Circulation

AHA SCIENTIFIC STATEMENT

State of the Science: The Relevance of Symptoms in Cardiovascular Disease and Research: A Scientific Statement From the American Heart Association

Corrine Y. Jurgens, PhD, RN, ANP, FAHA, Chair; Christopher S. Lee, PhD, RN, FAHA, Vice Chair; Dawn M. Aycock, PhD, RN, ANP-BC, FAHA; Ruth Masterson Creber, PhD, MSc, RN, FAHA; Quin E. Denfeld, PhD, RN, FAHA; Holli A. DeVon, PhD, RN, FAHA; Linda R. Evers, JD; Miyeon Jung, PhD, RN, FAHA; Gianluca Pucciarelli, PhD, RN, FAHA; Megan M. Streur, PhD, RN, FNP; Marvin A. Konstam, MD, FAHA; on behalf of the American Heart Association Council on Cardiovascular and Stroke Nursing; Council on Hypertension; and Stroke Council

ABSTRACT: Symptoms of cardiovascular disease drive health care use and are a major contributor to quality of life. Symptoms are of fundamental significance not only to the diagnosis of cardiovascular disease and appraisal of response to medical therapy but also directly to patients' daily lives. The primary purpose of this scientific statement is to present the state of the science and relevance of symptoms associated with cardiovascular disease. Symptoms as patient-reported outcomes are reviewed in terms of the genesis, manifestation, and similarities or differences between diagnoses. Specifically, symptoms associated with acute coronary syndrome, heart failure, valvular disorders, stroke, rhythm disorders, and peripheral vascular disease are reviewed. Secondary aims include (1) describing symptom measurement methods in research and application in clinical practice and (2) describing the importance of cardiovascular disease symptoms in terms of clinical events and other patient-reported outcomes as applicable.

Key Words: AHA Scientific Statements ■ arrhythmias ■ cardiovascular disease ■ coronary artery disease ■ heart failure ■ patient-reported outcomes ■ peripheral vascular disease ■ stroke

Symptoms are subjective experiences that may indicate disease or significant change in health status. Symptoms have been linked to cardiovascular disease (CVD) since Egyptian physicians and Hippocrates described fatigue and dyspnea, respectively, as being related to the failing heart.[1,2] In a contemporary view of CVD, symptoms often are critical elements of the diagnosis, evaluation, management, and certainly lived experience of illness. Symptoms also drive health care use and are a major contributor to broad patient-reported outcomes such as quality of life in chronic CVD.[3,4] More commonly, research in CVD is focused on major adverse cardiovascular events such as hospitalization or death in response to cardiovascular therapies and less so on symptoms despite their fundamental significance. The primary purpose of this scientific statement is to present the state of the science and relevance of symptoms associated with CVD. Symptoms as patient-reported outcomes are reviewed in terms of the genesis, manifestation, and similarities or differences between diagnoses. Secondary aims are to describe symptom measurement methods in research and to describe the importance of symptoms in terms of clinical events and other patient-reported outcomes as appropriate.

SYMPTOM TRAITS AND CAVEATS IN CVD

Although we frequently assume that symptoms are subjective experiences that accurately reflect underlying bodily changes, several caveats must be taken into consideration in the interpretation of symptoms in CVD (Table 1).

Supplemental material is available at https://www.ahajournals.org/doi/suppl/10.1161/CIR.0000000000001089.

Circulation is available at www.ahajournals.org/journal/circ

Table 1. Symptom Definition, Characteristics, Traits, and Caveats

Definition	Subjective experiences that may indicate disease or change therein
Characteristics	Intensity, quality, duration, timing, distress, interference with life
Traits	Localized (for example, substernal chest pain) or generalized (for example, fatigue) experiences that can involve any of the body's senses[5]
Caveats	Bodily changes must be (1) different in intensity or frequency and (2) sufficient in magnitude, newness, or significance compared with normal bodily sensations to be detected as symptoms.[5,6]
	Bodily changes are interpreted as a function of their attribution (for example, fatigue from heart failure vs a normal aging process)[7,8] and within cultural norms.[9]
	Bodily changes may be misinterpreted (that is, symptoms can be experienced without underlying change in pathogenesis, or change in underlying pathogenesis may not be experienced as symptoms).
	External stressors may cause unawareness of major body changes or hypervigilance to even small changes in health.[10]
	Symptoms may be highly variable among patients with similar cardiovascular disorders.[10,11]
	Symptoms of CVD commonly occur in clusters.[12–14]

CVD indicates cardiovascular disease.

Most notably, patients with CVD may experience symptoms in the absence of major changes in underlying pathogenesis. The absence of symptoms also does not necessarily confer the absence of change in underlying pathogenesis, particularly in advanced CVD.[15] Nevertheless, symptoms have relevance in CVD, particularly in acute coronary syndrome (ACS), heart failure (HF), valvular disorders, stroke, rhythm disorders, and peripheral vascular disease.

ACUTE CORONARY SYNDROME

Chest Pain and Associated Symptoms

The most frequently reported symptom of ACS is chest pain. Chest pain has often been described as substernal pressure or discomfort and may radiate to the jaw, shoulder, arm, or upper back. The most common co-occurring symptoms with chest pain are dyspnea, diaphoresis, unusual fatigue, nausea, and lightheadedness.[16] Symptoms such as unusual fatigue and weakness have often been labeled as atypical in ACS, but this labeling may be a function of men being the standard for typical symptom presentation as opposed to true symptom frequency. In a review of 7 studies assessing prodromal symptoms of ACS,[17] chest discomfort/pain, arm pain/discomfort, jaw pain, back/shoulder blade pain, unusual fatigue, shortness of breath, sleep disturbance, dizziness, headache, anxiety, and gastrointestinal complaints were reported in ACS. Patients with persistent angina also experience higher rates of depression and anxiety.[18] It remains unknown how depression may affect the report of physical symptoms of ischemic heart disease; however, shortness of breath and chest pain may be more prevalent among depressed patients with ischemic heart disease.[19]

A central challenge in interpreting symptoms in ACS is the lack of consensus on the duration of the prodromal phase, which in the literature ranges from 1 month to 48 hours before an ACS event.[16,17] Women reporting arm pain or discomfort and unusual fatigue during initial ischemic heart disease evaluation are more likely to have a cardiac event at any point in the next 90 days.[20] However, few cardiac symptoms are actually sensitive and specific for ischemic heart disease. Consequently, women are at risk for additional morbidity such as sustaining an ST-segment–elevation myocardial infarction secondary to misjudging or attributing symptoms to a minor cause. Put simply, it can be challenging to determine whether prodromal symptoms are specific to an ACS episode, as well as their clinical relevance to patient outcomes.

Sex Differences

More similarities in symptom presentation in ACS have been reported among women compared with men, but salient differences have been found. For example, in the EPIHeart study, there were no significant differences in the frequency or location of chest pain by sex, but women reported significantly more severe pain and more referred pain compared with men.[21] In a large American cohort, women were significantly more likely to experience nausea, shoulder pain, upper back pain, and a greater number of ACS symptoms compared with men.[16] Last, in the VIRGO study (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients), younger women with acute myocardial infarction were more likely to present with a cluster of ≥3 symptoms (ie, epigastric symptoms, palpitation, and pain or discomfort in the jaw, neck, arms, or shoulders) compared with men.[12]

On average, women with ACS are significantly older than men, with differences ranging from 2 to 10 years.[16,21,22] Ischemic heart disease is less prevalent among women than men for every age group in the United States except 20 to 39 years of age.[23] The incidence of myocardial infarction or fatal ischemic heart disease is higher for women only after 85 years of age.[23] Younger individuals with ACS are more likely to be male, to smoke, and to have a family history of premature CVD. Younger adults are also less likely to have extensive disease or ST-segment–elevation myocardial infarction.[24] There is a caveat in that the term young varies across the literature, ranging from ≤40 to ≤55 years of age, and there is no universally accepted cutoff.[24] The contributions of chronological (passage of time) and biological (functional decline) aging[25] to symptoms experienced by patients with ACS are unknown.

Clinical Application of Measurement

A majority of ACS symptom measures are disease-specific and multidimensional, and many are valid and

 Circulation. 2022;146:00–00. DOI: 10.1161/CIR.0000000000001089

reliable (Online Table).[26] However, the availability of multiple measures means that there is no standard instrument in use. A lack of standard measures means that there could be a bias in favor of certain symptom assessments and an inability to compare symptoms across cohorts. Moreover, lack of harmonization of ACS symptom measurement in research hampers growth in cumulative evidence. Therefore, little can be done to synthesize salient findings about symptoms across ischemic heart disease/ACS studies and to incorporate evidence-based information about symptoms into treatment guidelines and patient education materials. In clinical practice, tracking symptoms over time with respect to both severity and life interference with a valid and reliable measure would help contribute to the limited evidence base compared with the more typical arbitrary approaches to symptom appraisal. The Online Table outlines the strengths, limitations, and content of and key references for the various measures available for CVD.

HEART FAILURE

Dyspnea

Dyspnea (aka, shortness of breath, breathing discomfort, or breathlessness) is a hallmark of HF. Increased dyspnea is one of the most common reasons that adults with HF seek hospitalization, and severe dyspnea is associated with a greater risk of mortality.[27] Dyspnea is often characterized in terms of provocation, meaning dyspnea at rest, dyspnea on exertion, orthopnea, paroxysmal nocturnal dyspnea, and bendopnea.[28,29] It is important to account for dyspnea heterogeneity in both clinical practice and research by using nuanced measures and probing questions to capture this common and multifaceted symptom. Profiling techniques have been helpful in pinpointing patients with different clinical phenotypes of dyspnea in HF.[30] Moreover, it is important to consider non–HF-related causes when evaluating dyspnea, especially comorbid conditions such as chronic obstructive pulmonary disorder.[31]

Early Physical Symptoms

Early and subtle symptoms also can be harbingers of worsening HF and impending hospitalization or death.[27] For example, gastrointestinal-related symptoms such as upset stomach, nausea and vomiting, and loss of appetite can be related to intestinal congestion.[32] Fatigue is rated as both the most common and the most bothersome hallmark HF symptom.[33] Fatigue has variable causes both related and unrelated to HF pathophysiology and results in exercise intolerance, especially with co-occurring dyspnea. Together, these symptoms may herald muscle wasting and cachexia, which are indicators of HF progressing to more advanced stages.[34]

Other Symptoms and Symptom Clusters

Adults with HF commonly report insomnia and wake disturbances related to both HF (eg, pulmonary congestion) and non-HF causes (eg, sleep apnea), as well as side effects from medications (eg, nocturia).[35] Pain is a common but often unsolicited symptom in HF and can be attributable to cardiac causes (eg, deconditioning) or noncardiac causes (eg, diabetic neuropathy).[36] For some patients with HF, pain increases toward the end of life and can be exacerbated by physical limitations.[37] In addition to physical symptoms, 25% to 30% of adults with HF report mood disturbances, manifesting primarily as depressive and anxiety symptoms, that are independently associated with poor clinical outcomes.[38] In HF, physical and affective symptoms frequently cluster together regardless of cultural differences,[39] and such symptom clusters are associated with a gradient in clinical event risk.[13,40]

Cognitive dysfunction is common among patients with HF. It is likely attributable to lowered cerebral blood flow resulting from HF and associated with structural and functional changes to the brain.[41] A central challenge in dealing with cognitive dysfunction is that it is both a sign of HF and it directly affects a patient's ability to recognize and respond to other symptoms when they occur.[42] Accordingly, patients with HF who experience cognitive dysfunction have higher 30-day and 1-year mortality.[43] However, by definition, cognitive dysfunction is not subjective and is therefore not a symptom.

Sex and Age Differences

Women report higher physical symptom burden, higher depression and anxiety, and lower quality of life.[44–47] Symptoms reported more frequently by women are similar to what occurs in ACS (eg, nausea, palpitations, epigastric symptoms).[44,46] Women also were more likely to report higher pain (other than chest pain), nervousness, edema, and sweating.[44] Differences may partly be explained by a higher comorbid illness burden or diagnosis of HF at a later age among women.

Older adults in general perceive less dyspnea compared with younger adults.[48] Indeed, among adults with HF, older age is associated with problems recognizing and interpreting dyspnea.[49] In addition, physically frail adults with HF have significantly worse dyspnea, sleep-wake disturbances, and depressive symptoms compared with adults with HF who are not physically frail.[50] Taken together, both chronological age and biological age contribute to patient experience with symptoms in HF.

Clinical Application of Measurement

Several measures of symptoms in HF are commonly used and have evidence of validity and reliability (Online Table). Although quality of life and health status measures are

Table 2. Valve Lesions and Salient Symptom Differences

Aortic stenosis	AS may present with angina, syncope, or dyspnea, with none being specific for this disease.[52,54] All symptoms of AS portend progressive deterioration and limited survival. Mortality correlates with the presenting symptom, with angina being the least onerous; HF symptoms, notably dyspnea, carrying the worst prognosis; and syncope being in between.[55] Recommendation for delayed intervention in the absence of symptoms assumes that sudden cardiac death (that is, without antecedent symptoms) is rare in adults and is exceeded by surgical risk.[53] Intervention in severe disease is considered before symptom onset attributable to a decline in procedural morbidity and mortality and an estimated annual rate of sudden death between 0.5% and 1%.[53,54] Transcatheter aortic valve replacement has a favorable impact on symptoms and functional capacity in inoperable patients. It is at least equivalent to surgical intervention in high- to moderate-risk patients.[56,57]
Aortic regurgitation	Acute AR, as with acute bacterial endocarditis or acute aortic dissection, can be catastrophic, with acute pulmonary edema or cardiogenic shock. In chronic AR, after an often-protracted asymptomatic period, symptoms of HF reflect advancing LV remodeling and dysfunction. Early surgery is indicated when associated symptoms appear or in the presence of reduced LVEF (≤55%) to avoid progressive, irreversible LV damage.[52,53,58]
Mitral stenosis	With incident rheumatic MS virtually abolished, more cases are now recognized to be attributable to severe mitral annular calcification. Left-sided HF, with progressive dyspnea and exercise intolerance, is a manifestation of mitral flow obstruction, resulting in increased pulmonary vein pressure and impaired LV filling. Pulmonary hypertension, with associated RV dilation and dysfunction and symptoms of edema, hepatic congestion, and ascites, is more evident and less reversible with MS than with other valve lesions. Unlike with aortic valve disease, relatively mild symptoms may be manageable with diuresis and rate control. Advancing valve pathology and symptoms, including increased dyspnea and functional incapacity, call for mitral valvuloplasty or replacement.[53] Such intervention often results in dramatic symptom improvement and prevention of progressive symptoms of pulmonary arterial hypertension and right-sided HF.
Mitral regurgitation	MR may be functional, associated with LV and mitral annular dilation of any cause, or structural, with congenital or acquired valve deformity. Acute, severe MR often presents as acute pulmonary edema, which may require urgent intervention. In chronic MR, unlike aortic valve disorders, symptoms of left-sided HF result from direct LV ejection into the left atrium and therefore may occur in advance of significant LV damage. Mild symptoms may be manageable with diuretics, rate control, and vasodilators to reduce both LV afterload and preload. Factors affecting the decision for mitral repair or replacement include the severity and progression of symptoms, the nature of the valve lesion, the severity of regurgitant flow, and evidence for advancing LV dilation (end-systolic diameter ≥40 mm) and dysfunction (LVEF ≤60%).[53] Transcutaneous valve intervention for MR, in addition to reducing morbid and fatal events, has been shown to significantly improve health status.[59]
Tricuspid valve disease	Tricuspid stenosis is rare and results in symptoms of right-sided HF. Structural TR results from valve pathology, whereas TR is most commonly functional, associated with RV dilation attributable to myopathy, myocardial infarction, pulmonic valve obstruction, pulmonary emboli, or any other cause of pulmonary hypertension. TR symptoms are those of right-sided HF, including functional incapacity, edema, ascites, and hepatic congestion. In severe and chronic TR, hepatic failure may occur with its attendant symptoms, including jaundice, and may obviate procedures requiring general anesthesia. TR may be better tolerated when not associated with excessive RV afterload. Diuretics, pulmonary vasodilators, and nitrates often reduce symptoms of right-sided heart failure, particularly in functional TR. Structural intervention is considered in severe disease,[53] particularly in the case of valvular structural cause.

AR indicates aortic regurgitation; AS, aortic stenosis; HF, heart failure; LV, left ventricular; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; MS, mitral stenosis; RV, right ventricular; and TR, tricuspid regurgitation.

most commonly used in HF, the number of symptoms indirectly covered by such measures is limited. Current and future work in HF symptoms is now focused on symptom patterns and clustering over time, which have received limited attention in other CVDs.

VALVULAR HEART DISEASE

Valvular heart disease is a frequent cause of HF, with symptoms generally indistinguishable from other HF causes. Rheumatic heart disease, although still prevalent in low- and middle-income countries,[51] has largely disappeared elsewhere and has been replaced by population aging and cardiomyopathies as predominant drivers of valve disease. In the absence of acute severe valve dysfunction, patients generally have a prolonged asymptomatic period, followed by a period of progressive symptoms,[52] resulting from the valve lesion itself or secondary myocardial remodeling and dysfunction. The staging of valvular heart disease is based on a combination of valve findings, symptoms, and ventricular function.[53] Over time, left-sided valve dysfunction may result in pulmonary hypertension with tricuspid regurgitation and right-sided HF. Functional assessment may be aided by maximal exercise testing (ie, cardiopulmonary exercise testing). The 6-minute walk test and quality-of-life questionnaires are among the more common tools used to quantify benefit after valve intervention and to compare different interventional approaches. Among the valve lesions, there are subtle differences in terms of the role of symptoms in guiding the timing of intervention (Table 2).[56]

Sex Differences

Symptoms differ between the sexes for aortic valve disease. Aortic stenosis is typically asymptomatic for years. Women report dyspnea and exercise intolerance more often than men as stenosis progresses. Women also are more likely to be physically frail and to have a higher New York Heart Association class (III/IV) than men. Men are more likely to have chest pain.[60,61]

Clinical Application of Measurement

Symptom presence and severity are key in determining the stage of disease and timing of surgical or transcatheter intervention. However, the implication of symptoms differs across the various lesions. Quantitative symptom and functional assessments have been important research tools in gauging the efficacy of interventional treatment (Online Table). Given the importance of symptom assessment, more work is needed to determine the incremental value of quantitative symptom measurement as an aid to clinical management.

STROKE

Acute Stroke Symptoms

Acute symptoms often predict disability and quality of life after stroke.[62] Identifying and responding to stroke signs and symptoms quickly is essential for proper treatment.[63] Acronyms like FAST[64] (face, arm, speech, time) and related derivations were developed to facilitate lay public recognition and prehospital response to the most common signs of stroke. Weakness and numbness, speech problems, confusion, dizziness and loss of coordination/balance, and visual changes have been associated with the likelihood of seeking emergency care,[65,66] but timeliness of response differs by symptom.

For clinicians, classic stroke symptoms, in addition to nonclassic symptoms such as partial sensory deficit, dysarthria, vertigo, and diplopia,[67] require consideration for activating a stroke response team.[68] The Rapid Arterial Occlusion Evaluation Scale[69] and National Institutes of Health Stroke Scale show the best diagnostic accuracy values,[70] with the latter advocated for most because of rapid performance, along with both accuracy and reliability (Online Table).[71]

Poststroke Symptoms

After a stroke, acute symptoms may linger, becoming disabilities, or improve with time or rehabilitation. Although there are others, the Stroke Specific Quality of Life scale is the dominant means to assess physical function and is shorter and easier to administer in daily practice compared with alternatives.[72] Stroke severity, physical disability, and cognitive impairments after stroke are associated with common poststroke symptoms of anxiety, depression, fatigue, and pain.[73–76] About one-fourth of stroke survivors experience anxiety,[77] one-third experience depression,[75] at least half report fatigue,[78] and up to half report pain,[79] all at various stages in stroke recovery.

Sex Differences

A systematic review and meta-analysis revealed that women were more likely to present with nonfocal symptoms (eg, headache, altered mentality, and coma/stupor) than men.[80] To enhance public education about stroke symptoms and to facilitate the diagnosis and treatment of stroke, research is needed to better understand the presentation of stroke symptoms by other select demographic characteristics (eg, race and ethnicity, age, stroke subtype).

Clinical Application of Measurement

The significance of time is evident for when to assess stroke symptoms in the hyperacute and acute phases of stroke, but the optimal frequency of symptom assessment is less clear for the subacute and chronic phases. All people who experience a stroke should be screened for poststroke anxiety and depression and other physical and psychological issues (Online Table).[81] Stroke survivors at high risk of depression (eg, high stroke severity, age ≤50 years, history of depression, cognitive impairment) should be assessed at various stages throughout the continuum of stroke care, especially at transition points.[81] Although there are other means of assessing anxiety and depressive symptoms, in a systematic review, only the Hospital Anxiety and Depression Scale was recommended for its high sensitivity and specificity in stroke.[82] The 2016 American Heart Association/American Stroke Association "Guidelines for Adult Stroke Rehabilitation and Recovery" recommend the use of a structured depression inventory (eg, Patient Health Questionnaire-2) to routinely screen for poststroke depression.[83]

In a 2017 American Heart Association scientific statement on poststroke fatigue, the frequently used Fatigue Severity Scale was recommended.[73] Another tool, the Neurological Fatigue Index for Stroke, has been shown to screen fatigue at all levels of severity; it is easy to use and freely available from the authors.[84] It is recommended to assess for poststroke fatigue at discharge from acute care; at 3, 6, and 12 months; and then annually.[73]

Last, poststroke pain may involve neuropathic pain and nociceptive pain, musculoskeletal pains, shoulder pain, spasticity-related pain[76]; there are no stroke-specific measures of pain because of the heterogeneity of neurological deficits in this population.[79] Hence, general self-report questionnaires, pain scales, and

clinical assessment are used to assess poststroke pain. Poststroke pain can take weeks to months to develop, with the highest prevalence rates at 4 to 6 months.[79,85] Prevalence rates and individual responses should guide the assessment of pain and anxiety after stroke.

RHYTHM DISORDERS

Cardiac arrhythmias, including atrial fibrillation (AF), atrial flutter, supraventricular tachycardias, bradyarrhythmias, and ventricular tachycardia, present with common symptoms. Palpitations (ie, perceiving the heartbeat as irregular, rapid, fluttering, skipping, or pausing) is a characteristic symptom of many cardiac arrhythmias. The most common cardiac arrhythmia, AF, may present with palpitations or less specific symptoms (eg, fatigue, dyspnea, dizziness) that occur in association with a broad range of disease conditions.[86] Palpitations are considered the typical symptom presentation for AF, yet patients with new-onset AF often present either asymptomatically or with nonspecific symptoms.[86] Palpitations (27%–70%), fatigue (26%–75%), and dyspnea (28%–76%) are the most common symptoms reported by patients with AF, whereas chest pain (12%–30%), dizziness (19%–44%), presyncope/syncope (3%–4%), and anxiety (12%–50%) occur less frequently.[87–90] Psychological distress also may be associated with worse AF symptom severity.[91] Last, AF symptoms do not correspond to objectively measured AF episodes in all cases.[92] Even within the same individual, AF may fluctuate between symptomatic and asymptomatic.[93]

Tachycardia accounts for some symptom variability, although achieving heart rate control does not always eliminate symptoms.[94] AF ablation reduces symptoms,[95] but the effect is not attributable solely to a reduction in AF burden. It is interesting to note that in 1 study 52% of AF episodes were asymptomatic before AF ablation and 79% were asymptomatic after ablation.[96] AF also is a well-known risk factor for developing stroke and dementia.[97] Moreover, even among patients without prior stroke, the diagnosis of AF is a risk factor for poor cognitive function.[98] Symptoms of AF are often erroneously attributed to deconditioning, stress, or sleepiness, leading to delays in seeking medical attention for a week or longer.[99] Nonspecific (fatigue and dyspnea) and intermittent symptoms are associated with a delay in seeking treatment for AF, whereas cardiac-specific symptoms, including palpitations and chest pain, are not.[100] In a longitudinal cohort, patients with AF who initially presented with palpitations had lower stroke and mortality rates, even after adjustment for thromboembolic risk and anticoagulation.[86] In ORBIT-AF (Outcomes Registry for Better Informed Treatment of AF)[101] and RACE II (Rate Control Efficacy in Permanent AF),[102] worse AF symptom severity was associated with higher hospitalization rates. Symptoms also are the reason for presentation in 50% of patients presenting to the emergency department for AF.[103]

Sex, Age, and Racial Differences

Women and younger individuals with AF typically present with palpitations,[14,86] whereas men are more commonly asymptomatic.[86,104,105] Older age also increases the likelihood of a nonclassic or asymptomatic presentation of AF.[14,86,105] With regards to race, 2 systematic reviews reported an AF paradox in terms of symptoms associated with AF. Despite non-Hispanic Black individuals being at lower risk for development of AF, Black patients are burdened more with palpitations, dyspnea on exertion, exercise intolerance, dizziness, dyspnea at rest, and chest discomfort compared with White or Hispanic patients.[106,107]

Clinical Application of Measurement

Symptom monitoring and the association between symptoms and heart rate and rhythm are essential components of medication titration for rate control and selection of a rate versus rhythm control management strategy.[108] Clinicians underrepresent AF symptom severity[102]; hence, clinician-reported AF symptom measures should be avoided unless absolutely necessary. Several measures are available to quantify rhythm disorders; however, some are limited in terms of validity testing or comprehensiveness of symptoms assessed (Online Table). Correlating symptoms and rhythm also can present a challenge when symptoms occur infrequently and unpredictably, but mobile health devices increase AF detection compared with standard practice (eg, mobile devices, in-office ECGs, 24-hour Holter) and therefore reduce diagnostic delay and improve symptom-rhythm correlation.[109]

PERIPHERAL VASCULAR DISEASE

Peripheral Arterial Disease

Peripheral vascular disease and its associated symptoms can arise from either arterial or venous pathology. Peripheral arterial disease (PAD) is a progressive atherosclerotic disease resulting in insufficient blood flow to the lower extremities. PAD symptoms vary, ranging from none (despite disease progression) to leg pain at rest. Classic claudication occurs in approximately one-third of patients and is defined as calf pain that occurs in 1 or both legs with exertion (walking), does not begin at rest, and resolves within 10 minutes of standing still or rest. Nonclassic symptoms (eg, noncalf exercise pain) are reported more frequently than classic claudication symptoms. Assessing symptoms at rest, during exercise, and during recovery can assist with classifying symptoms as ischemic or not.[110,111]

Table 3. Common Symptoms Across CVD Diagnoses

Anxiety	Chest pain	Depression	Dizziness	Dyspnea	Fatigue
ACS	ACS	ACS	AF	ACS	ACS
AF	Aortic stenosis	HF	Stroke	Aortic stenosis	AF
HF	AF	PAD		AF	HF
Stroke		Stroke		HF	PVD
					Stroke

ACS indicates acute coronary syndrome; AF, atrial fibrillation; CVD, cardiovascular disease; HF, heart failure; PAD, peripheral arterial disease; and PVD, peripheral venous disease.

Limb ischemia is the most severe form of PAD, with individuals experiencing pain in their legs, feet, or toes. Symptomatic PAD is associated with an increased risk of major adverse cardiovascular events, with men at higher risk.[112,113] Last, depression is common in PAD, with a prevalence (3%–48%) similar to that of other types of CVD. Women, the elderly, individuals of underrepresented races and ethnicities, and those with worse disease and physical function are at increased risk of depression.[114]

Peripheral Venous Disease

Similar to patients with PAD, individuals with peripheral venous disease (PVD) can be symptomatic or asymptomatic. Clinical classification of PVD includes symptoms such as leg pain, aching, fatigue, heaviness, cramping, tightness, restless legs syndrome, and skin irritation. In a study of symptoms in chronic venous disorders (n=38 750; 78% female), pain, heaviness, aching, and fatigue were more common in people <65 years of age.[115] Pain and heaviness are believed to be caused by venous dilatation and hypoxia of the venous wall.[115,116] Symptoms also may occur without visible signs of PVD.

Sex Differences

Sex differences in peripheral vascular disease are specific to PAD. Women with PAD are more likely to have nonclassic symptoms or an absence of symptoms. Symptom attribution among women is complicated by comorbid musculoskeletal diseases (eg, osteoarthritis) or the mistaken belief that PAD is more common in men. Women with PAD also have a more rapid decline, worse quality of life, and higher burden of depression.[117]

Clinical Application of Measurement

Existing measures for PVD are quality-of-life measures that include symptoms, limitations of activities of daily living, and psychological impact (Online Table). Current PVD measures have limitations similar to other CVDs in terms of data supporting responsiveness to change or minimally important differences. Moreover, existing legacy measures of PVD are centered on clinician appraisal versus patient-reported symptoms.

CONCLUSIONS

Amelioration of CVD symptoms is an integral part of CVD management. It is important to recognize that CVD symptoms are simply not static and may vary in occurrence or severity over time. Moreover, several symptoms such as dyspnea and fatigue are common across disorders. Therefore, it is prudent to use established measures or to develop reliable, valid, relevant, and responsive measures of CVD symptoms for tracking over time. It is important to acknowledge that several existing measures have limitations in terms of responsiveness to change or lack of established minimally important differences. Most measures have not been evaluated for measurement error based on sex, race, or ethnicity, which is problematic given the lack of sex balance and racial representation in CVD research. Many measures are used on the basis of legacy application versus appropriateness for informing research or clinical care. Monitoring symptoms with reliable and valid measures in research and clinical practice may enhance clinical care by identifying those who may be at risk for poor outcomes more quickly (eg, lower quality of life, hospitalization, death).

People living with CVD commonly have symptoms directly related to their CVD and their other chronic conditions, as well as associated symptoms such as sleep disturbance and depression (Table 3). Therefore, it is challenging for people living with CVD to disambiguate and appropriately attribute their symptoms to any one disorder. Furthermore, cognitive dysfunction and depression have a bearing on patients' ability to detect underlying changes in symptoms[42,118–120]; therefore, both should be measured to establish a baseline and in response to significant clinical changes. More information is needed on the relationship between symptoms and clinical events, as well as underlying CVD pathogenesis, especially among people living with multiple chronic conditions. Despite limitations in measurement and complexities in how they are experienced, symptoms have clear relevance to the diagnosis, monitoring, and treatment of CVD.

ARTICLE INFORMATION

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.

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on April 27, 2022, and the American Heart Association Executive Committee on May 16, 2022. A copy of the document is available at https://professional.heart.org/statements by using either "Search for Guidelines & Statements" or the "Browse by Topic" area. To purchase additional reprints, call 215-356-2721 or email Meredith.Edelman@wolterskluwer.com.

The American Heart Association requests that this document be cited as follows: Jurgens CY, Lee CS, Aycock DM, Masterson Creber R, Denfeld QE, DeVon HA, Evers LR, Jung M, Pucciarelli G, Streur MM, Konstam MA; on behalf of the American Heart Association Council on Cardiovascular and Stroke Nursing; Council on Hypertension; and Stroke Council. State of the science: the relevance of symptoms in cardiovascular disease and research: a scientific statement from the American Heart Association. *Circulation.* 2022;146:e•••–e•••. doi: 10.1161/CIR.0000000000001089

The expert peer review of AHA-commissioned documents (eg, scientific statements, clinical practice guidelines, systematic reviews) is conducted by the AHA Office of Science Operations. For more on AHA statements and guidelines development, visit https://professional.heart.org/statements. Select the "Guidelines & Statements" drop-down menu, then click "Publication Development."

Disclosures

Writing Group Disclosures

Writing group member	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Corrine Y. Jurgens	Boston College School of Nursing	None	None	None	None	None	None	None
Christopher S. Lee	Boston College	NIH (MPI/co-I)†; PCORI (DSMB chair)*	None	None	None	None	None	None
Dawn M. Aycock	Georgia State University	Gordon and Betty Irene Moore Foundation (funded grant)†	None	None	None	None	None	None
Quin E. Denfeld	Oregon Health & Science University School of Nursing	NIH/NINR (R01NR019054)†; NIH/ORWH (K12HD043488)†	None	None	None	None	None	None
Holli A. DeVon	University of California Los Angeles School of Nursing	None	None	None	None	None	None	None
Linda R. Evers	Linda Evers, Stevens & Lee	None	None	None	None	None	None	None
Miyeon Jung	Indiana University School of Nursing	AHA (PI)†; NIH/NINR (co-I)†; Indiana University School of Nursing (PI)*; Midwest Nursing Research Society (a mentor on a dissertation grant)*	None	None	None	None	None	None
Marvin A. Konstam	Tufts Medical Center, The CardioVascular Center	None	LivaNova†; scPharma† (all clinical trials)	None	None	None	Boehringer Ingelheim†; Carduriant†; Cytokineticst; LivaNova†; Luitpold*; Merckt; Pfizert; scPharma†	None
Ruth Masterson Creber	Weill Cornell Medicine	None	None	None	None	None	None	None
Gianluca Pucciarelli	University of Rome Tor Vergata (Italy)	None	None	None	None	None	None	None
Megan M. Streur	University of Washington	NIH/NINR (K23NR017632 [PI])†	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
Jonathan Auld	University of Washington	National Institute of Nursing Research (K23 award)†	None	None	None	None	None	None
Kenneth M. Faulkner	Stony Brook University	None	None	None	None	None	None	None
Lisa Kitko	Penn State University	None	None	None	None	None	None	None
Lea Ann Matura	University of Pennsylvania	Bayer (funding for an RCT to treat [nonpharmacologically] insomnia and fatigue)†	None	None	Peter A. Allegra*	None	None	None
Bunny J. Pozehl	University of Nebraska Medical Center	None	None	None	None	None	None	None
Jessica H. Thompson	University of Kentucky	NIH (K award–BIRCWH recipient, fellow, University of Kentucky)*	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.

*Modest.

†Significant.

REFERENCES

1. Katz AM. Evolving concepts of heart failure: cooling furnace, malfunctioning pump, enlarging muscle, part I. *J Card Fail.* 1997;3:319–334. doi: 10.1016/s1071-9164(97)90032-4
2. Katz AM. The "modern" view of heart failure: how did we get here? *Circ Heart Fail.* 2008;1:63–71. doi: 10.1161/CIRCHEARTFAILURE.108.772756
3. Adams KF Jr, Fonarow GC, Emerman CL, LeJemtel TH, Costanzo MR, Abraham WT, Berkowitz RL, Galvao M, Horton DP; ADHERE Scientific Advisory Committee and Investigators. Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100,000 cases in the Acute Decompensated Heart Failure National Registry (ADHERE). *Am Heart J.* 2005;149:209–216. doi: 10.1016/j.ahj.2004.08.005
4. Goldberg RJ, Spencer FA, Szklo-Coxe M, Tisminetzky M, Yarzebski J, Lessard D, Gore JM, Gaasch W. Symptom presentation in patients hospitalized with acute heart failure. *Clin Cardiol.* 2010;33:E73–E80. doi: 10.1002/clc.20627
5. Whitaker KL, Scott SE, Wardle J. Applying symptom appraisal models to understand sociodemographic differences in responses to possible cancer symptoms: a research agenda. *Br J Cancer.* 2015;112(suppl 1):S27–S34. doi: 10.1038/bjc.2015.39
6. Scott SE, Walter FM, Webster A, Sutton S, Emery J. The model of pathways to treatment: conceptualization and integration with existing theory. *Br J Health Psychol.* 2013;18:45–65. doi: 10.1111/j.2044-8287.2012.02077.x
7. Leventhal H, Benyamini Y, Brownlee S, Deifenbach M, Leventhal EA, Patrick-Miller L, Robitaille C. Illness representations: theoretical foundations. In: Petrie KG, Weinman JA, eds. *Perceptions of Health and Illness.* Hardwood Publishers; 1997:19–45.
8. Cioffi D. Beyond attentional strategies: cognitive-perceptual model of somatic interpretation. *Psychol Bull.* 1991;109:25–41. doi: 10.1037/0033-2909.109.1.25
9. Alonzo AA. Everyday illness behavior: a situational approach to health status deviations. *Soc Sci Med (1967).* 1979;13A:397–404.
10. Pennebaker JW. *The Psychology of Physical Symptoms.* Springer-Verlag; 1982.
11. Lee CS, Hiatt SO, Denfeld QE, Mudd JO, Chien C, Gelow JM. Symptom-hemodynamic mismatch and heart failure event risk. *J Cardiovasc Nurs.* 2015;30:394–402. doi: 10.1097/JCN.0000000000000175
12. Lichtman JH, Leifheit EC, Safdar B, Bao H, Krumholz HM, Lorenze NP, Daneshvar M, Spertus JA, D'Onofrio G. Sex differences in the presentation and perception of symptoms among young patients with myocardial infarction: evidence from the VIRGO study (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients). *Circulation.* 2018;137:781–790. doi: 10.1161/CIRCULATIONAHA.117.031650
13. Lee CS, Gelow JM, Denfeld QE, Mudd JO, Burgess D, Green JK, Hiatt SO, Jurgens CY. Physical and psychological symptom profiling and event-free survival in adults with moderate to advanced heart failure. *J Cardiovasc Nurs.* 2014;29:315–323. doi: 10.1097/JCN.0b013e318285968a
14. Streur M, Ratcliffe SJ, Callans D, Shoemaker MB, Riegel B. Atrial fibrillation symptom clusters and associated clinical characteristics and outcomes: a cross-sectional secondary data analysis. *Eur J Cardiovasc Nurs.* 2018;17:707–716. doi: 10.1177/1474515118778445
15. Lee CS, Denfeld QE, Aouizerat BE, Jurgens CY, Chien CV, Aarons E, Gelow JM, Hiatt SO, Mudd JO. Comparative symptom biochemistry between moderate and advanced heart failure. *Heart Lung.* 2018;47:565–575. doi: 10.1016/j.hrtlng.2018.09.002
16. DeVon HA, Burke LA, Vuckovic KM, Haugland T, Eckhardt AL, Patmon F, Rosenfeld AG. Symptoms suggestive of acute coronary syndrome: when is sex important? *J Cardiovasc Nursing.* 2017;32:383–392. doi: 10.1097/JCN.0000000000000351
17. O'Keefe-McCarthy S, Ready L. Impact of prodromal symptoms on future adverse cardiac-related events: a systematic review. *J Cardiovasc Nurs.* 2016;31:E1–E10. doi: 10.1097/JCN.0000000000000207
18. Mehta PK, Bess C, Elias-Smale S, Vaccarino V, Quyyumi A, Pepine CJ, Bairey Merz CN. Gender in cardiovascular medicine: chest pain and coronary artery disease. *Eur Heart J.* 2019;40:3819–3826. doi: 10.1093/eurheartj/ehz784
19. Vaccarino V, Badimon L, Bremner JD, Cenko E, Cubedo J, Dorobantu M, Duncker DJ, Koller A, Manfrini O, Milicic D, et al; ESC Scientific Document Group Reviewers. Depression and coronary heart disease: 2018 position paper of the ESC working group on coronary pathophysiology and microcirculation. *Eur Heart J.* 2020;41:1687–1696. doi: 10.1093/eurheartj/ehy913
20. McSweeney JC, Cleves MA, Fischer EP, Pettey CM, Beasley B. Using the McSweeney Acute and Prodromal Myocardial Infarction Symptom Survey to predict the occurrence of short-term coronary heart disease events in women. *Womens Health Issues.* 2017;27:660–665. doi: 10.1016/j.whi.2017.07.002
21. Araújo C, Laszczyńska O, Viana M, Melão F, Henriques A, Borges A, Severo M, Maciel MJ, Moreira I, Azevedo A. Sex differences in presenting symptoms of acute coronary syndrome: the EPIHeart cohort study. *BMJ Open.* 2018;8:e018798. doi: 10.1136/bmjopen-2017-018798
22. Pelletier R, Khan NA, Cox J, Daskalopoulou SS, Eisenberg MJ, Bacon SL, Lavoie KL, Daskupta K, Rabi D, Humphries KH, et al; GENESIS-PRAXY Investigators. Sex versus gender-related characteristics: which predicts outcome after acute coronary syndrome in the young? *J Am Coll Cardiol.* 2016;67:127–135. doi: 10.1016/j.jacc.2015.10.067
23. Virani SS, Alonso A, Aparicio HJ, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Cheng S, Delling FN, et al; on behalf of the American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee.

Heart disease and stroke statistics—2021 update: a report from the American Heart Association. *Circulation.* 2021;143:e254–e743. doi: 10.1161/CIR.0000000000000950
24. Shah N, Kelly AM, Cox N, Wong C, Soon K. Myocardial infarction in the "young": risk factors, presentation, management and prognosis. *Heart Lung Circ.* 2016;25:955–960. doi: 10.1016/j.hlc.2016.04.015
25. Hamczyk MR, Nevado RM, Barettino A, Fuster V, Andrés V. Biological versus chronological aging: *JACC* Focus Seminar. *J Am Coll Cardiol.* 2020;75:919–930. doi: 10.1016/j.jacc.2019.11.062
26. Zimmerman L, Pozehl B, Vuckovic K, Barnason S, Schulz P, Seo Y, Ryan CJ, Zerwic JJ, DeVon HA. Selecting symptom instruments for cardiovascular populations. *Heart Lung.* 2016;45:475–496. doi: 10.1016/j.hrtlng.2016.08.012
27. Jurgens CY, Lee CS, Riegel B. Psychometric analysis of the heart failure somatic perception scale as a measure of patient symptom perception. *J Cardiovasc Nurs.* 2017;32:140–147. doi: 10.1097/JCN.0000000000000320
28. Thibodeau JT, Turer AT, Gualano SK, Ayers CR, Velez-Martinez M, Mishkin JD, Patel PC, Mammen PP, Markham DW, Levine BD, et al. Characterization of a novel symptom of advanced heart failure: bendopnea. *JACC Heart Fail.* 2014;2:24–31. doi: 10.1016/j.jchf.2013.07.009
29. Alpert CM, Smith MA, Hummel SL, Hummel EK. Symptom burden in heart failure: assessment, impact on outcomes, and management. *Heart Fail Rev.* 2017;22:25–39. doi: 10.1007/s10741-016-9581-4
30. Faulkner KM, Jurgens CY, Denfeld QE, Lyons KS, Harman Thompson J, Lee CS. Identifying unique profiles of perceived dyspnea burden in heart failure. *Heart Lung.* 2020;49:488–494. doi: 10.1016/j.hrtlng.2020.03.026
31. Parshall MB, Schwartzstein RM, Adams L, Banzett RB, Manning HL, Bourbeau J, Calverley PM, Gift AG, Harver A, Lareau SC, et al; American Thoracic Society Committee on Dyspnea. An official American Thoracic Society statement: update on the mechanisms, assessment, and management of dyspnea. *Am J Respir Crit Care Med.* 2012;185:435–452. doi: 10.1164/rccm.201111-2042ST
32. Valentova M, von Haehling S, Bauditz J, Doehner W, Ebner N, Bekfani T, Elsner S, Sliziuk V, Scherbakov N, Murín J, et al. Intestinal congestion and right ventricular dysfunction: a link with appetite loss, inflammation, and cachexia in chronic heart failure. *Eur Heart J.* 2016;37:1684–1691. doi: 10.1093/eurheartj/ehw008
33. AbouEzzeddine OF, Wong YW, Mentz RJ, Raza SS, Nativi-Nicolau J, Kociol RD, McNulty SE, Anstrom KJ, Hernandez AF, Redfield MM; NHLBI Heart Failure Clinical Research Network. Evaluation of novel metrics of symptom relief in acute heart failure: the worst symptom score. *J Card Fail.* 2016;22:853–858. doi: 10.1016/j.cardfail.2015.12.015
34. von Haehling S, Ebner N, Dos Santos MR, Springer J, Anker SD. Muscle wasting and cachexia in heart failure: mechanisms and therapies. *Nat Rev Cardiol.* 2017;14:323–341. doi: 10.1038/nrcardio.2017.51
35. Redeker NS, Adams L, Berkowitz R, Blank L, Freudenberger R, Gilbert M, Walsleben J, Zucker MJ, Rapoport D. Nocturia, sleep and daytime function in stable heart failure. *J Card Fail.* 2012;18:569–575. doi: 10.1016/j.cardfail.2012.05.002
36. Goebel JR, Doering LV, Shugarman LR, Asch SM, Sherbourne CD, Lanto AB, Evangelista LS, Nyamathi AM, Maliski SL, Lorenz KA. Heart failure: the hidden problem of pain. *J Pain Symptom Manage.* 2009;38:698–707. doi: 10.1016/j.jpainsymman.2009.04.022
37. Årestedt K, Brännström M, Evangelista LS, Strömberg A, Alvariza A. Palliative key aspects are of importance for symptom relief during the last week of life in patients with heart failure. *ESC Heart Fail.* 2021;8:2202–2209. doi: 10.1002/ehf2.13312
38. Sokoreli I, de Vries JJG, Pauws SC, Steyerberg EW. Depression and anxiety as predictors of mortality among heart failure patients: systematic review and meta-analysis. *Heart Fail Rev.* 2016;21:49–63. doi: 10.1007/s10741-015-9517-4
39. Moser DK, Lee KS, Wu JR, Mudd-Martin G, Jaarsma T, Huang TY, Fan XZ, Strömberg A, Lennie TA, Riegel B. Identification of symptom clusters among patients with heart failure: an international observational study. *Int J Nurs Stud.* 2014;51:1366–1372. doi: 10.1016/j.ijnurstu.2014.02.004
40. Denfeld QE, Bidwell JT, Gelow JM, Mudd JO, Chien CV, Hiatt SO, Lee CS. Cross-classification of physical and affective symptom clusters and 180-day event-free survival in moderate to advanced heart failure. *Heart Lung.* 2020;49:151–157. doi: 10.1016/j.hrtlng.2019.11.004
41. Havakuk O, King KS, Grazette L, Yoon AJ, Fong M, Bregman N, Elkayam U, Kloner RA. Heart failure-induced brain injury. *J Am Coll Cardiol.* 2017;69:1609–1616. doi: 10.1016/j.jacc.2017.01.022
42. Lee CS, Gelow JM, Bidwell JT, Mudd JO, Green JK, Jurgens CY, Woodruff-Pak DS. Blunted responses to heart failure symptoms in adults with mild cognitive dysfunction. *J Cardiovasc Nurs.* 2013;28:534–540. doi: 10.1097/JCN.0b013e31826620fa
43. Pressler SJ, Kim J, Riley P, Ronis DL, Gradus-Pizlo I. Memory dysfunction, psychomotor slowing, and decreased executive function predict mortality in patients with heart failure and low ejection fraction. *J Card Fail.* 2010;16:750–760. doi: 10.1016/j.cardfail.2010.04.007
44. Haedtke CA, Moser DK, Pressler SJ, Chung ML, Wingate S, Goodlin SJ. Influence of depression and gender on symptom burden among patients with advanced heart failure: insight from the Pain Assessment, Incidence and Nature in Heart Failure study. *Heart Lung.* 2019;48:201–207. doi: 10.1016/j.hrtlng.2019.02.002
45. Lam CSP, Arnott C, Beale AL, Chandramouli C, Hilfiker-Kleiner D, Kaye DM, Ky B, Santema BT, Sliwa K, Voors AA. Sex differences in heart failure. *Eur Heart J.* 2019;40:3859–3868c. doi: 10.1093/eurheartj/ehz835
46. Sethares KA, Chin E. Age and gender differences in physical heart failure symptom clusters. *Heart Lung.* 2021;50:832–837. doi: 10.1016/j.hrtlng.2021.07.001
47. Stolfo D, Uijl A, Vedin O, Strömberg A, Faxén UL, Rosano GMC, Sinagra G, Dahlström U, Savarese G. Sex-based differences in heart failure across the ejection fraction spectrum: phenotyping, and prognostic and therapeutic implications. *JACC Heart Fail.* 2019;7:505–515. doi: 10.1016/j.jchf.2019.03.011
48. Petersen S, von Leupoldt A, Van den Bergh O. Geriatric dyspnea: doing worse, feeling better. *Ageing Res Rev.* 2014;15:94–99. doi: 10.1016/j.arr.2014.03.001
49. Riegel B, Dickson VV, Cameron J, Johnson JC, Bunker S, Page K, Worrall-Carter L. Symptom recognition in elders with heart failure. *J Nurs Scholarsh.* 2010;42:92–100. doi: 10.1111/j.1547-5069.2010.01333.x
50. Denfeld QE, Winters-Stone K, Mudd JO, Hiatt SO, Lee CS. Identifying a relationship between physical frailty and heart failure symptoms. *J Cardiovasc Nurs.* 2018;33:E1–E7. doi: 10.1097/JCN.0000000000000408
51. Vervoort D, Antunes MJ, Pezzella AT, Rheumatic heart disease: the role of global cardiac surgery. *J Card Surg.* 2021;36:2857–2864. doi: 10.1111/jocs.15597
52. Borer JS, Sharma A. Drug therapy for heart valve diseases. *Circulation.* 2015;132:1038–1045. doi: 10.1161/CIRCULATIONAHA.115.016006
53. Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP 3rd, Gentile F, Jneid H, Krieger EV, Mack M, McLeod C, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines [published correction appears in *Circulation.* 2021;143:e229]. *Circulation.* 2021;143:e72–e227. doi: 10.1161/CIR.0000000000000923
54. Carabello BA. Introduction to aortic stenosis. *Circ Res.* 2013;113:179–185. doi: 10.1161/CIRCRESAHA.113.300156
55. Ross J Jr, Braunwald E. Aortic stenosis. *Circulation.* 1968;38(suppl):61–67. doi: 10.1161/01.cir.38.1s5.v-61
56. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, et al; PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med.* 2010;363:1597–1607. doi: 10.1056/NEJMoa1008232
57. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, et al; PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med.* 2011;364:2187–2198. doi: 10.1056/NEJMoa1103510
58. Siemienczuk D, Greenberg B, Morris C, Massie B, Wilson RA, Topic N, Bristow JD, Cheitlin M. Chronic aortic insufficiency: factors associated with progression to aortic valve replacement. *Ann Intern Med.* 1989;110:587–592. doi: 10.7326/0003-4819-110-8-587
59. Arnold SV, Chinnakondepalli KM, Spertus JA, Magnuson EA, Baron SJ, Kar S, Lim DS, Mishell JM, Abraham WT, Lindenfeld JA, et al; COAPT Investigators. Health status after transcatheter mitral-valve repair in heart failure and secondary mitral regurgitation: COAPT trial. *J Am Coll Cardiol.* 2019;73:2123–2132. doi: 10.1016/j.jacc.2019.02.010
60. Nitsche C, Koschutnik M, Kammerlander A, Hengstenberg C, Mascherbauer J. Gender-specific differences in valvular heart disease. *Wien Klin Wochenschr.* 2020;132:61–68. doi: 10.1007/s00508-019-01603-x
61. Shan Y, Pellikka PA. Aortic stenosis in women. *Heart.* 2020;106:970–976. doi: 10.1136/heartjnl-2019-315407
62. Gattringer T, Posekany A, Niederkorn K, Knoflach M, Poltrum B, Mutzenbach S, Haring HP, Ferrari J, Lang W, Willeit J, et al; Austrian Stroke Unit Registry Collaborators. Predicting early mortality of acute ischemic stroke. *Stroke.* 2019;50:349–356. doi: 10.1161/STROKEAHA.118.022863

63. Musuka TD, Wilton SB, Traboulsi M, Hill MD. Diagnosis and management of acute ischemic stroke: speed is critical. *CMAJ.* 2015;187:887–893. doi: 10.1503/cmaj.140355
64. Berglund A, Svensson L, Wahlgren N, von Euler M; HASTA Collaborators. Face Arm Speech Time Test use in the prehospital setting, better in the ambulance than in the emergency medical communication center. *Cerebrovasc Dis.* 2014;37:212–216. doi: 10.1159/000358116
65. Kleindorfer D, Lindsell CJ, Moomaw CJ, Alwell K, Woo D, Flaherty ML, Adeoye O, Zakaria T, Broderick JP, Kissela BM. Which stroke symptoms prompt a 911 call? A population-based study. *Am J Emerg Med.* 2010;28:607–612. doi: 10.1016/j.ajem.2009.02.016
66. Gargano JW, Wehner S, Reeves MJ. Presenting symptoms and onset-to-arrival time in patients with acute stroke and transient ischemic attack. *J Stroke Cerebrovasc Dis.* 2011;20:494–502. doi: 10.1016/j.jstrokecerebrovasdis.2010.02.022
67. Lavallée PC, Sissani L, Labreuche J, Meseguer E, Cabrejo L, Guidoux C, Klein IF, Touboul PJ, Amarenco P. Clinical significance of isolated atypical transient symptoms in a cohort with transient ischemic attack. *Stroke.* 2017;48:1495–1500. doi: 10.1161/STROKEAHA.117.016743
68. Ashcraft S, Wilson SE, Nyström KV, Dusenbury W, Wira CR, Burrus TM; on behalf of the American Heart Association Council on Cardiovascular and Stroke Nursing and the Stroke Council. Care of the patient with acute ischemic stroke (prehospital and acute phase of care): update to the 2009 comprehensive nursing care scientific statement: a scientific statement from the American Heart Association. *Stroke.* 2021;52:e164–e178. doi: 10.1161/STR.0000000000000356
69. Perez de la Ossa N, Carrera D, Gorchs M, Querol M, Millan M, Gomis M, Dorado L, Lopez-Cancio E, Hernandez-Perez M, Chicharro V, et al. Design and validation of a prehospital stroke scale to predict large arterial occlusion: the Rapid Arterial Occlusion Evaluation Scale. *Stroke.* 2014;45:87–91.
70. Antipova D, Eadie L, Macaden A, Wilson P. Diagnostic accuracy of clinical tools for assessment of acute stroke: a systematic review. *BMC Emerg Med.* 2019;19:49. doi: 10.1186/s12873-019-0262-1
71. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, et al; on behalf of the American Heart Association Stroke Council. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association [published correction appears in *Stroke.* 2019;50:e440–e441]. *Stroke.* 2019;50:e344–e418. doi: 10.1161/STR.0000000000000211
72. Otterman N, Veerbeek J, Schiemanck S, van der Wees P, Nollet F, Kwakkel G. Selecting relevant and feasible measurement instruments for the revised Dutch clinical practice guideline for physical therapy in patients after stroke. *Disabil Rehabil.* 2017;39:1449–1457. doi: 10.1080/09638288.2016.1196399
73. Hinkle JL, Becker KJ, Kim JS, Choi-Kwon S, Saban KL, McNair N, Mead GE; on behalf of the American Heart Association Council on Cardiovascular and Stroke Nursing and Stroke Council. Poststroke fatigue: emerging evidence and approaches to management: a scientific statement for healthcare professionals from the American Heart Association. *Stroke.* 2017;48:e159–e170. doi: 10.1161/STR.0000000000000132
74. Menlove L, Crayton E, Kneebone I, Allen-Crooks R, Otto E, Harder H. Predictors of anxiety after stroke: a systematic review of observational studies. *J Stroke Cerebrovasc Dis.* 2015;24:1107–1117. doi: 10.1016/j.jstrokecerebrovasdis.2014.12.036
75. Towfighi A, Ovbiagele B, El Husseini N, Hackett ML, Jorge RE, Kissela BM, Mitchell PH, Skolarus LE, Whooley MA, Williams LS; on behalf of the American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; and Council on Quality of Care and Outcomes Research. Poststroke depression: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2017;48:e30–e43. doi: 10.1161/STR.0000000000000113
76. Paolucci S, Iosa M, Toni D, Barbanti P, Bovi P, Cavallini A, Candeloro E, Mancini A, Mancuso M, Monaco S, et al; Neuropathic Pain Special Interest Group of the Italian Neurological Society. Prevalence and time course of post-stroke pain: a multicenter prospective hospital-based study. *Pain Med.* 2016;17:924–930. doi: 10.1093/pm/pnv019
77. Knapp P, Dunn-Roberts A, Sahib N, Cook L, Astin F, Kontou E, Thomas SA. Frequency of anxiety after stroke: an updated systematic review and meta-analysis of observational studies. *Int J Stroke.* 2020;15:244–255. doi: 10.1177/1747493019896958
78. Paciaroni M, Acciarresi M. Poststroke fatigue. *Stroke.* 2019;50:1927–1933. doi: 10.1161/STROKEAHA.119.023552
79. Harrison RA, Field TS. Post stroke pain: identification, assessment, and therapy. *Cerebrovasc Dis.* 2015;39:190–201. doi: 10.1159/000375397
80. Ali M, van Os HJA, van der Weerd N, Schoones JW, Heymans MW, Kruyt ND, Visser MC, Wermer MJH. Sex differences in presentation of stroke: a systematic review and meta-analysis. *Stroke.* 2022;53:345–354. doi: 10.1161/STROKEAHA.120.034040
81. Mountain A, Patrice Lindsay M, Teasell R, Salbach NM, de Jong A, Foley N, Bhogal S, Bains N, Bowes R, Cheung D, et al. Canadian stroke best practice recommendations: rehabilitation, recovery, and community participation following stroke. part two: transitions and community participation following stroke. *Int J Stroke.* 2020;15:789–806. doi: 10.1177/1747493019897847
82. Burton LJ, Tyson S. Screening for mood disorders after stroke: a systematic review of psychometric properties and clinical utility. *Psychol Med.* 2015;45:29–49. doi: 10.1017/S0033291714000336
83. Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, Deruyter F, Eng JJ, Fisher B, Harvey RL, et al; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Quality of Care and Outcomes Research. Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American Stroke Association [published corrections appear in *Stroke.* 2017;48:e78 and *Stroke.* 2017;48:e369]. *Stroke.* 2016;47:e98–e169. doi: 10.1161/STR.0000000000000098
84. Mills RJ, Pallant JF, Koufali M, Sharma A, Day S, Tennant A, Young CA. Validation of the Neurological Fatigue Index for Stroke (NFI-Stroke). *Health Qual Life Outcomes.* 2012;10:51. doi: 10.1186/1477-7525-10-51
85. Nesbitt J, Moxham S, Ramadurai G, Williams L. Improving pain assessment and managment in stroke patients. *BMJ Qual Improv Rep.* 2015;4:u203375.w3105. doi: 10.1136/bmjquality.u203375.w3105
86. Siontis KC, Gersh BJ, Killian JM, Noseworthy PA, McCabe P, Weston SA, Roger VL, Chamberlain AM. Typical, atypical, and asymptomatic presentations of new-onset atrial fibrillation in the community: characteristics and prognostic implications. *Heart Rhythm.* 2016;13:1418–1424. doi: 10.1016/j.hrthm.2016.03.003
87. Lip GY, Laroche C, Ioachim PM, Rasmussen LH, Vitali-Serdoz L, Petrescu L, Darabantiu D, Crijns HJ, Kirchhof P, Vardas P, et al. Prognosis and treatment of atrial fibrillation patients by European cardiologists: one year follow-up of the EUROObservational Research Programme-Atrial Fibrillation General Registry Pilot Phase (EORP-AF Pilot registry). *Eur Heart J.* 2014;35:3365–3376. doi: 10.1093/eurheartj/ehu374
88. Gleason KT, Nazarian S, Dennison Himmelfarb CR. Atrial fibrillation symptoms and sex, race, and psychological distress: a literature review. *J Cardiovasc Nurs.* 2018;33:137–143. doi: 10.1097/JCN.0000000000000421
89. Schnabel RB, Pecen L, Rzayeva N, Lucerna M, Purmah Y, Ojeda FM, De Caterina R, Kirchhof P. Symptom burden of atrial fibrillation and its relation to interventions and outcome in Europe. *J Am Heart Assoc.* 2018;7:e007559. doi: 10.1161/JAHA.117.007559
90. Blum S, Muff C, Aeschbacher S, Ammann P, Erne P, Moschovitis G, Di Valentino M, Shah D, Schläpfer J, Fischer A, et al. Prospective assessment of sex-related differences in symptom status and health perception among patients with atrial fibrillation. *J Am Heart Assoc.* 2017;6:e005401. doi: 10.1161/JAHA.116.005401
91. Bamgbade BA, Sanghai SR, McManus DD, Lessard D, Waring ME, Forrester S, Pierre-Louis I, Saczynski JS. Psychosocial and cognitive multimorbidity and health-related quality of life and symptom burden in older adults with atrial fibrillation: the Systematic Assessment of Geriatric Elements in Atrial Fibrillation (SAGE-AF) cohort study. *Arch Gerontol Geriatr.* 2020;90:104117. doi: 10.1016/j.archger.2020.104117
92. Garimella RS, Chung EH, Mounsey JP, Schwartz JD, Pursell I, Gehi AK. Accuracy of patient perception of their prevailing rhythm: a comparative analysis of monitor data and questionnaire responses in patients with atrial fibrillation. *Heart Rhythm.* 2015;12:658–665. doi: 10.1016/j.hrthm.2015.01.012
93. Page RL, Wilkinson WE, Clair WK, McCarthy EA, Pritchett EL. Asymptomatic arrhythmias in patients with symptomatic paroxysmal atrial fibrillation and paroxysmal supraventricular tachycardia. *Circulation.* 1994;89:224–227. doi: 10.1161/01.cir.89.1.224
94. Groenveld HF, Crijns HJ, Van den Berg MP, Van Sonderen E, Alings AM, Tijssen JG, Hillege HL, Tuininga YS, Van Veldhuisen DJ, Ranchor AV, et al; RACE II Investigators. The effect of rate control on quality of life in patients with permanent atrial fibrillation: data from the RACE II (Rate Control Efficacy in Permanent Atrial Fibrillation II) study. *J Am Coll Cardiol.* 2011;58:1795–1803. doi: 10.1016/j.jacc.2011.06.055

95. Allan KS, Aves T, Henry S, Banfield L, Victor JC, Dorian P, Healey JS, Andrade JG, Carroll SL, McGillion MH. Health-related quality of life in patients with atrial fibrillation treated with catheter ablation or antiarrhythmic drug therapy: a systematic review and meta-analysis. *CJC Open.* 2020;2:286–295. doi: 10.1016/j.cjco.2020.03.013
96. Verma A, Champagne J, Sapp J, Essebag V, Novak P, Skanes A, Morillo CA, Khaykin Y, Birnie D. Discerning the incidence of symptomatic and asymptomatic episodes of atrial fibrillation before and after catheter ablation (DISCERN AF): a prospective, multicenter study. *JAMA Intern Med.* 2013;173:149–156. doi: 10.1001/jamainternmed.2013.1561
97. Gorelick PB, Scuteri A, Black SE, Decarli C, Greenberg SM, Iadecola C, Launer LJ, Laurent S, Lopez OL, Nyenhuis D, et al; on behalf of the American Heart Association Stroke Council, Council on Epidemiology and Prevention, Council on Cardiovascular Nursing, Council on Cardiovascular Radiology and Intervention, and Council on Cardiovascular Surgery and Anesthesia. Vascular contributions to cognitive impairment and dementia: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2011;42:2672–2713. doi: 10.1161/STR.0b013e3182299496
98. Stefanidis KB, Askew CD, Greaves K, Summers MJ. The effect of non-stroke cardiovascular disease states on risk for cognitive decline and dementia: a systematic and meta-analytic review. *Neuropsychol Rev.* 2018;28:1–15. doi: 10.1007/s11065-017-9359-z
99. McCabe PJ, Chamberlain AM, Rhudy L, DeVon HA. Symptom representation and treatment-seeking prior to diagnosis of atrial fibrillation. *West J Nurs Res.* 2016;38:200–215. doi: 10.1177/0193945915570368
100. McCabe PJ, Rhudy LM, Chamberlain AM, DeVon HA. Fatigue, dyspnea, and intermittent symptoms are associated with treatment-seeking delay for symptoms of atrial fibrillation before diagnosis. *Eur J Cardiovasc Nurs.* 2016;15:459–468. doi: 10.1177/1474515115603901
101. Freeman JV, Simon DN, Go AS, Spertus J, Fonarow GC, Gersh BJ, Hylek EM, Kowey PR, Mahaffey KW, Thomas LE, et al; on behalf of the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) Investigators and Patients. Association between atrial fibrillation symptoms, quality of life, and patient outcomes: results from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). *Circ Cardiovasc Qual Outcomes.* 2015;8:393–402. doi: 10.1161/CIRCOUTCOMES.114.001303
102. Vermond RA, Crijns HJ, Tijssen JG, Alings AM, Van den Berg MP, Hillege HL, Van Veldhuisen DJ, Van Gelder IC, Rienstra M; RACE II Investigators. Symptom severity is associated with cardiovascular outcome in patients with permanent atrial fibrillation in the RACE II study. *Europace.* 2014;16:1417–1425. doi: 10.1093/europace/euu151
103. Hong KL, Babiolakis C, Zile B, Bullen M, Haseeb S, Halperin F, Hohl CM, Magee K, Sandhu RK, Tian SY, et al. Canada-wide mixed methods analysis evaluating the reasons for inappropriate emergency department presentation in patients with a history of atrial fibrillation: the multicentre AF-ED trial. *BMJ Open.* 2020;10:e033482. doi: 10.1136/bmjopen-2019-033482
104. Streur MM, Ratcliffe SJ, Callans DJ, Shoemaker MB, Riegel BJ. Atrial fibrillation symptom profiles associated with healthcare utilization: a latent class regression analysis. *Pacing Clin Electrophysiol.* 2018;41:741–749. doi: 10.1111/pace.13356
105. Reynolds MR, Lavelle T, Essebag V, Cohen DJ, Zimetbaum P. Influence of age, sex, and atrial fibrillation recurrence on quality of life outcomes in a population of patients with new-onset atrial fibrillation: the Fibrillation Registry Assessing Costs, Therapies, Adverse events and Lifestyle (FRACTAL) study. *Am Heart J.* 2006;152:1097–1103. doi: 10.1016/j.ahj.2006.08.011
106. Tamirisa KP, Al-Khatib SM, Mohanty S, Han JK, Natale A, Gupta D, Russo AM, Al-Ahmad A, Gillis AM, Thomas KL. Racial and ethnic differences in the management of atrial fibrillation. *CJC Open.* 2021;3(suppl):S137–S148. doi: 10.1016/j.cjco.2021.09.004
107. Ugowe FE, Jackson LR 2nd, Thomas KL. Racial and ethnic differences in the prevalence, management, and outcomes in patients with atrial fibrillation: a systematic review. *Heart Rhythm.* 2018;15:1337–1345. doi: 10.1016/j.hrthm.2018.05.019
108. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC Jr, Conti JB, Ellinor PT, Ezekowitz MD, Field ME. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society [published correction appears in *Circulation.* 2014;130:e270–e71]. *Circulation.* 2014;130:2071–2104. doi: 10.1161/CIR.0000000000000040
109. Biersteker TE, Schalij MJ, Treskes RW. Impact of mobile health devices for the detection of atrial fibrillation: systematic review. *JMIR Mhealth Uhealth.* 2021;9:e26161. doi: 10.2196/26161
110. Rose GA. The diagnosis of ischaemic heart pain and intermittent claudication in field surveys. *Bull World Health Organ.* 1962;27:645–658.
111. Schorr EN, Treat-Jacobson D. Methods of symptom evaluation and their impact on peripheral artery disease (PAD) symptom prevalence: a review. *Vasc Med.* 2013;18:95–111. doi: 10.1177/1358863X13480001
112. Gerhard-Herman MD, Gornik HL, Barrett C, Barshes NR, Corriere MA, Drachman DE, Fleisher LA, Fowkes FG, Hamburg NM, Kinlay S, et al. 2016 AHA/ACC Guideline on the management of patients with lower extremity peripheral artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines [published correction appears in *Circulation.* 2017;135:e791–e792]. *Circulation.* 2017;135:e726–e779. doi: 10.1161/CIR.0000000000000471
113. Haine A, Kavanagh S, Berger JS, Hess CN, Norgren L, Fowkes FGR, Katona BG, Mahaffey KW, Blomster JI, Patel MR, et al; International Steering Committee and Investigators of the EUCLID Trial. Sex-specific risks of major cardiovascular and limb events in patients with symptomatic peripheral artery disease. *J Am Coll Cardiol.* 2020;75:608–617. doi: 10.1016/j.jacc.2019.11.057
114. Brostow DP, Petrik ML, Starosta AJ, Waldo SW. Depression in patients with peripheral arterial disease: a systematic review. *Eur J Cardiovasc Nurs.* 2017;16:181–193. doi: 10.1177/1474515116687222
115. Pappas PJ, Lakhanpal S, Nguyen KQ, Vanjara R. The Center for Vein Restoration Study on presenting symptoms, treatment modalities, and outcomes in Medicare-eligible patients with chronic venous disorders. *J Vasc Surg Venous Lymphat Disord.* 2018;6:13–24. doi: 10.1016/j.jvsv.2017.08.018
116. Nicolaides AN. Chronic venous disease and the leukocyte-endothelium interaction: from symptoms to ulceration. *Angiology.* 2005;56(suppl 1):S11–S19. doi: 10.1177/00033197050560i103
117. Pabon M, Cheng S, Altin SE, Sethi SS, Nelson MD, Moreau KL, Hamburg N, Hess CN. Sex differences in peripheral artery disease. *Circ Res.* 2022;130:496–511. doi: 10.1161/CIRCRESAHA.121.320702
118. Kupper N, Bonhof C, Westerhuis B, Widdershoven J, Denollet J. Determinants of dyspnea in chronic heart failure. *J Card Fail.* 2016;22:201–209. doi: 10.1016/j.cardfail.2015.09.016
119. Leto L, Feola M. Cognitive impairment in heart failure patients. *J Geriatr Cardiol.* 2014;11:316–328. doi: 10.11909/j.issn.1671-5411.2014.04.007
120. Sedlar N, Lainscak M, Mårtensson J, Strömberg A, Jaarsma T, Farkas J. Factors related to self-care behaviours in heart failure: a systematic review of European Heart Failure Self-Care Behaviour Scale studies. *Eur J Cardiovasc Nurs.* 2017;16:272–282. doi: 10.1177/1474515117691644