of exercise preferences in 23 stroke survivors and 42 healthy control participants,³⁰ some preferred organized group sessions, whereas others preferred to exercise with family or to incorporate exercise into their daily routine.

The perceived barriers identified in the systematic review included those likely to reduce self-efficacy, that is, individuals' beliefs that they can engage in the activity. In a survey of 312 stroke survivors, self-efficacy, outcome expectations, and physician recommendations all influenced self-reported activity after stroke,¹⁸³ although these factors accounted for only 30% of the variance in exercise behavior. Theory can be used to develop an intervention to improve self-efficacy and outcome expectations for exercise and, by extension, improve exercise behavior.¹⁹¹ It is possible to change health beliefs about susceptibility to stroke and the perceived benefit of exercise to reduce risk using a psychological intervention designed to modify stroke survivors' readiness to exercise and beliefs about physical activity.¹⁹² Whether this increases the amount of exercise in stroke survivors will need to be explored further.

How might we put this evidence into practice? Physical barriers such as costs and lack of transportation should ideally be removed, and stroke survivors should have access to exercise guidance delivered by instructors with suitable knowledge and training.¹⁸² The provision of social support appears important; adherence to exercise may be better if it is done in a group.³⁰ Professional advice to increase activity is perceived to be important, but professional advice on its own is unlikely to increase physical activity.⁷⁴ Health and exercise professionals should understand that enhancement of self-efficacy and outcome expectations and allowing patients to establish goals might all help with the uptake of exercise; and stroke survivors should be reassured that exercise is likely to reduce (rather than increase) the risk of a recurrent stroke⁶¹ and may improve fatigue.²³

Healthcare professionals are in a position to help establish appropriate exercise prescription and programming in the longer term. For example, if a stroke survivor had already started exercise training in the hospital, information about the mode of training, duration, and intensity achieved in the hospital is highly relevant to fitness instructors who will work with the stroke survivor after discharge from hospital.

In summary, several barriers and motivators to physical activity have been identified in the literature. Addressing these barriers and building on the motivators may increase participation with physical activity.

Treatment Gaps and Future Research Directions

Adherence to physical activity and exercise recommendations is critical to promote effectiveness but difficult to achieve in practice. Despite the availability of national guidelines for risk factor management, there remain large treatment gaps. These gaps exist between the practices recommended by the guidelines for clinicians to provide to stroke survivors and the actual physical activity— and exercise-prescribing behaviors practiced by clinicians. Historically, the intensity of stroke rehabilitation interventions was insufficient to induce aerobic challenge.⁹⁴ Although the importance of implementing exercise training into neurological rehabilitation programs is now recognized, intensity is still primarily determined on the basis of observation and subjective reports rather than objective measures such as peak heart rate or peak $\dot{V}O_2$.¹⁹³

There also are significant gaps between the recommendations made to patients by clinicians who adhere to the guidelines and the actual behaviors performed by the patients. Lack of adherence to stated guidelines by clinicians and patients accounts for a great deal of the failure by patients at heightened risk for stroke and other cardiovascular events to achieve health lifestyles.¹⁹⁴ Clearly, there is an urgent need to bridge these treatment gaps by developing and implementing approaches that provide all stroke survivors with access to effective, comprehensive stroke risk-reduction interventions, including exercise.¹⁹⁵ It is also important to ensure that health professionals and the clients they serve follow the recommendations provided.

Since the original recommendations were published in 2004, there has been steady growth in the body of research examining the effects of physical activity and structured exercise programs after stroke. There is now a solid foundation of evidence regarding the benefits of such interventions on improving aerobic capacity and walking ability in this population,^{12,15} but gaps remain in our knowledge, and there are many areas yet to explore through ongoing research.

Examining the Influence of Exercise on Free-Living Physical Activity

Although the effectiveness of exercise interventions in improving gait speed and ambulatory capacity is well established,^{12,15} whether and to what extent these changes translate to actual increases in free-living physical activity is not yet known. Self-report questionnaires may be used to capture this information but lack the accuracy of more objective methods of collecting physical activity data in real time. Given that stroke survivors often present with slower gait speeds and asymmetrical patterns, triaxial accelerometers are superior to standard pedometers or uniaxial accelerometers in measuring physical activity in this population.^{8,29} To date, these devices have largely been used to measure physical activity under research conditions. As devices have become more comfortable to wear, cheaper, and more robust, with longer battery life, we are seeing them used more broadly. In the future, accelerometry may be used as a primary outcome in clinical trials to measure changes in free-living physical activity as a result of participation in exercise programs, as a method of tracking intervention compliance in programs, or even as a motivational or self-management tool for participants.

Benefits to Cardiovascular Health and Lowered Risk for Secondary Events

We need to better understand the influence of physical activity and exercise training on the long-term cardiovascular health of stroke survivors. The inverse association between aerobic capacity and CVD risk is well established in healthy populations,¹⁹⁶ as is the association between sedentary behavior and cardiovascular risk.^{197–199} As discussed in previous sections, for stroke survivors, the effects of exercise on reducing occurrence of secondary events, or on outcomes related to cardiovascular health (eg, mortality, vascular risk factors), are either not known or not well established.¹⁵ Aerobic exercise training after stroke has been shown to improve insulin sensitivity⁶⁴ but not lipid profiles,¹⁷² and the evidence regarding

training-related improvements in blood pressure and heart rate has been conflicting.^{66,167,171,172} To date, we lack prospective studies with long-term follow-up evaluating the effects of poststroke physical activity levels or exercise on the hard end points of all-cause or cardiovascular-related mortality or the incidence of recurrent events. Such studies would significantly improve the evidence base for exercise prescription to reduce cardiovascular risk.

Exploring Effective Models of Care

What is the best model to support an overall increase in physical activity and exercise training as a key component of secondary prevention? Behavioral interventions are effective in changing lifestyle behaviors after stroke.²⁰⁰ In noncontrolled studies, hospital treatment utilization rates (medications, education on lifestyle factors) were increased when secondary stroke prevention strategies were initiated early²⁰¹ and continued through outpatient care and after discharge,²⁰² and a randomized controlled trial is currently under way to compare the effectiveness of usual care versus in-hospital and ongoing education through stroke community health workers on control of stroke risk factors and knowledge of stroke and lifestyle modification.²⁰³

Secondary prevention programs may also be modeled after comprehensive risk factor modification programs such as cardiac rehabilitation. Core components of this model of care include participant assessment, exercise training, nutritional counseling, management of risk factors (blood pressure, lipids, weight, diabetes mellitus, smoking, physical activity), and psychosocial interventions,²⁰⁴ all of which are also relevant to individuals with stroke. The effectiveness of these exercise-based programs in reducing mortality and hospital admissions for individuals with CAD are well established.²⁰⁵ Moreover, behavioral interventions focused on education, self-management, and goal setting have been shown to be more effective than traditional cardiac rehabilitation interventions for individuals with cardiac disease.²⁰⁶ The application of cardiac rehabilitation models to stroke has been the focus of recent work. Studies have established the feasibility and effectiveness of adapting exercise-based cardiac rehabilitation interventions for individuals with mild to moderate disability from stroke,^{172,207} and comprehensive models that integrate exercise, lifestyle modification, and medications have been shown to be beneficial for individuals after TIA or stroke with little to no residual deficits.^{68,208} Larger clinical trials are currently under way to examine whether similar models of care involving exercise and risk factor modification can be adapted and implemented among individuals with TIA or a broader range of clinical presentation after stroke.^{209,210} These trials represent important steps toward the development of optimal secondary prevention strategies that integrate exercise interventions into a comprehensive risk-reduction program for stroke survivors.

Concurrent Benefits to Markers of Vascular Health

Silent ischemic strokes resulting from vascular disease are also an important consideration, given their high prevalence and significant clinical and public health impact.^{211,212} These

subclinical events manifest as cognitive decline and dementia and are associated with cardiovascular risk factors such as hypertension, dyslipidemia, and diabetes mellitus^{213,214} that may be mediated through exercise and physical activity. Indeed, higher physical activity levels were associated with lower risk of silent brain infarcts among older adults without history of stroke,²¹⁵ and enhanced physical activity and fitness can improve cognitive function in older adults without known impairment.¹⁵⁰ Among stroke survivors, there is some evidence demonstrating improved cognition after exercise,^{19–21,216} but the mechanisms that underlie these changes are not known. Future clinical trials may build on the evidence concerning the effects of exercise on neuroplastic changes in animal models²¹⁷ to bridge the gap between basic science and human stroke research. Ongoing work may examine the effects of exercise on cognition concurrent with changes in cardiovascular health, including vascular risk factors such as blood pressure, lipid profiles, glucose control and insulin sensitivity, and markers of brain health, such as white matter hyperintensity volume, brain-derived neurotrophic factor levels, and B-amyloid plaque formation.

Economic Analyses

There are significant economic costs associated with stroke. Direct and indirect costs of stroke are \$65.5 billion in the United States alone and €27 billion in the European Union.²¹⁸ The potential for exercise and physical activity as a secondary prevention strategy would also have economic benefits. Intervention-related cost-benefit analyses may include morbidity, mortality, and hospitalization rates; productivity; and quality of life-years.²¹⁹ Economic evaluations related to exercise interventions will provide additional evidence to support their use as a secondary prevention strategy.

Capitalizing on Technology

Novel methods of supporting exercise and physical activity in stroke survivors should also be explored and developed. Information and communication technologies have already been used successfully with other chronic disease populations, including CAD, hypertension, and diabetes mellitus.²²⁰ Mobile phone telemonitoring was effective for maintenance of regular exercise among individuals with chronic obstructive pulmonary disease,²²¹ and telemedicine-based cardiac rehabilitation programs have derived comparable benefit compared with conventional on-site programs with respect to improved risk factors, physical activity levels, anthropometric measures, and dietary intake.²²² Studies are currently under way to establish mobile- and Internet-based support for cardiac rehabilitation interventions,^{223,224} and future work may extend these remote-monitoring programs for stroke survivors. Although short-term behavior change using these approaches is indicated, whether these models result in longer-term benefits is yet to be demonstrated. Historically, key practical challenges with implementing technology-based programs for stroke survivors have included that technology solutions have not been easy to use, nor are they reliable, and that some older adults have lacked confidence in using technology. Rapid changes in both access and usability of technology will lead to these kinds of programs becoming increasingly relevant.

There is also potential to develop Web-, mobile-, and tablet-based applications (“apps”) for a variety of uses.²²⁵ Fitness-based applications are already widely used by the general public to track and measure progress related to fitness and nutrition goals. Similar applications may be developed for people with disabilities, including stroke, that provide clinicians with the means to enter customized exercise programs on their clients’ devices and remotely track and monitor exercise activities and progress. Web sites or mobile applications for knowledge uptake may also be designed for health professionals that synthesize the current state of research and facilitate implementation into clinical practice.

Other new technologies may also provide novel ways of monitoring and delivering interventions with cardiovascular challenge. Through miniaturization, wearable technologies are advancing rapidly and allow individuals to monitor and track physiological responses and progress over time. As the market for such devices as smart watches, bracelets, sensors, or interactive glasses continues to grow, scientists and health professionals may turn to these technologies for use in research and clinical practice. Video-based interactive gaming platforms have gained recent popularity for their potential application in older adult and clinical populations. These systems are commercially available; designed to be fun, motivational, and incrementally challenging; and provide visual and auditory feedback to participants during repetitive, high-intensity, and task-specific activities. Active video games have been shown to elicit cardiorespiratory responses of light (<3 METs)^{226,227} to moderate (3–6 METs) intensity among older adults²²⁶ and moderate-level intensity among stroke survivors.²²⁸ Future work may examine the cardiovascular benefit derived from engaging in these activities over a period of time.

Interventions for Individuals With Severe Stroke

To date, the majority of research has focused on individuals with mild to moderate disability from stroke, but a large gap remains regarding how those with severe stroke may be supported to increase physical activity patterns and engage in an exercise program. One potential area for this subset of the stroke population is the application of electromechanical-assisted walking interventions. Historically, these interventions have focused on the recovery of walking function and thus typically target changes in gait and mobility outcomes.²²⁹ New research, however, is emerging regarding the potential aerobic benefits of such training among individuals with limited ambulatory capacity. Treadmill training with a robotic exoskeleton after incomplete spinal cord injury resulted in improved left ventricular and endothelial function.²³⁰ For stroke survivors, robot-assisted treadmill training combined with conventional inpatient rehabilitation physical therapy was more effective in increasing peak $\dot{V}O_2$ than conventional physical therapy alone.¹⁶⁵ Ongoing work may explore the broader application and effectiveness of interactive gaming systems or electromechanical-assisted gait training to induce cardiovascular benefit after stroke.

Other areas of future research are likely to include the following:

- Identifying factors (eg, stroke characteristics, clinical presentation, and personal or social factors) that influence

the degree to which a stroke survivor can respond to an exercise program,^{184,231} gaining a better understanding of the barriers and facilitators to exercise, including the exercise preferences of these individuals,³⁰ and identifying effective models of behavior change related to exercise and secondary prevention.⁷⁴ The results of such research will help to establish optimal protocols to maximize benefit for various patient subgroups, including those with limited mobility, and will aid in the development of programs that embed physical activity and exercise into the daily lives of stroke survivors.

- Understanding whether sedentary behaviors are just as important as exercise behaviors in maintaining health after stroke.
- Determining the effectiveness of different types of training (ie, aerobic, resistance, and combined aerobic and resistance training) on cardiovascular health and functional outcomes.
- Determining whether and to what extent standard post-stroke functional rehabilitation programs result in increased aerobic fitness and improved cardiovascular health.
- Exploring the cost-effectiveness of different models of exercise participation for stroke survivors across a range of settings (institution, community, home), including integration of individuals into community programs. This will likely include tracking long-term engagement and health outcomes.
- Analyzing the cost-benefit ratio of vigorous physical activity across various patient subsets, with specific reference to cerebrovascular, cardiovascular, and musculoskeletal benefit and complications.
- Establishing the effectiveness of exercise training on quality of life in individuals with residual impairments from stroke.
- Establishing exercise testing protocols that provide high sensitivity and specificity for concomitant CAD.

The measurement of exercise capacity has been shown to improve risk discrimination and classification of all-cause and cardiovascular mortality among individuals without history of CVD,²³² but whether it is a similarly powerful predictor of CVD risk in the stroke population is not yet known.

- Establishing effective strategies to facilitate long-term adherence to regular exercise and physical activity after stroke.
- Establishing effective interventions that take place in both healthcare and home settings to optimize outcomes, maximize adherence, and facilitate involvement of caregivers.

Conclusions

As an important sentinel event, the stroke can serve as an “alert” or “wake-up call” to the individual. The care and services that are provided to the individual after the stroke, which should include exercise training recommendations and physical activity programs, can serve as important opportunities to implement effective and lasting behavioral and medical interventions that would improve overall health and might prevent the future occurrence of cardiovascular events such as subsequent stroke or myocardial infarction.

Exercise is a very valuable yet underused component of poststroke care. The evidence strongly supports the benefits of physical activity exercise for stroke survivors. With education in and encouragement for the benefits and safety of exercise after stroke, and with development of appropriate programs in hospitals and in communities, the ability to recruit patients to these programs should increase. These programs, developed by trained exercise professionals, should be offered early after stroke, when change can often make an impact, and should continue to be monitored throughout chronic stages to impact lifestyle-changing behaviors and improve overall health.

Disclosures

Writing Group Disclosures

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
Sandra A. Billinger	Kansas University Medical Center	NIH†	None	None	None	None	None	None
Ross Arena	University of Illinois at Chicago	None	None	None	None	None	None	None
Julie Bernhardt	Florey Institute of Neuroscience and Mental Health	National Health and Medical Research Council*; National Stroke Foundation Australia*	None	None	None	None	None	None
Janice J. Eng	University of British Columbia	Canadian Institutes of Health Research (CIHR)†; Heart and Stroke Foundation of Canada†	None	None	None	None	None	None
Barry A. Franklin	Beaumont Health System, Royal Oak, MI	None	None	None	None	None	None	None
Cheryl Mortag Johnson	UW Hospital and Clinics	NIH†	None	None	None	None	None	None
Marilyn MacKay-Lyons	Dalhousie University	Canadian Institutes of Health Research (CIHR)†; Canadian Stroke Network†; Heart and Stroke Foundation of Canada†	None	None	None	None	Canadian Stroke Network (board of directors)*; Institute of Circulatory and Respiratory Health, Canadian Institutes of Health Research (advisory board)*	None
Richard F. Macko	VA Maryland/University of Maryland School of Medicine	NIH†	None	None	None	Interactive Motion Technologies*	IKKOS Inc (unpaid to date)*	None
Gillian E. Mead	University of Edinburgh	Chief Scientist, Office of Scottish Government†; Welsh Stroke Organisation (paid to University Edinburgh; research for exercise after stroke)†	None	Elsevier (annual royalties for a book on exercise after stroke)*; Late Life Training (not-for-profit company; annual royalties paid to University of Edinburgh)*; World Stroke Organisation (single royalty payment to University Edinburgh in 2013 for an education module to support research on exercise after stroke)*	None	None	None	None
Elliot J. Roth	Northwestern University Feinberg School of Medicine/Rehabilitation Institute of Chicago	Kiwanis Foundation of Illinois and Eastern Iowa*; NIDRR†; NIH/NINDS†	None	None	None	None	None	None
Marianne Shaughnessy	Baltimore VA Geriatric Research Education and Clinical Centers/University of Maryland School of Nursing	None	None	None	None	None	None	None
Ada Tang	McMaster University	Canadian Institutes of Health Research†	None	None	None	None	None	None

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*Modest.

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Reviewer Disclosures

Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
Janet Fulton	Centers for Disease Control and Prevention	None	None	None	None	None	None	None
Barbara Lutz	University of Florida	None	None	None	None	None	None	None

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