

Prioritizing Functional Capacity as a Principal End Point for Therapies Oriented to Older Adults With Cardiovascular Disease

A Scientific Statement for Healthcare Professionals From the American Heart Association

ABSTRACT: Adults are living longer, and cardiovascular disease is endemic in the growing population of older adults who are surviving into old age. Functional capacity is a key metric in this population, both for the perspective it provides on aggregate health and as a vital goal of care. Whereas cardiorespiratory function has long been applied by cardiologists as a measure of function that depended primarily on cardiac physiology, multiple other factors also contribute, usually with increasing bearing as age advances. Comorbidity, inflammation, mitochondrial metabolism, cognition, balance, and sleep are among the constellation of factors that bear on cardiorespiratory function and that become intricately entwined with cardiovascular health in old age. This statement reviews the essential physiology underlying functional capacity on systemic, organ, and cellular levels, as well as critical clinical skills to measure multiple realms of function (eg, aerobic, strength, balance, and even cognition) that are particularly relevant for older patients. Clinical therapeutic perspectives and patient perspectives are enumerated to clarify challenges and opportunities across the caregiving spectrum, including patients who are hospitalized, those managed in routine office settings, and those in skilled nursing facilities. Overall, this scientific statement provides practical recommendations and vital conceptual insights.

Since 1900, the average longevity in the United States has increased >30 years.¹ As more adults survive into old age, healthcare challenges that stem from the age-related biological and physiological predispositions have become increasingly prevalent. Between 2010 and 2050, the population ≥65 years of age is expected to more than double to reach ≈88.5 million, ≈25% of the anticipated population.¹ Within this total, the very old subgroup (ie, those ≥85 years of age) is growing the most rapidly and is expected to triple over the same period to ≈4.5% of the population.² Although some may assume that adults who survive to old age are naturally selected to be more resilient and hardy, in fact, these individuals are more likely to have many health deficiencies. Aging encompasses systemic, organ-level, and cellular changes that predispose individuals to cardiovascular and comorbid diseases and geriatric syndromes (eg, sarcopenia, multimorbidity, frailty, disability, cognitive impairment, sensory impairments, balance impairment, and falls)³ with progressions that can be insidious, debilitating, and harmful. Functional decline is integral to these patterns. Adults who survive into old age are predictably more vulnerable to becoming sedentary and to a cycle wherein multimorbidities and hospitalizations compound functional decrements, which exacerbate risks of disability, dependency, and frailty. Whereas most major randomized controlled trials of therapies for cardiovascular disease (CVD) are usually oriented to outcomes metrics of mortality, morbidity (clini-

Daniel E. Forman, MD, FAHA, Chair*
 Ross Arena, PhD, PT, FAHA, Co-Chair
 Rebecca Boxer, MD, MS
 Mary A. Dolansky, RN, PhD
 Janice J. Eng, PhD, MSc, BSR
 Jerome L. Fleg, MD, FAHA*
 Mark Haykowsky, PhD
 Arshad Jahangir, MD, FAHA
 Leonard A. Kaminsky, PhD, FAHA
 Dalane W. Kitzman, MD
 Eldrin F. Lewis, MD, MPH
 Jonathan Myers, PhD, FAHA*
 Gordon R. Reeves, MD, MPT
 Win-Kuang Shen, MD, FAHA
 On behalf of the American Heart Association Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Quality of Care and Outcomes Research; and Stroke Council

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cal events), and hospitalizations, they rarely address the associated risks of functional loss that can occur even if the initial therapies seem to go well.⁴ Not only are strategies to better preserve physical capacity and to minimize declines important steps to reduce disease-related mortality and morbidity, but many older patients regard preserved function, independence, and related self-efficacy as their primary goals of care; that is, for many patients, conserved functional capabilities become more important than traditional disease-specific therapeutic end points.⁵ Amid worldwide demographics of aging, researchers and clinicians can enrich care by focusing on the interactions between physical function, aging, and disease and their relevance to patient-centered goals.

Although clinical and research methods oriented to functional capacity overlap, there are also important differences. Research tends to evaluate functional attributes or therapies with comprehensive protocols by which specific mechanisms and techniques can be clarified. Clinical applications are often relatively more challenged by contexts that provide little time for assessments and wide variability of patient types and capacities, and functional evaluations are often selected for maximal practicality and efficiency.

DETERMINANTS OF PHYSICAL FUNCTION IN OLDER ADULTS: IMPACT OF AGE AND DISEASE

Cardiorespiratory Fitness

The primary metric of functional capacity is cardiorespiratory fitness (CRF), usually assessed as peak oxygen uptake ($\dot{V}O_2$).⁶ Cardiovascular and pulmonary physiological components are key determinants of $\dot{V}O_2$ and usually predominate in younger adults, but vascular, skeletal muscle, autonomic, hematologic, and other physiological mechanisms are also contributory and often factor relatively more significantly in older age. Oxygen use is ideally measured by cardiopulmonary exercise testing (CPET). Peak $\dot{V}O_2$ is an assessment of maximal aerobic performance that implies that activity has intensified to a point of maximal volition; hence, peak $\dot{V}O_2$ is usually assessed as part of a symptom-limited or maximum exercise test.⁷ Metabolic equivalents (METs) achieved are a surrogate indicator of exercise performance that are calculated from workload (ie, treadmill speed/grade or Watts) and often used as an alternative to CPET when ventilatory expired gas analysis is not available. However, calculated METs provide a less accurate form of CRF assessment because individual metabolic efficiencies and other age-related changes (eg, body composition) are not accounted for in the calculations.

Peak $\dot{V}O_2$ corresponds to the product of heart rate (HR), stroke volume, and systemic arteriovenous oxygen difference ($\Delta A\dot{V}O_2$) at maximal effort. Cardiologists have tended to regard peak $\dot{V}O_2$ as a particularly valuable index for heart function because $\dot{V}O_2$ can be applied as a

proxy for cardiac output,⁸ and this is most commonly used as part of heart failure (HF) management. However, not only do CPET indexes reveal physiological components in addition to the cardiac physiology that underlies CRF (eg, CPET indexes indicative of pulmonary, skeletal muscle, and autonomic impact), but the overall implication of functional assessment extends beyond such mere delineation of underlying physiologies. Myers et al⁹ used the METs calculated from standard ETT and showed that even this relatively less intricate measure of CRF was a powerful predictor of mortality in adults with coronary heart disease and in adults without CVD. In multiple studies, CRF metrics, whether measured by CPET, ETT, or 6-minute walking testing (6MWT), have shown significant prognostic bearing for patients with coronary artery disease (CAD), valvular heart disease, arrhythmia, peripheral arterial diseases, pulmonary hypertension, and other CVDs.⁷ CRF is a leading measure of health; declining functional capacity typically surpasses all other cardiovascular risks; and the hazard of declining CRF tends to worsen with aging. Thus, elucidating CRF and interrelated dynamics of function provides key insights into aggregate well-being.

In healthy adults, peak $\dot{V}O_2$ declines on average by 8% to 10% per decade, with accelerating declines as age advances.¹⁰ Thus, peak $\dot{V}O_2$ at 80 years is typically $\approx 50\%$ of that in the third decade. This dramatic reduction in peak $\dot{V}O_2$ is mediated in large part by declines in both maximal HR and $\Delta A\dot{V}O_2$ of $\approx 5\%$ per decade, with stroke volume relatively preserved.¹¹ The reduction in maximal HR appears to result from a blunted sensitivity to circulating catecholamines caused by impaired β -adrenergic receptor and postreceptor signaling.^{11,12} Mechanisms for the reduction in $\Delta A\dot{V}O_2$ likely involve both less efficient distribution of blood flow to exercising muscle and impaired mitochondrial function within the muscles.¹³ The common occurrence of deconditioning and cardiovascular, pulmonary, and other disease states in older adults compounds age-associated declines in peak $\dot{V}O_2$.

Determinants of Function Beyond the Heart, Lungs, and Vasculature

In addition to cardiovascular physiological components,⁴ strength and neuromuscular function contribute to CRF with a proportionally greater role in determining peak $\dot{V}O_2$ as strength and coordination decline.¹⁴ Just as peak $\dot{V}O_2$ decreases with advancing age, muscle mass and strength also decline, with proportionately greater impact as age, disease, and sedentariness synergistically escalate.^{15,16} Age-associated loss of skeletal muscle mass, called sarcopenia, involves both loss of muscle fibers and reduced fiber size.¹⁶ Whereas muscle mass constitutes 30% of body weight in younger adults, it decreases to $\approx 15\%$ of body weight by 75 years of age.¹⁷ The loss of strength that accompanies the loss of mus-

cle mass and function in older adults typically leads to the need for greater relative effort to perform equivalent work for daily tasks. Many individuals then choose to avoid tasks that have become relatively more stressful, with the result that physical activity and CRF become further reduced.

Balance and flexibility are also required for many daily activities and decline with age, especially in the context of changing muscle mass and function, neurogenic factors, bone loss, and degenerative changes in connective tissue.¹⁸ Medications further exacerbate these vulnerabilities via additional hemodynamic perturbations, fatigue, somnolence, and falls, especially in the common context of multimorbidity and polypharmacy and age-related shifts in pharmacokinetics and pharmacodynamics.¹⁹ An 86-year-old woman with a non-ST-segment-elevation myocardial infarction, HF, Parkinson disease, and insomnia, for example, may be prescribed β -blockers, angiotensin-converting enzyme inhibitors, diuretics, statins, selegiline, and trazodone with evidence-based rationales but with the potential effect of increasing risk for falls and functional decline via chronotropic, hemodynamic, myalgic, and sedating effects.

Cognitive decline and depression are also more likely to develop amid the inflammatory substrate that underlies CVD. Not only can cognitive limitation fundamentally undermine functional capability,²⁰ but depression compounds impediments with intensified cardiovascular, immune, and hormonal pathophysiologies,^{21,22} as well as poorer adherence to multiple healthy lifestyle activities (eg, smoking cessation, exercise, diet) and medications.^{23,24} Diminished sleep quality (shorter and more fragmented) is also common in older cardiovascular patients and often adds to fatigue and exercise intolerance.²⁵ In effect, the CRF model of function in older adults becomes integrated with a spectrum of geriatric physiological and clinical complexities.

Systemic, Cellular, and Subcellular Determinants of Functional Capacity

Beyond cardiac and other organ-specific determinants of functional capacity, relatively more fundamental systemic and cellular components underlie physical function, including mitochondrial dysfunction, oxidative stress, abnormal calcium handling, chronic inflammation, cellular senescence, extracellular matrix production, loss of telomeric structures, and poor DNA repair capability. Together, these processes contribute to susceptibility to disease and declines in functional status that extend beyond any one disease and that can even occur in health.²⁶ Changes in mitochondrial function alter the bioenergetic capacity of the heart, leading to diminished ability to meet energy demands with reduced ATP generation.^{13,27} These mitochondrial changes are accompanied by enhanced reactive oxidative species generation,

increasing susceptibility to injury by oxidative damage to lipid membranes, proteins, nuclear and mitochondrial DNA, and other macromolecules.^{28,29}

Alterations in redox status and impairment in oxidative phosphorylation also sensitize mitochondria in older adults to permeability transition pore opening that in turn leads to cellular energetic failure and necrotic or programmed cell death in cardiomyocytes or other tissue.³⁰ In addition, cellular mitochondrial quality control mechanisms such as autophagy and ubiquitin-protease system, which removes damaged mitochondria or protein to maintain a functional mitochondrial network, become impaired with aging, resulting in an accumulation of dysfunctional mitochondria, which further contribute to myocardial functional impairment and CVD.³¹

Age-related increases in low-level inflammation, perhaps resulting from chronic stimulation by mitochondrial dysfunction or dysregulation of the immune system, result in elevated circulating proinflammatory cytokines such as interleukin-6 or tissue necrosis factor- α .^{32,33} This inflammatory milieu further contributes to aging-associated functional decline via reactive oxidative species-mediated exacerbation of telomere dysfunction³⁴ and accelerated muscle catabolism, promoting cell senescence and subsequent disease, frailty, and mortality.^{33,35,36} Interrelated effects of inflammation on cognition,³⁷ depression,³⁸ and sleep^{27,28} may then exacerbate the clinical risks.

Changes in body composition with aging, particularly loss of lean mass, and increases in metabolically active visceral and muscle fat that secrete hormones and cytokines also contribute to the persistent low-level inflammation and cellular senescence³⁴ that promote further decline in functional capacity, stress intolerance, and progressive cellular dysfunction, sarcopenia, and frailty.

The impact of high ambient inflammation is exacerbated by the depletion of vital nutrient and energy stores with worsening fatigue and cellular harm. Age-related nutritional decline is common amid age-related changes in taste, dentition, digestion, absorption, and cognition, as well as limitations in access (logistics, cost, and the challenge of food preparation).

Relevance of Frailty in Older Patients With CVD

Frailty is neither disease nor age specific but refers to the reduced ability to tolerate physiological stresses, including reduced or delayed ability to recover from a stressor. Frailty is also associated with increased incidence of CVD³⁹ through interrelating inflammatory pathways.⁴⁰ Although many different measures of frailty exist, physical frailty is conceptually distinctive from the frailty index^{39,41,42} and relates more directly to functional attributes.^{41,42} Physical frailty is usually defined as a phenotype that includes 5 domains (unintentional weight loss, exhaustion, muscle weakness, slowness while walking,

and low levels of activity).⁴³ Afilalo et al⁴⁴ observed that physical frailty may lead to CVD, just as CVD may lead to frailty. Thus, physical frailty includes specific domains of functional decline (weakness, slowness, and reduced activity) that relate to CVD but not through any specific impact on cardiac output.⁴¹ Frailty increases hospital length of stay and adverse outcomes in patients admitted for CVD, HF, CAD,⁴¹ and associated procedures (eg, cardiac valve replacement or arterial vascular surgery [aortic or lower limb arterial intervention])^{45,46} and exacerbates risks of long-term disability thereafter.

Functional Decline: More Than the Tally of Mechanisms

Whereas cardiac output and numerous other factors are now recognized to affect CRF, functional capacity is still more than a tally of causal physiological mechanisms. The patient experience is more personal and distinctive. Pinsky et al⁴⁷ reported that angina pectoris was more predictive of disability than extent of underlying CHD, suggesting that a patient's sense of discomfort and apprehension was likely more impactful than the underlying physiology. The challenge for research is not only to study therapies based on mechanistic insights pertaining to CVD but also to assess efficacy of therapies from patient-centered perspectives; that is, the number of events may be less important than the patient's personal experience. The ASPREE trial (Aspirin in Reducing Events in the Elderly) stands out as a novel approach to assessing the utility of platelet medication in senior adults.⁴⁸ Instead of measuring thromboembolic events, bleeding, and the traditional metrics that one might expect, the primary end point is disability-free life, including dementia and persistent disability. Thus, in ASPREE, the realm of functional capacity and disability-free life is targeted as an ultimate goal of a mechanistic therapeutic approach.

ASSESSING FUNCTION IN OLDER INDIVIDUALS: MEDICAL PERSPECTIVES

Functional capacity in older adults can be quantified in a number of ways. Often, the choice of assessment tool will depend on the individual being tested, the purpose of the evaluation, or even the geographic location. Research and clinical priorities often differ; research options are more likely to be more comprehensive and complex and enabling more detailed and discriminating evaluations, whereas clinical options often raise priorities for speed, reliability, cost, and efficacy for a wide range of patients and clinical venues. Whereas CRF measured by CPET or exercise tolerance test (ETT) is often used in younger individuals, the utility of CPET and ETT for older adults is often complicated by weakness and other limitations, although these tests may

still be feasible when appropriate protocols and modes are used. Physical performance domains are also interdependent; assessments of multiple domains can often help clarify functional limitations and then can be applied together as integrated bases of management. Table 1 lists commonly used tests (as detailed below) and their relative utility within many routine research and clinical applications.

Aerobic Capacity

Directly measured oxygen use as measured during CPET remains the gold standard for CRF and is a powerful prognostic marker across the spectrum of conditions, habitual activity, and age.⁸ Peak $\dot{V}O_2$ is considered an especially useful index because it encompasses the effects of age, habitual activity, and comorbidities that affect performance. Moreover, in addition to peak $\dot{V}O_2$, CPET facilitates assessment of complementary ventilatory indexes (eg, the ratio of minute ventilation to exhaled carbon dioxide or breathing efficiency [$\dot{V}_E/\dot{V}CO_2$] and the ratio of exhaled carbon dioxide to inhaled oxygen or respiratory exchange ratio) that augment the assessment of aerobic performance in health and disease.⁸ Nonventilatory exercise test indexes (eg, HR, blood pressure, electrocardiogram) are also routinely integrated with ventilatory gas analysis during CPET to further refine determinants of function and related features of diagnosis, prognosis, and goals of care (eg, to detect abnormal chronotropic responses or rhythm abnormalities).^{8,49,50}

Standard ETT, without ventilatory assessments, can also be used to assess functional dynamics in older adults. Although ETTs are often criticized for their low sensitivity to diagnose CAD, especially for older adults, their utility for performance evaluation is undervalued.⁵¹ Calculated METs, although a less accurate indicator of CRF than directly measured $\dot{V}O_2$, still provide an effective assessment of aerobic capacity that can be very useful in the diagnosis, prognosis, and management of CVD (eg, distinguishing very high from very low performance) with synergistic assessments of HR, blood pressure, rhythms, and symptoms.

Nonetheless, both CPET and ETT among senior populations can be confounded by the increased prevalence of orthopedic, neurological, or other conditions that may compromise ability to exercise. Thus, the test modality and protocol should be carefully selected to optimize performance and safety and to ensure meaningful assessment despite physical limitations. Cycle ergometry may, for example, be more appropriate for seniors who have a residual motor deficit from a stroke. In addition, regardless of the modality, the testing protocol should be tailored to the expected levels of exercise capacity. More individualized or gradually incremented protocols such as the Balke, ramp, or Naughton protocol are generally more suitable for older adults who are limited by

Table 1. Common Functional Assessments in Clinical and Research Environments

		Test	Outcomes	Protocol	Hospital	Office	SNF	CR	Research
Aerobic	Maximal	CPET/CPX	$\dot{V}co_2$, $\dot{V}E/\dot{V}co_2$ slope, ischemia, HR, HR recovery, arrhythmia, hemodynamics	High intensity*	X	X		X	X
				Low intensity†	X	X		X	X
		ETT	METs, ischemia, HR, HR recovery, BP, arrhythmia	High intensity*	X	X		X	X
				Low intensity†					
Submaximal	CPET/CPX	VAT, $\dot{V}E/\dot{V}co_2$ slope, ischemia, HR, HR recovery, arrhythmia, hemodynamics	High intensity*	X	X		X	X	
			Low intensity†						
	ETT	Ischemia, HR, HR recovery, BP, arrhythmia	High intensity*	X	X		X	X	
			Low intensity†						
	6MWT	Distance walked over 6 min at brisk speed		X	X	X	X	X	
	Strength	Maximal	1RM Grip strength			X	X	X	X
Submaximal		TUG			X	X	X	X	X
Power					X			X	X
Endurance		STS			X	X	X	X	X
Balance		Berg Balance Scale Performance-Oriented Mobility Assessment Functional reach	Fall risk		X	X	X	X	X
Physical frailty	Physical domains associated with frailty	Gait speed Grip strength SPPB Fried scale	Overall prognosis and well-being		X	X	X	X	X
Cognition		MoCA	Cognitive capacity		X	X	X	X	X
Physical activity	Questionnaires	DASI Minnesota Leisure Time Physical Activity Questionnaire DASI	Minutes of activity, energy expenditure		X	X	X	X	X
	Activity monitoring devices	Accelerometers Wearable devices Pedometers	Minutes and intensity of activity, energy expenditure		X	X	X	X	X
ADLs	Questionnaires	ADL-IADL Katz, Barthel, FIM	Capacity to maintain house and care for self		X	X	X	X	X
Disability	Physical disability	400-m hall walk	Time to walk 400 m at usual pace		X	X	X	X	X

Table 1 is primarily meant to demonstrate the breadth of functional assessments and the different contexts in which they can be implemented as enhancements of clinical care and research. Many may regard the feasibility of functional assessments as inherently more difficult in clinical contexts, but this chart highlights the viewpoint that assessments are more feasible than many often assume. Furthermore, the tests listed in this chart are not definitive; that is, many more tests and questionnaires exist, many of which may be particularly well suited to specific patients, offices, or research applications.

1RM indicates 1-repetition maximum; 6MWT, 6-minute walk test; ADL, activity of daily living; BP, blood pressure; CPET/CPX, cardiopulmonary exercise stress test; CR, cardiac rehabilitation; DASI, Duke Activity Status Index; ETT, exercise tolerance test; FIM, Functional Independence Measure; HR, heart rate; IADL, instrumental activities of daily living; MET, metabolic equivalent; MoCA, Montreal Cognitive Assessment; SNF, skilled nursing facility; SPPB, Short Physical Performance Battery; STS, Sit to Stand; TUG, Timed Up and Go; VAT, ventilatory anaerobic threshold; and $\dot{V}E/\dot{V}co_2$ slope, minute ventilation/carbon dioxide production slope.

*High intensity (eg, Bruce; high-intensity ramp, treadmill, or bicycle).

†Low intensity (eg, modified Bruce, Naughton, modified Balke; low-intensity ramp, treadmill, or bicycle).

age physiology, multimorbidity, or medications. Patients should be assessed as to potential exercise limitations and may require submaximal testing protocols to optimize safety.^{52,53} When conducted in this manner, exercise testing is feasible and safe even among patients with advanced age and significant comorbidity.^{52,54}

Symptom-limited (maximal) exercise testing may not be appropriate in all older adults. Orthopedic, neurological, or excessive cardiovascular risks may limit maximal exercise, or the tests may be available only in a setting where adequate physician supervision is unavailable.⁵⁵ With CPET, ventilatory indexes can be selected that provide sensitive and specific assessments of important physiological relationships even at submaximal workloads (eg, $\dot{V}O_2$ at the anaerobic threshold and $\dot{V}E/\dot{V}CO_2$ slope can provide key insights into cardiac and pulmonary performance at submaximal workloads).⁸ Submaximal ETTs (with CPET or ETT) can also be useful and have been successfully applied to assess rate of perceived exertion, HR responses, rhythm, and other key parameters at lower exercise intensities. Steady-state exercise at submaximal workloads can be applied as testing end points. HRs (eg, 70% of the HR reserve or 85% of age-predicted maximal HR) can also be used as submaximal testing targets,⁵⁶ although the wide variation in the age-predicted estimate of maximal HR or the confounding effects of medications⁵⁷ limit the interpretation of results.

The 6MWT is commonly applied as a simple, low-cost submaximal assessment of aerobic exercise capacity with significant prognostic value. Standardized 6MWT protocols have been established to minimize variability and to ensure quality, including patient preparation and instructions, safety considerations, and guidelines for interpretation.⁵⁸ An assistive device for ambulation may be used during the test, which may constitute a relative advantage compared with treadmill testing for many older adults. The 6MWT is often applied to assess capacity for daily activities⁵⁹; however, in severely impaired populations, a 6MWT may represent maximal effort. This may help explain variations in correlations of 6MWT distance with peak $\dot{V}O_2$ in different study populations, ranging from 0.50 to 0.80.^{60,61}

Muscle Strength and Endurance

Muscle strength is an important determinant of physical function, particularly in older adults who are relatively frail. Low muscle strength and endurance are predictive of a future decline in functional performance and higher incidence of disability^{62,63} and mortality.^{64–66}

The standard measure of strength, the 1-repetition maximum (1RM), is commonly measured with the heaviest weight that can be lifted concentrically throughout a complete range of motion. This is usually measured on a variable weight machine with a sitting chest press used for upper-body strength and knee extension used

for lower-body strength; these 2 exercises have been shown to be surrogates for overall upper- and lower-body strength. The 1RM is advantageous in that it is similar to functional tasks such as moving a heavy load through a range of motion.⁶⁷ There have been concerns about injuries associated with 1RM testing in elderly individuals, and it has generally been considered less safe than isokinetic testing, given that there is no set control on the speed of movement and often no set range of motion. However, under careful supervision and with appropriate familiarization procedures, the 1RM can be safely conducted even in very frail seniors.^{68–70}

Handgrip strength is another common measure of strength that is relatively simple to perform, requiring only a hand dynamometer, and has been shown to correlate well with other strength tests, including more general upper- and lower-body 1RM testing. Numerous studies have reported that handgrip strength is strongly related to physical function, frailty, and disability,^{71,72} as well as long-term morbidity and mortality.^{72–74} The handgrip test should be performed with the use of standardized protocols with attention to positioning, number of trials performed, and hand used.⁷⁵

Measures of fatigability are also useful, particularly as they correspond to activities of daily living (ADLs; eg, carrying groceries). Assessment options include the number of submaximal repetitions (usually at 60% of the 1RM) until limited by fatigue or impaired form, the relative decline in maximal force of a set number of repeated dynamic contractions performed with an isokinetic dynamometer,^{76,77} the relative decline in maximal force of repeated isometric contractions, and the maximal time to maintain a submaximal isometric contraction.^{76–80}

Functional muscle strength and endurance testing such as timed repeated chair rise also provides meaningful measures of skeletal muscle performance associated with functional independence and clinical outcomes.⁸¹ This testing is easy to perform in a variety of clinical settings, can be integrated into composite measures of functional capacity, and is often complementary to balance assessments.⁸² Assessments of power, that is, the speed of movement, are also important, with growing recognition that slowing of movement is a particularly sensitive marker of disability. Whereas direct assessments of power usually entail sophisticated research techniques,⁸³ indirect assessments can be inferred from other time-based maneuvers (eg, gait speed) that gauge rapidity of movement.^{84,85}

Balance

Balance requires the coordinated integration of multiple systems (sensory, neurocognitive, neuromuscular, and musculoskeletal). Balance deficits are common in older adults amid aging-related declines and mounting diseases and medications that further erode these

systems. Balance impairment jeopardizes functional independence and is a strong primary risk factor for the occurrence of falls. One in every 3 adults ≥ 65 years of age and nearly half of those >80 years of age experience at least 1 fall annually.⁸⁶ Injuries caused by falls are a major cause of mortality among older adults, and they are increasing.^{86,87}

Balance testing typically involves some combination of static and dynamic balance assessment with interval or ordinal scaling, with sensitivities for predicting falls ranging from 50% to 90%.⁸⁸ These tools are generally responsive to clinical changes and have reasonable sensitivity to predict fall risk.^{88,89}

The Berg Balance Scale has been widely used as a screening and assessment tool for balance impairment.⁹⁰ It consists of 14 items that involve the ability to perform physical tasks and is a strong predictor of falls. Tinetti⁹¹ developed a balance and gait evaluation that is more detailed, involving observations of gait initiation and step height, length, symmetry, and continuity, along with path deviation, trunk stability, and turning. There are other tools that are relatively simpler to use and that achieve similar types of assessments using very basic maneuvers (eg, sitting to standing or reaching).^{88,89} The sit-to-rise test is a simple assessment that involves subtracting points on the basis of the need to use hand support while moving from sitting on the floor to a standing position. It incorporates strength, balance, and flexibility and was recently shown to be a strong predictor of mortality.⁹² In the Functional Reach Test,⁹³ the patient stands next to a wall with feet stationary and one arm outstretched and then leans forward as far as he or she can without stepping. A reach distance of <6 inches is considered abnormal. A modified Sit and Reach test was developed for individuals who have difficulty standing such as those who have had a stroke.⁹⁴

Multidomain Assessments

These tests involve combinations of balance, mobility, and gait speed over short distances. The Short Physical Performance Battery (SPPB) is a brief (10–12 minutes) 3-component test combining gait speed with assessments of functional strength (timed repeated chair rise) and standing balance.⁸² Performance on each component is scored from 0 to 4 for a total score of 0 to 12. A score of ≤ 6 has been proposed as a frailty cutoff.⁴¹ In addition to the composite score, performance in each component can give insights into specific functional limitations. A change of 1 point in the overall SPPB score has been identified as representing a substantial change and 0.5 points as a minimal meaningful change⁹⁵ that is predictive of mortality, hospital admission, or nursing home admission.

The Get Up and Go Test is a practical test integrating balance and gait assessment into a single assessment. The test requires the individual to rise from an armless chair (without using hands), walk 10 ft to a wall, turn around without touching the wall, walk back to the chair, pivot, and sit. The Timed Up and Go Test⁹³ is a similar test of basic functional mobility but also requires that the movements be performed as quickly as possible, which generally adds to the overall sensitivity of assessment.^{96–98}

Functional Independence and Daily Activity

Numerous questionnaires have been developed to assess the degree of dependency with ADLs. These tools have the advantage of simplicity and safety, and they require no equipment and a minimal amount of time. The Katz Index of Independence in Activities of Daily Living⁹⁹ is a widely used instrument that assesses an individual's ability to perform 6 basic ADLs: bathing, dressing, use of toilet facilities, transferring, continence, and feeding. The Lawton-Brody Instrumental Activities of Daily Living questionnaire¹⁰⁰ focuses on activities related to independent living beyond these basic ADLs, including preparing meals, managing money, shopping for groceries or personal items, performing light or heavy housework, and using a telephone. Participants are scored on the basis of their ability to carry out these activities independently without assistance from caregivers. The Barthel Index and the Functional Independence Measure are also widely used to assess functional independence, particularly in patients who have suffered a stroke, or to assess response to functional rehabilitation.^{101,102} Another commonly used example is the Frail Elderly Functional Assessment.¹⁰³ It includes 19 questions related to the capacity to perform ADLs, resulting in a composite score between 0 and 55. The tool has been demonstrated to be reliable and valid and to be responsive to functional change.^{103,104}

Although ADL assessment can be performed via direct observation, ADLs are typically evaluated as questionnaires based on perceptions that lack objective measures of physical function. In contrast, the 400-m walk test is an objective test of major mobility disability; that is, the inability to complete a 400-m walk within 15 minutes without sitting and without the help of another person. This test was designed to serve as an index of independence with community ambulation, not as an assessment of aerobic capacity. In contrast to the 6MWT, in which subjects are asked to walk as quickly as possible, seniors are asked to walk at their usual pace in the 400-m walk.

In addition to assessments of exercise capacity and functional independence, methods have been developed to assess a person's level of daily physical activity.¹⁰⁵ Questionnaires such as the Duke Activity Status Index or the Minnesota Leisure Time Physical Activity Question-

naire have been used to estimate average daily energy expenditure on the basis of the patient's report of routine activities.^{106,107} With advances in technology, there is an expanding role for accelerometry-based assessment of physical activity. Many of these devices can now be worn on the wrist, greatly increasing an individual's adherence and the potential to provide valuable insights into physical activity and sleep patterns as part of large observational studies¹⁰⁸ or as patient-centered end points in clinical trials.¹⁰⁹ Although the devices and related software are becoming increasingly user-friendly, expertise in their use among older adults and the interpretation and use of the large amount of data are still evolving.

Frailty

Many different tools exist to assess frailty. Physical frailty is particularly oriented to physical function and is conceptually distinctive from the frailty index, which is a proportion of deficits relative to a total number of age-related health variables considered.^{39,41,42} Weakness, slowness of gait, and generalized fatigue are all components of the Fried physical frailty phenotype, which remains particularly popular as an assessment a clinician can integrate into the physical examination.⁴³ Many of the measures discussed previously, including the SPPB, Timed Up and Go Test, grip strength, ADL assessment, and physical activity questionnaires, have been used to estimate physical frailty.^{41,43}

Gait speed has been widely used as a single measure of frailty and is supported by a robust body of literature demonstrating its prognostic importance across a wide range of patient populations and performance levels.⁸⁵ Gait speed is a highly relevant metric because slowing of movement with aging is a universal biological phenomenon that reflects the integrated performance of numerous organ systems. Methods to assess gait speed have varied, but typically these tests involve measuring the time required to walk a specified short distance, usually 4 to 5 m, at an individual's usual pace. Although gait speed is usually assessed relative to age- and sex-based standards, a cutoff value <0.8 m/s (eg, taking >5 seconds to walk 4 m) is often regarded as an indicator of frailty⁹⁸ with high sensitivity (0.99) and moderate specificity (0.64). Gait speed provides prognostic information across a wide spectrum of performance, including a significant association with survival at increments of 0.1 m/s.⁸⁴ Gait speed has also been demonstrated to be a consistent risk factor for disability, cognitive impairment, institutionalization, falls, and postoperative outcomes.⁸⁵

ASSESSING FUNCTION IN OLDER ADULTS: PATIENT PERSPECTIVES

Physical function is an important indicator of prognostic risk and a key influence on the daily life of older adults with CVD.¹¹⁰ In particular, inability to perform ADLs re-

duces quality of life (QOL), but even the progressive loss of strength and CRF can translate into reduced confidence and mood. Although the importance of physical function is well defined in published literature, the use of this important outcome measure for establishing the efficacy of a particular intervention among older adults should be considered in the context of regulatory stringency,^{111,112} in relation to other components of patient-reported outcomes,^{113,114} and in respect to the impact that non-CVDs may also have on this measure. From a regulatory perspective, a clinically meaningful improvement in physical function in response to an intervention requires that it be directly measured from the patient and is important to the patient, thus emphasizing the importance of objective, validated tools.

Health-related QOL is a person's perception of his or her position in life in the context of culture and value systems and in relation to goals, expectations, standards, and concerns.¹¹⁵ Multiple domains often influence patient perceptions, which makes it difficult to understand the influence of a particular intervention on the summary QOL scores. There are also variable changes in health-related QOL domains in patients with similar disease states, and much of the change may be influenced by 1 or 2 particular items in the instrument. Therefore, functional limitations are often targeted as the key end points. Given the importance of QOL to older patients, understanding the elements of physical function that correspond to health-related QOL is important.

Several key elements correspond to a reduced health-related QOL among older patients with CVD. The most common functional classification in HF is the New York Heart Association functional class, which is highly associated with QOL.¹¹⁶ Measures obtained from exercise testing such as exercise duration and peak $\dot{V}O_2$ (or METs) have modest correlations with health-related QOL. The respiratory exchange ratio and 6MWT distance have been associated with depression scores.¹¹⁷ Instruments that measure physical function have also been associated with health-related QOL. Variables that also mediate physical function and health-related QOL include sarcopenia, muscle strength/endurance, balance/mobility, and undiagnosed depression. The interplay between physical function and physical activity may be driven by a patient's needs and motivation, social support, and comorbid illnesses and the requirements that need to be met to perform daily activities. These complex associations between function and activity lead to high interpatient variability and may blunt the association among older adults with CVD.

Self-efficacy is broadly defined by Bandura¹¹⁸ as patients' belief that they have the ability to influence their lives via self-imposed actions. This has been modified in health care to include knowledge base, management of medicines, symptom recognition, and strategies for interfacing with the healthcare system when short-term

changes occur in clinical status. Self-efficacy is closely related to health-related QOL in older adults. Self-efficacy is influenced by physical function^{119,120}; among older women, improvements in physical activity resulted in increased self-efficacy and physical function. Higher self-efficacy has also led to greater self-esteem.¹²¹ Greater self-esteem may increase QOL, facilitate a wider range of ADLs, reduce depression and anxiety, and enable better disease management. Moreover, physical self-worth may improve as a result of this increased activity and image. Global and disease-specific health-related QOL may improve as a consequence of this greater physical self-worth and self-esteem. Self-efficacy potentially mediates the impact of physical activity on perception of self-esteem and QOL¹²² and can serve as a modifiable variable for improving health-related QOL in older CVD populations. Conversely, health-related QOL at baseline may also influence self-efficacy. Patients with less impaired health-related QOL may be more willing to participate actively in the management of their disease, may be more interested in preserving their health-related QOL via changes in behavior, and may focus their attention on improving their knowledge base, understanding symptom recognition, and preventing declines in their functional capacity.

PHYSICAL FUNCTION AS A THERAPEUTIC TARGET IN OLDER ADULTS

Physical function is an important target of interventions, given its importance to the patient and its association with subsequent nonfatal and fatal cardiovascular events. There are several tenets to incorporating physical function into clinical pathways and research.¹²³ The physical function measured should fit within a well-developed conceptual framework that links the disease with the patient's physical function and the potential ability to modify this function.¹¹² Patients with CVD should perceive the importance of the physical function on their sense of well-being, and well-characterized, expected baseline metrics and changes should be measured within different patient groups with and without comorbid illnesses.

Exercise training remains a primary therapy to improve functional capacity. Aerobic training and strength training augment multiple biological and physiological mechanisms to enable gains. Aerobic benefits include subcellular shifts in gene expression (triggered in part by reduced inflammation), boosted cellular metabolism (improved bioenergetics and insulin sensitivity), greater organ efficiency (including increased cardiac, vascular, pulmonary, muscular, neurologic, and cognitive performance), and enhanced systemic biological and physiological integration.⁶ Exercise training benefits are often promoted by health providers primarily for their primary and secondary prevention cardiovascular health

benefits, with a preponderance of data demonstrating decreased cardiovascular events and increased longevity.¹²⁴ For older patients with CVD, these benefits persist but are often surpassed by the value of exercise training to improve capacity to improve physical function and to thereby better enable ADLs and improved QOL.

When the energy requirement for an activity exceeds an individual's CRF or muscle endurance, the person is less likely to perform that activity. In 161 community-dwelling adults 65 to 90 years of age, a peak $\dot{V}O_2$ of $\approx 18 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ optimally distinguished between high and low physical function.¹²⁵ Because the peak $\dot{V}O_2$ of most healthy female octogenarians is often below this level, many are close to a threshold at which functional independence is no longer possible. Concomitant CVD, particularly HF, and noncardiovascular comorbidities tend to compound decrements in peak $\dot{V}O_2$, social risk, and the insidious vicious circle whereby sedentariness progressively worsens disease. Thus, in addition to healthful attributes for which physical exercise is known, for many older patients with CVD, a primary goal (and personal goal of care) of exercise training interventions is to enhance functional capacity sufficiently to preserve independence and QOL.

Considerable evidence exists for hospital-associated deconditioning^{126,127} and disability, including rapid loss of muscle mass and strength^{128–132} that contributes to slower gait speed^{133–135} and difficulty performing ADLs.^{136–139} Approximately 40% to 70% of older adults hospitalized for a cardiac event have significant physical disability the month after discharge,^{140,141} and without enrollment in an exercise training/rehabilitation program, disability often persists.¹⁴²

Although early investigations suggested that CRF could not be significantly improved by endurance exercise training in older adults, numerous subsequent studies have demonstrated up to 25% increases in peak $\dot{V}O_2$ in previously sedentary healthy adults through the ninth decade, similar to improvements found in younger adults.^{143–145} These increases are mediated primarily by enhanced limb blood flow and oxygen extraction by exercising muscle and to a lesser extent by augmented stroke volume from a larger left ventricular end-diastolic volume. It has also been shown that aerobic exercise training can lead to skeletal muscle hypertrophy.¹⁴⁶

Strength training provides synergistic benefit to aerobic exercise, and gains of muscle volume and function may be particularly beneficial in the context of sarcopenia and disease effects on skeletal muscle. Skeletal muscle adaptations to exercise include remodeling of the muscle fibers, enhancements to contractile protein and function, mitochondrial biogenesis, increases in skeletal muscle glucose uptake, and improvements in whole-body insulin sensitivity. However, for many older cardiovascular patients struggling with impending disability and dependency associated with illness and hos-

pitalizations, the focus of muscle strengthening is often to improve mobility such as rising from a chair or walking short distances to maintain independence. Balance deficits are also common in such patients, which, along with functional strength and mobility training, may be important targets to maximize gains and to reduce the risk of injuries and falls.

Whereas exercise training is often used to increase physical function for CAD and HF, its value is validated and reinforced by physiological health benefits that already justify its application. The use of procedures to increase function such as valve replacements or repairs, pacemakers, or atrial fibrillation ablation becomes less certain amid confounding aspects of the primary disease, comorbidity, frailty, and other clinical complexities.

CHANGES IN PHYSICAL FUNCTION WITH EXERCISE TRAINING

The benchmarks for meaningful training-induced increases in CRF or strength depend on the goals of training. Observational studies in older adults have shown that walking >1.5 miles a day was associated with better clinical outcomes than walking lesser distances.¹⁴⁷ If, however, the goal is a meaningful improvement in physical function, a more intensive exercise stimulus is usually needed. Because the coefficient of variation of peak $\dot{V}O_2$ is $\approx 6\%$ to 7% in older patients with HF,^{148,149} an increase of $>7\%$ from baseline suggests a clinically meaningful improvement in aerobic capacity. Such an increase in peak $\dot{V}O_2$ may allow these patients to perform meaningful aerobic activities that were previously not possible.

Similarly, a modest increase in strength may allow a frail elder to perform meaningful tasks such as carrying groceries or making a bed. Fiatarone et al⁷⁰ analyzed the benefits of strength training in institutionalized seniors in their 80s and 90s and found that strength increased $>100\%$ after several weeks, with many able to reduce their dependence on wheelchairs and walkers. Resistance and balance training can also decrease falls in elders.¹⁵⁰ Thus, exercise programs for such individuals should generally incorporate interventions to improve strength and balance, as well as aerobic endurance.

PHYSICAL FUNCTION AND CVD

The functional declines that occur with aging are magnified by the development of CVD. Therefore, CVD is likely to occur in older adults who are already functionally impaired, with greater potential to compound functional limitations to the point when ADLs and independence are threatened. Addressing these predictable risks as a therapeutic priority is an important consideration for healthcare providers of older adults.

Atherosclerosis

Atherosclerosis is inherent to aging and has pervasive effects, including cardiovascular instability, underperfusion of skeletal muscle, cognitive changes, and neuromotor/cognitive impairments after stroke. Exercise results in a multitude of effects that can delay the progression of atherosclerosis and improve physical function (Tables 2–4¹⁵¹⁻¹⁷²); reduced inflammation, improved endothelial function, increased insulin sensitivity, and other benefits have all been demonstrated for older patients with CAD,^{173,174} peripheral artery disease,^{175,176} and stroke,^{177,178} with compounding benefits as function increases.

Ades et al¹⁷⁹ documented a 16% increase in peak $\dot{V}O_2$ in 60 patients with CAD 65 ± 5 years of age after a 3-month training program; the increase was mediated entirely by an $\Delta \dot{A}V\dot{O}_2$; that is, enhanced oxygen extraction. In another study, men and women >70 years of age participating in traditional outpatient cardiac rehabilitation (CR) after an acute coronary event or revascularization procedure derived improvements in exercise capacity that were similar to those in younger patients.¹⁸⁰

Older patients with peripheral artery disease had improved exercise capacity, walking speed, and diminished claudication, along with underlying improvements in endothelial function,¹⁸¹ capillary density, and mitochondrial oxidative activity. Stroke patients benefit particularly from task-specific functional strengthening (eg, repetitive rise from a chair) to overcome deficits in motor-sensory coordination.¹⁵⁹

Vascular disease also predisposes to cognitive impairment in older adults.¹⁸² Cognition changes are often manifest as subtle executive declines, which have been demonstrated to diminish capacity to undertake ADLs¹⁸³ and to contribute to a worsening cycle of reduced CRF.¹⁸⁴ A number of potential mechanisms contribute to cognitive impairment and dementia in CVD; however, cerebral infarcts and neurovascular dysfunction are the most important cerebrovascular pathologies,¹⁸² both of which may benefit from regular physical activity.

Heart Failure

The primary chronic symptom in older patients with HF with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction is severe exercise intolerance, even when patients are clinically stable and euolemic. Studies by Kitzman et al¹⁸⁵ and others¹⁸⁶⁻¹⁸⁸ found that in older patients with HF (mean age ≥ 70 years), peak $\dot{V}O_2$ during upright treadmill or cycle exercise is $\approx 30\%$ lower than in age-matched healthy subjects, and the magnitude of the reduction is independent of HF phenotype (ejection fraction).¹⁸⁶ The peak $\dot{V}O_2$ of a typical older patient with HF ($\approx 14 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$)¹⁸⁵⁻¹⁸⁸ is also well below the established threshold value (ie, $18 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$),¹²⁵

Table 2. Approaches to Improve Function in CAD and HF

Treatment	Supporting Evidence	Main Results
Atherosclerotic risk factor modification	AHA/ACCF guideline ¹⁵¹	Recommends antiplatelets, statins, angiotensin-converting enzyme inhibitors, and β -blockers when warranted for secondary prevention in coronary and atherosclerotic vascular disease (relevant for CAD, stroke, and PAD)
	23 Studies (n=11 085) ¹⁵²	Lifestyle management programs reduced all-cause mortality, cardiac mortality, reinfarction, and readmission and improved risk factors (BP, smoking, exercise, dietary habits).
Heart failure	Extensive research base for HFrEF; relatively more limited research base for HFpEF ^{153,154}	Improves exercise capacity and QOL. Similar benefits seem likely for HFpEF. Benefits of HFrEF to reduce rehospitalization and increase survival, although survival benefits remain controversial
CR	63 Studies (n=14 486) ¹⁵⁵	Reduces cardiovascular mortality and hospitalization and improves health-related QOL
Home-based CR	17 Studies (n=2172) ¹⁵⁶	Home-based CR is equally as effective for improving exercise capacity, modifiable risk factors, and health-related QOL as center-based CR.
Telehealth CR	11 Studies (n=1189) ¹⁵⁷	Telehealth exercise-based CR was comparably effective for improving aerobic capacity and more effective for improving physical activity level, exercise adherence, diastolic BP, and low-density lipoprotein cholesterol than center-based CR.

ACCF indicates American College of Cardiology Foundation; AHA, American Heart Association; BP, blood pressure; CAD, coronary artery disease; CR, cardiac rehabilitation; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; PAD, peripheral artery disease; and QOL, quality of life.

distinguishing between high and low physical function. A consequence of the HF-mediated decline in peak $\dot{V}O_2$ is decreased physical functional performance and greater risk for poor outcomes.^{186,187,189–193}

Among patients with HF, multiple studies have demonstrated substantial improvement in peak $\dot{V}O_2$ in response to exercise training. Although early studies focused on younger, predominantly male cohorts with HFrEF, more

recent studies have included larger proportions of older adults, women, and individuals with HF with preserved ejection fraction. In 181 patients with HFrEF and a mean age of 65 years (19% women), McKelvie et al¹⁹⁴ showed a 14% increase in peak $\dot{V}O_2$ after 12 months of combined cycle exercise and resistance training. Similarly, Austin et al¹⁹⁵ observed a 16% increase in 6MWT distance and 16% decrease in mean New York Heart Association class

Table 3. Approaches to Improve Function in Stroke

Treatment	Supporting Evidence	Main Results
Atherosclerotic risk factor modification	26 Studies (n=8021) ¹⁵⁸	Educational and behavioral secondary stroke prevention interventions had no clear benefit on modifiable risk factors.
Interdisciplinary rehabilitation	AHA/ASA guidelines for adult stroke rehabilitation and recovery ¹⁵⁹	Interdisciplinary rehabilitation (including physical medicine, physical and occupational therapy, speech and language therapy) improves functional recovery and reduces disability.
Early supported discharge	14 Studies (n=1957) ¹⁶⁰	Early supported discharge from the hospital improves ADL, increases likelihood of being independent, and reduces hospital length of stay.
Physical rehabilitation	30 Studies (n=1750) ¹⁶¹	Large doses (indicated by time scheduled for therapy) had better motor recovery.
	96 Studies (n=10 401) ¹⁶²	Physical rehabilitation improved functional recovery (motor function, balance, walking speed), but no one approach was more effective than another.
Physical fitness exercise	45 Studies (n=2188) ¹⁶³	Cardiorespiratory exercise (most involving walking) improved physical function, including peak $\dot{V}O_2$, walking, and balance.
		Inconsistent or limited evidence for cardiorespiratory exercise to improve mood or cognition
	13 Studies (n=1022) ¹⁶⁴	Exercise improved depressive symptoms, especially with higher-intensity exercise.
	9 Studies ¹⁶⁵	Exercise enhances cognitive performance in acquired brain injury (including stroke and traumatic brain injury).

ADL indicates activities of daily living; AHA/ASA, American Heart Association/American Stroke Association; and $\dot{V}O_2$, oxygen uptake.

Table 4. Approaches to Improve Function in PAD

Treatment	Supporting Evidence	Main Results
Atherosclerotic risk factor modification	Society for Vascular Surgery Lower Extremity Guidelines Writing Group ¹⁶⁶	Risk factors associated with PAD are similar to those for CAD (although smoking and diabetes mellitus may have more weight). Although there are limited studies on the impact of improving risk factors on function in PAD, secondary prevention strategies are well-established management strategies in CAD.
Exercise (generally 2 times a week)	30 Studies (n=1816) ¹⁶⁷	Improvement in pain-free walking distance and time
	24 RCTs (n=2074) ¹⁶⁸	Supervised exercise is more effective than unsupervised exercise in improving pain-free walking distance.
Antiplatelet	15 Cilostazol studies (n=3718) ¹⁶⁹	Improvement in pain-free walking distance in those with intermittent claudication
	49 Antiplatelet studies (n=35 518) ¹⁷⁰	ADP receptor inhibitors (eg, clopidogrel, ticlopidine) prevented major cardiovascular events. Dual antiplatelets (aspirin and clopidogrel) can reduce risk of amputation after revascularization but have increased risk of bleeding.
Revascularization	Society for Vascular Surgery Lower Extremity Guidelines Writing Group ¹⁶⁶	Recommends endovascular or surgical treatment for intermittent claudication for patients with significant functional disability, when pharmacological or exercise therapy has failed, and when the benefits of treatment outweigh the potential risks
	12 Studies (n=1548) ¹⁷¹	Revascularization (surgery, endovascular therapy) improved walking distance, claudication symptoms, and QOL, but superiority over exercise was limited. Supervised exercise and revascularization may be superior on walking outcomes to exercise alone.
	9 Studies (n=3071) ¹⁷²	Similar effects of bypass surgery and endovascular approaches on mortality and amputation in critical limb ischemia but better patency with surgery

CAD indicates coronary artery disease; PAD, peripheral artery disease; QOL, quality of life; and RCT, randomized controlled trial.

in a randomized trial of 200 patients with HFrEF with a mean age of 72 years (34% women) after 24 weeks of combined aerobic/resistance training. However, some studies demonstrated no significant increases in peak $\dot{V}O_2$ with aerobic training in older patients with HF.¹⁹⁶ In the multicenter HF-ACTION trial (Heart Failure and a Controlled Trial Investigating Outcomes of Exercise Training) involving 2331 adults (28% women) with HFrEF randomized to 3 months of supervised aerobic training followed by home training for ≥ 1 year versus usual care, the mean increase in peak $\dot{V}O_2$ was only $\approx 4\%$, largely because of low training adherence.¹⁹⁷ Despite this modest improvement in peak $\dot{V}O_2$, an 11% reduction in the combined primary end point of all-cause hospitalizations or death occurred over a median follow-up of 30 months. Although the median age of the HF-ACTION cohort was 59 years, results in the 435 patients >70 years of age were generally similar. Self-reported health status¹⁹⁸ and depressive symptoms¹⁹⁹ also improved modestly with aerobic exercise training.

The mechanisms responsible for the increased peak $\dot{V}O_2$ with aerobic exercise training may depend partly on HF phenotype, but the clinical benefits of improved exercise capacity, decreased fatigability, improved self-efficacy, and improved QOL are consistent regardless

of the mechanisms determining functional gains. In older patients with HF with preserved ejection fraction, the increased peak $\dot{V}O_2$ after moderate-intensity continuous endurance exercise training was secondary to peripheral adaptations that resulted in increased peak exercise $\Delta\dot{V}O_2$ difference without a change in cardiovascular function (ie, no change in peak exercise cardiac output, central artery stiffness, or peripheral arterial endothelial function).^{200,201} In older patients with HFrEF, the improvement in peak $\dot{V}O_2$ was associated with favorable adaptations in both cardiovascular and peripheral compartments.^{202,203} In both patients with HF with preserved ejection fraction and those with HFrEF, the peripheral contributions to improved peak $\dot{V}O_2$ with training appear to be attributable largely to improved skeletal muscle function (ie, increased percent skeletal muscle oxidative fibers, mitochondrial volume density, oxidative capacity, capillarity, and muscle blood flow).^{204–206}

INITIATING PHYSICAL ACTIVITY

Initiation of physical activity in older adults with CVD presents multiple challenges. Many older adults have led a sedentary lifestyle for so long that the utility of physical activity may no longer seem intuitive or appealing.

Moreover, older adults with CVD are particularly prone to multimorbidity, frailty, disability associated with hospitalizations, polypharmacy, and other debilitating risks that may make changing physical activity seem overwhelming or hopeless.

CR is a valuable component of the care plan in patients with CVD that can help mitigate these risks and impediments. Outpatient phase II CR is a multifaceted program with emphasis on aerobic and strengthening exercises, associated education, and techniques to build confidence and to foster behaviors conducive to physical activity and wellness that endure after the program is completed.²⁰⁷ Several Cochrane systematic reviews have demonstrated the utility of outpatient phase II CR to reduce mortality and hospital readmissions and to improve QOL.¹⁵⁵ Outpatient phase II CR achieved a 20% to 31% reduction in mortality from CAD, along with improved functional capacity,²⁰⁸ reduced risk factors, improved emotional health and QOL,²⁰⁹ and improved cognition.²¹⁰ Even patients who are relatively frail at enrollment are likely to benefit.²¹¹

Referral to outpatient phase II CR is a Class I recommendation from the American Heart Association, the American College of Cardiology, and the European Society of Cardiology²¹² for patients after acute myocardial infarction, coronary revascularization, valvular heart surgery, and cardiac transplantation and in stable individuals with HFrEF. However, despite these strong endorsements, phase II site-based CR is used by only 13% to 34% of eligible adults.^{124,213} Older adults are even less likely to attend,²¹² particularly those discharged to a skilled nursing facility (SNF) or to home care services after hospitalization,²¹⁴ despite proven benefits.^{215,216}

Although one of the strongest predictors of enrollment is an endorsement by a physician,²¹⁷ many eligible patients, particularly older adults, are simply not referred. Furthermore, even when they are referred, fewer older adults actually enroll; many cite logistic, psychosocial, and financial impediments.²¹²

Paradoxically, low participation of older adults in outpatient phase II CR programs has been attributed to multimorbidity, baseline frailty, and disability (such that CR seems particularly daunting), but patients with these features particularly benefit from CR. Unfortunately, entrenched barriers impede participation of most eligible patients. Similarly, older patients may benefit from initial inpatient or outpatient physical therapy to build sufficient strength before initiating CR, but this requires coordination and encouragement. Other common impediments to CR enrollment and participation include illness severity, complications during hospitalization, impaired cognitive or physical function, depression, pain, lack of social support, and logistic barriers.²¹⁸

Given the low use of outpatient phase II CR by older individuals, there is growing interest in new CR approaches. Transitional and home-based phase II CR

models have been shown to be effective and safe,^{219–222} although they are not standardized and often not reimbursed by insurance. Some of these programs include weekly telephone-based services.²²³ Novel mobile health applications are also a burgeoning field, with the potential to promote comprehensive CR interventions.²²⁴ The HEART trial (Heart Exercise and Remote Technologies)²²⁵ showed that text messaging and Internet use increased physical activity levels in individuals with CVD. A New Zealand trial, Text4Heart,²²⁶ is ongoing, and an Australian trial indicated benefit of a smartphone-based CR program to improve 6MWT distance and QOL²²⁷ in a home-based protocol. The utility of these approaches for older adults and all the associated challenges of cognition, frailty, and multimorbidity have yet to be established.

Novel exercise strategies may also improve outcomes in older patients with CVD. For example, tai chi may have distinctive value for older adults because it integrates strength, aerobic, and balance components. Yoga affords similar advantages.^{177,178} High-intensity interval training has also been suggested for its training efficacy in older, vulnerable patients with CVD.¹⁷⁸ However, high-intensity interval training entails short bursts of high-intensity aerobic exercise with longer periods of lower-intensity training that requires close supervision, and its utility for broader application to older adults is still unproven.

Although training strategies and adjuncts to reinforce them continue to evolve, the fact remains that exercise training is still a daunting challenge for the majority of older patients with CVD. Relatively simpler emphasis on increasing physical activity is often more successful than formal exercise training. Encouragement to make a bed, carry laundry, climb stairs, dance, or walk as part of a daily routine may better achieve healthful physically active behavior in many older adults.

PHYSICAL FUNCTION GOALS FOR SNFS

Typically, patients are referred from the hospital to postacute care settings because of greater disease complexity, deconditioning, or cognitive declines that have left them particularly debilitated.^{228–230} There are 2 fundamentally different tracks in institutionalized postacute care: SNFs provide care for adults intending to return home, and long-term care provides services to adults who require permanent institutional-level care. Although these are 2 distinctive populations with very different needs, they often coexist in the same building and are managed by the same staff. This is particularly problematic because it often adds to the likelihood that SNF residents will not receive care that prioritizes vigorous functional enhancement or that best facilitates their anticipated transitions to home or their long-term well-being.

SNFs serve many of the oldest and frailest cardiac patients who are discharged from the hospital.²³⁰ These patients are usually so deconditioned or encumbered by illness that they must regain basic mobility before returning home or entering standard rehabilitation. Many of these patients must first regain the ability to transfer from a bed to a chair, maintain balance to reduce the risk of falling, and recover ADL independence.

Current SNF rehabilitation does not adequately address deficits in physical function, which directly contributes to poor outcomes (low community discharge rates of only 28%²³¹). Although many factors play a role in the need for long-term institutionalization (ie, psychosocial, environmental), the low percentage of community discharge correlates particularly with functional status.²²⁹ In fact, impaired physical function is among the most important predictors of reinstitutionalization after SNF discharge.^{229,230} Similarly, for those patients who are able to return home from an SNF, impaired physical function often persists as a poorly addressed component of failing health,^{232–234} rehospitalization,^{233,234} or death.²³⁵

Current SNF rehabilitation paradigms dose the “intensity” of rehabilitation on the basis of standardized minutes of therapy per week, as opposed to standards oriented to specific domains (cardiovascular, strength, balance) that are pertinent and more effective. Evidence suggests that patients in rehabilitation at SNF settings are ≈80% less active compared with community-dwelling older adults, and they do not engage in an adequate intensity of rehabilitation to facilitate meaningful improvements in physical function.^{236–238} Notably, gait speeds at SNF discharge averaged 0.39 m/s,²³⁹ which is less than half of the 1.0 m/s necessary for community ambulation.²⁴⁰

There is little disease-specific research in SNFs with regard to physical function. Although 70% of older adults who use SNFs are eligible for some type of CR, there typically are no standard cardiac assessments and no cardiac education delivered in these facilities,²⁴¹ as well as no specific mechanisms to facilitate CR once patients leave SNFs and return to the community.

SUMMARY

Older individuals now constitute the predominant population of individuals with CVD; functional impairment is a predictable consequence, particularly because CVD compounds the functional deficits associated with aging. Therefore, optimally managing these patients requires an understanding of the importance and complexities of measuring and modifying functional capacity. The consequences of functional impairment in older adults with CVD include increased morbidity and mortality and reduced ability to perform ADLs, remain independent, and delay disability. Numerous studies have documented the importance of functional capacity as a predictor of out-

comes across the spectrum of age, including the very old. Optimization of functional capacity and other measures of physical function and frailty will become even more critical as the population continues to age.

Although the gold standard for assessing CRF, peak $\dot{V}O_2$, has a well-established history and is often the primary efficacy measure for interventions in CVD, it is not always readily available, nor is it the best metric for many older individuals. Moreover, exercise testing in the elderly can be problematic given the increased prevalence of orthopedic, neurological, or other conditions compromising the ability to exercise. Measurements including strength and balance are also important metrics of function and in many cases more strongly determine an older individual's ability to remain independent, continue working, or safely perform ADLs than maximal exercise tolerance. Numerous tests have been developed that are easily applied and that reflect combinations of strength, balance, mobility, and frailty that quantify a senior's ability to function independently and avoid falls, disability, or hospitalization. Advances in technology have provided an expanding role for wearable devices in quantifying physical function and activity patterns.

There is no specific guideline that dictates a schedule of assessments for older patients with CVD, but clinical management provides many logical considerations. Given the dynamic nature of CVD and aging, a routine periodic assessment of function seems reasonable. A simple assessment of physical and cognitive function can be used to quantify interval changes. The SPPB and Montreal Cognitive Assessment tests are easily administered in an office setting and provide relatively sensitive measures of longitudinal changes. Measurement of gait speed is even simpler than the SPPB to administer and is also effective. Routine assessment of ADLs can also be helpful; a change in ADLs often signifies a useful time to initiate further functional testing. A key underlying point is that there is no perfect tool for functional assessment; the more important priority is periodic and standardized monitoring.

Exercise intervention programs for older adults should be designed not only to increase maximal functional capacity but also to target the capacity to perform ADLs, maintain independence, and optimize QOL. Because deficits can differ considerably among older individuals, exercise therapy should be individualized. The incorporation of goals meaningful to a given patient for performing ADLs (eg, climbing stairs, basic household chores) or particular recreational activities should be emphasized because such goals are more tangible to the patient and are likely to be more motivating than an abstract measure such as peak $\dot{V}O_2$. Many of the multidomain tests designed to quantify strength, balance, mobility, and frailty in older adults are responsive to clinical change and to interventions. In general, it is logical to assess multiple domains of functional capacity as a part

of routine transitions of care, particularly as a means to assess vulnerability to falls, frailty, and progressive disability. A composite of a 6MWT, SPPB, and the Montreal Cognitive Assessment exemplifies a type of assessment that can provide important perspective for a patient's physical capacities at hospital discharge and before and after CR as a means to establish goals of care and organize management. Pre- and post-SNF assessments would be especially helpful in identifying the likely extent of risk and adding impetus for further rehabilitation.

A large and growing body of literature has demonstrated that older adults respond favorably to exercise training programs, with relative changes in function similar to those in younger adults. Novel programs using mobile technology or telehealth and home-based programs may increase accessibility to participants and improve adherence and have been demonstrated to be as effective as traditional center-based programs. Particular clinical conditions germane to older adults should be considered in the design of exercise programs, including concomitant CVD, metabolic and neurological disorders, pain, cognitive impairment, reduced strength, and balance deficits that increase the risk of falls. Exercise type, intensity, and progression will frequently need to be modified relative to younger individuals. Unfortunately, despite the fact that older adults stand to benefit considerably from rehabilitation programs, both their referral and participation rates are lower than those in younger adults.

There is a need for better recognition by clinicians of the importance of physical function in older adults. Current standards of medications and disease management have glaring deficiencies in attention to function and prioritization of interventions to enhance and maintain exercise capacity. Therapeutic options such as CR and SNFs are surprisingly underdeveloped and underused for functional enhancement in the elderly despite obvious potential. Moreover, current standards of evidence-based medications often manifest greater functional risks than anticipated benefits in the elderly. The approach of addressing and modifying physical function cohesively and logically has even more potential value when combined with therapeutic advances in valvular, pacing, and other

cardiovascular technologies that are increasingly used in older adults.

FOOTNOTES

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

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DISCLOSURES**Writing Group Disclosures**

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
Daniel E. Forman	University of Pittsburgh Medical Center; VA Pittsburgh Healthcare System	PCORI†; NIH†; Veterans Affairs†	None	None	None	None	None	None
Ross Arena	University of Illinois Chicago Physical Therapy	None	None	None	None	None	None	None
Rebecca Boxer	University of Colorado School of Medicine	NIH*	None	None	None	None	None	None
Mary A. Dolansky	Case Western Reserve University Nursing	None	None	None	None	None	None	None
Janice J. Eng	University of British Columbia Physical Therapy	Canadian Institutes of Health*	None	None	None	None	None	None
Jerome L. Fleg	NHLBI	None	None	None	None	None	None	None
Mark Haykowsky	University of Texas at Arlington College of Nursing and Health Innovation	NIH/NINR†; Moritz Chair in Geriatrics†	None	None	None	None	None	None
Arshad Jahangir	Aurora University of Wisconsin Medical Group Center for Integrative Research on Cardiovascular Aging	NHLBI, NIH†	None	None	None	None	None	None
Leonard A. Kaminsky	Ball State University Fisher Institute for Health and Well-Being	None	None	None	None	None	None	None
Dalane W. Kitzman	Wake Forest University School of Medicine	Novartis†	None	None	None	Gilead†	Merck*; Medtronic*; Bayer*	None
Eldrin F. Lewis	Brigham & Women's Hospital	Novartis†; Sanofi†; Amgen†	None	None	None	None	Novartis*	None
Jonathan Myers	Veterans Affairs Palo Alto Health Care System and Stanford University	None	None	None	None	None	None	None
Gordon R. Reeves	Sidney Kimmel Medical College at Thomas Jefferson University	NIH†; ResMed Foundation†; Thoratec Corp†	None	None	None	None	None	None
Win-Kuang Shen	Mayo Clinic	None	None	None	None	None	None	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives \$10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns \$10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

Reviewer Disclosures

Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
Philip Ades	University of Vermont	None	None	None	None	None	None	None
Nanette K. Wenger	Emory University	None	None	None	None	None	None	None
Mark A. Williams	Creighton University	None	None	None	None	None	None	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives \$10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns \$10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

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**Prioritizing Functional Capacity as a Principal End Point for Therapies Oriented to Older Adults With Cardiovascular Disease: A Scientific Statement for Healthcare Professionals
From the American Heart Association**

Daniel E. Forman, Ross Arena, Rebecca Boxer, Mary A. Dolansky, Janice J. Eng, Jerome L. Fleg, Mark Haykowsky, Arshad Jahangir, Leonard A. Kaminsky, Dalane W. Kitzman, Eldrin F. Lewis, Jonathan Myers, Gordon R. Reeves, Win-Kuang Shen and On behalf of the American Heart Association Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Quality of Care and Outcomes Research; and Stroke Council

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