2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society

WRITING COMMITTEE MEMBERS*
Win-Kuang Shen, MD, FACC, FAHA, FHRS, Chair†
Robert S. Sheldon, MD, PhD, FHRS, Vice Chair
David G. Benditt, MD, FACC, FHRS*‡
Mitchell I. Cohen, MD, FACC, FHRS‡
Daniel E. Forman, MD, FACC, FAHA‡
Zachary D. Goldberger, MD, MS, FACC, FAHA, FHRS‡
Blair P. Grubb, MD, FACC§
Mohamed H. Hamdan, MD, MBA, FACC, FHRS*‡
Andrew D. Krahn, MD, FHRS*§
Mark S. Link, MD, FACC‡
Brian Olshansky, MD, FACC, FAHA, FHRS*‡
Satish R. Raj, MD, MSc, FACC, FHRS*§
Roopinder Kaur Sandhu, MD, MPH‡
Dan Sorajja, MD‡
Benjamin C. Sun, MD, MPP, FACEP‖
Clyde W. Yancy, MD, MSc, FACC, FAHA‡¶

Developed in Collaboration with the American College of Emergency Physicians and Society for Academic Emergency Medicine

Endorsed by the American College of Emergency Physicians, the Society of Academic Emergency Medicine, and the Pediatric and Congenital Electrophysiology Society

ACC/AHA Task Force Members, see page e98

Key Words: AHA Scientific Statements ■ syncope ■ risk assessment ■ diagnosis ■ prognosis ■ cardiac syncope ■ reflex syncope ■ vasovagal syncope ■ orthostatic hypotension ■ neurogenic syncope ■ dehydration ■ pediatrics ■ adult congenital heart disease ■ geriatrics ■ driving ■ athletes

*Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry may apply; see Appendix 1 for detailed information. †ACC/AHA Task Force on Clinical Practice Guidelines Liaison. ‡ACC/AHA Representative. §HRS Representative. ‖ACEP and SAEM Joint Representative. ¶ACC/AHA Task Force on Performance Measures Liaison.

The American Heart Association requests that this document be cited as follows: Shen W-K, Sheldon RS, Benditt DG, Cohen MI, Forman DE, Goldberger ZD, Grubb BP, Hamdan MH, Krahn AD, Link MS, Olshansky B, Raj SR, Sandhu RK, Sorajja D, Sun BC, Yancy CW. 2017 ACC/AHA/HRS guideline for the evaluation and management of patients with syncope: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *Circulation*. 2017;136:e60–e122. DOI: 10.1161/CIR.0000000000000499.

TABLE OF CONTENTS

PREAMBLE

Since 1980, the American College of Cardiology (ACC) and American Heart Association (AHA) have translated scientific evidence into clinical practice guidelines (guidelines) with recommendations to improve cardiovascular health. These guidelines, which are based on systematic methods to evaluate and classify evidence, provide a cornerstone for quality cardiovascular care. The ACC and AHA sponsor the development and publication of guidelines without commercial support, and members of each organization volunteer their time to the writing and review efforts. Guidelines are official policy of the ACC and AHA.

Intended Use

Practice guidelines provide recommendations applicable to patients with or at risk of developing cardiovascular disease. The focus is on medical practice in the United States, but guidelines developed in collaboration with other organizations may have a global impact. Although guidelines may be used to inform regulatory

or payer decisions, their intent is to improve patients' quality of care and align with patients' interests. Guidelines are intended to define practices meeting the needs of patients in most, but not all, circumstances and should not replace clinical judgment.

Clinical Implementation

Guideline-recommended management is effective only when followed by healthcare providers and patients. Adherence to recommendations can be enhanced by shared decision making between healthcare providers and patients, with patient engagement in selecting interventions based on individual values, preferences, and associated conditions and comorbidities.

Methodology and Modernization

The ACC/AHA Task Force on Clinical Practice Guidelines (Task Force) continuously reviews, updates, and modifies guideline methodology on the basis of published standards from organizations including the Institute of Medicine[1,2] and on the basis of internal re-evaluation. Similarly, the presentation and delivery of guidelines are re-evaluated and modified on the basis of evolving technologies and other factors to facilitate optimal dissemination of information at the point of care to healthcare professionals. Given time constraints of busy healthcare providers and the need to limit text, the current guideline format delineates that each recommendation be supported by limited text (ideally, <250 words) and hyperlinks to supportive evidence summary tables. Ongoing efforts to further limit text are underway. Recognizing the importance of cost–value considerations in certain guidelines, when appropriate and feasible, an analysis of the value of a drug, device, or intervention may be performed in accordance with the ACC/AHA methodology.[3]

To ensure that guideline recommendations remain current, new data are reviewed on an ongoing basis, with full guideline revisions commissioned in approximately 6-year cycles. Publication of new, potentially practice-changing study results that are relevant to an existing or new drug, device, or management strategy will prompt evaluation by the Task Force, in consultation with the relevant guideline writing committee, to determine whether a focused update should be commissioned. For additional information and policies regarding guideline development, we encourage readers to consult the ACC/AHA guideline methodology manual[4] and other methodology articles.[5–8]

Selection of Writing Committee Members

The Task Force strives to avoid bias by selecting experts from a broad array of backgrounds. Writing committee members represent different geographic regions, sexes, ethnicities, races, intellectual perspectives/biases, and scopes of clinical practice. The Task Force may also invite organizations and professional societies with related interests and expertise to participate as partners, collaborators, or endorsers.

Relationships With Industry and Other Entities

The ACC and AHA have rigorous policies and methods to ensure that guidelines are developed without bias or improper influence. The complete relationships with industry and other entities (RWI) policy can be found online. Appendix 1 of the current document lists writing committee members' relevant RWI. For the purposes of full transparency, writing committee members' comprehensive disclosure information is available online, as is comprehensive disclosure information for the Task Force.

Evidence Review and Evidence Review Committees

When developing recommendations, the writing committee uses evidence-based methodologies that are based on all available data.[4–7] Literature searches focus on randomized controlled trials (RCTs) but also include registries, nonrandomized comparative and descriptive studies, case series, cohort studies, systematic reviews, and expert opinion. Only key references are cited.

An independent evidence review committee (ERC) is commissioned when there are 1 or more questions deemed of utmost clinical importance that merit formal systematic review. This systematic review will determine which patients are most likely to benefit from a drug, device, or treatment strategy and to what degree. Criteria for commissioning an ERC and formal systematic review include: a) the absence of a current authoritative systematic review; b) the feasibility of defining the benefit and risk in a time frame consistent with the writing of a guideline; c) the relevance to a substantial number of patients; and d) the likelihood that the findings can be translated into actionable recommendations. ERC members may include methodologists, epidemiologists, healthcare providers, and biostatisticians. The recommendations developed by the writing committee on the basis of the systematic review are marked with "SR".

Guideline-Directed Management and Therapy

The term *guideline-directed management and therapy* (GDMT) encompasses clinical evaluation, diagnostic

Circulation. 2017;136:e60–e122. DOI: 10.1161/CIR.0000000000000499

Table 1. ACC/AHA Recommendation System: Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care* (Updated August 2015)

CLASS (STRENGTH) OF RECOMMENDATION

CLASS I (STRONG) — **Benefit >>> Risk**

Suggested phrases for writing recommendations:
- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

CLASS IIa (MODERATE) — **Benefit >> Risk**

Suggested phrases for writing recommendations:
- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS IIb (WEAK) — **Benefit ≥ Risk**

Suggested phrases for writing recommendations:
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

CLASS III: No Benefit (MODERATE) — **Benefit = Risk**
(Generally, LOE A or B use only)

Suggested phrases for writing recommendations:
- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS III: Harm (STRONG) — **Risk > Benefit**

Suggested phrases for writing recommendations:
- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

LEVEL (QUALITY) OF EVIDENCE‡

LEVEL A
- High-quality evidence‡ from more than 1 RCT
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

LEVEL B-R (Randomized)
- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

LEVEL B-NR (Nonrandomized)
- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

LEVEL C-LD (Limited Data)
- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

LEVEL C-EO (Expert Opinion)

Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

testing, and pharmacological and procedural treatments. For these and all recommended drug treatment regimens, the reader should confirm the dosage by reviewing product insert material and evaluate the treatment regimen for contraindications and interactions. The recommendations are limited to drugs, devices, and treatments approved for clinical use in the United States.

Class of Recommendation and Level of Evidence

The Class of Recommendation (COR) indicates the strength of the recommendation, encompassing the estimated magnitude and certainty of benefit in proportion to risk. The Level of Evidence (LOE) rates the quality of scientific evidence that supports the inter-

vention on the basis of the type, quantity, and consistency of data from clinical trials and other sources (Table 1).[4–6]

Glenn N. Levine, MD, FACC, FAHA
Chair, ACC/AHA Task Force on Clinical Practice Guidelines

1. INTRODUCTION

1.1. Methodology and Evidence Review

The recommendations listed in this guideline are, whenever possible, evidence based. An initial extensive evidence review, which included literature derived from research involving human subjects, published in English, and indexed in MEDLINE (through PubMed), EMBASE, the Cochrane Library, the Agency for Healthcare Research and Quality, and other selected databases relevant to this guideline, was conducted from July to October 2015. Key search words included but were not limited to the following: *athletes, autonomic neuropathy, bradycardia, carotid sinus hypersensitivity, carotid sinus syndrome, children, death, dehydration, diagnosis, driving, electrocardiogram, electrophysiological study, epidemiology, falls, implantable loop recorder, mortality, older populations, orthostatic hypotension, pediatrics, psychogenic pseudosyncope, recurrent syncope, risk stratification, supraventricular tachycardia, syncope unit, syncope, tilt-table test, vasovagal syncope,* and *ventricular arrhythmia.* Additional relevant studies published through October 2016, during the guideline writing process, were also considered by the writing committee and added to the evidence tables when appropriate. The finalized evidence tables, included in the Online Data Supplement, summarize the evidence used by the writing committee to formulate recommendations. Lastly, the writing committee reviewed documents related to syncope previously published by the ACC and AHA and other organizations and societies. References selected and published in this document are representative and not all inclusive.

An independent ERC was commissioned to perform a systematic review of clinical questions, the results of which were considered by the writing committee for incorporation into this guideline. The systematic review report "Pacing as a Treatment for Reflex-Mediated (Vasovagal, Situational, or Carotid Sinus Hypersensitivity) Syncope" is published in conjunction with this guideline.[9]

1.2. Organization of the Writing Committee

The writing committee was composed of clinicians with expertise in caring for patients with syncope, including cardiologists, electrophysiologists, an emergency physician, and a pediatric cardiologist. The writing committee included representatives from the ACC, AHA, Heart Rhythm Society (HRS), American Academy of Neurology, American College of Emergency Physicians, and Society for Academic Emergency Medicine.

1.3. Document Review and Approval

This document was reviewed by 2 official reviewers each nominated by the ACC, AHA, and HRS; 1 reviewer each from the American Academy of Neurology, American College of Emergency Physicians and Society for Academic Emergency Medicine, and Pediatric and Congenital Electrophysiology Society; a lay/patient representative; and 25 individual content reviewers. Reviewers' RWI information was distributed to the writing committee and is published in this document (Appendix 2).

This document was approved for publication by the governing bodies of the ACC, AHA, and HRS and was endorsed by the American College of Emergency Physicians, the Society for Academic Emergency Medicine, and the Pediatric and Congenital Electrophysiology Society.

1.4. Scope of the Guideline

The purpose of this ACC/AHA/HRS guideline is to provide contemporary, accessible, and succinct guidance on the management of adult and pediatric patients with suspected syncope. This guideline is intended to be a practical document for cardiologists, arrhythmia specialists, neurologists, emergency physicians, general internists, geriatric specialists, sports medicine specialists, and other healthcare professionals involved in the care of this very large and heterogeneous population. It is not a review of physiology, pathophysiology, or mechanisms of underlying conditions associated with syncope. The nature of syncope as a symptom required that the writing committee consider numerous conditions for which it can be a symptom, and as much as possible, we have addressed the involvement of syncope only as a presenting symptom. Because of the plausible association of syncope and sudden cardiac death (SCD) in selected populations, this document discusses risk stratification and prevention of SCD when appropriate. The use of the terms *selected populations* and *selected patients* in this document is intended to direct healthcare providers to exercise clinical judgment, which is often required during the evaluation and management of patients with syncope. When a recommendation is made to refer a patient to a specialist with expertise for further evaluation, such as in the case of autonomic neurology, adult congenital heart disease (ACHD), older populations, or athletes, the writing committee

Circulation. 2017;136:e60–e122. DOI: 10.1161/CIR.0000000000000499

Table 2. Relevant ACC/AHA Guidelines

Title	Organization	Publication Year (Reference)
ACC/AHA guideline policy relevant to the management of syncope		
Supraventricular tachycardia	ACC/AHA/HRS	2015[10]
Valvular heart disease	AHA/ACC	2014[11]
Device-based therapies for cardiac rhythm abnormalities	ACCF/AHA/HRS	2012[12]
Ventricular arrhythmias and sudden cardiac death	ACC/AHA/ESC	2006[13]*
Other ACC/AHA guidelines of interest		
Hypertension*	ACC/AHA	–
Stable ischemic heart disease	ACC/AHA/ACP/AATS/ PCNA/SCAI/STS	2012 and 2014[14,15]
Atrial fibrillation	AHA/ACC/HRS	2014[16]
Non–ST-elevation acute coronary syndromes	AHA/ACC	2014[17]
Assessment of cardiovascular risk	ACC/AHA	2013[18]
Heart failure	ACC/AHA	2013[19]*
Hypertrophic cardiomyopathy	ACC/AHA	2011[20]
Assessment of cardiovascular risk in asymptomatic adults	ACC/AHA	2010[21]
Adult congenital heart disease	ACC/AHA	2008[22]*
Other related references		
Scientific statement on electrocardiographic early repolarization	AHA	2016[23]
Expert consensus statement on the diagnosis and treatment of postural tachycardia syndrome, inappropriate sinus tachycardia, and vasovagal syncope	HRS	2015[24]
Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death	ESC	2015 and 2013[25,26]
Expert consensus statement on the recognition and management of arrhythmias in adult congenital heart disease	PACES/HRS	2014[27]
Expert consensus statement on the use of implantable cardioverter-defibrillator therapy in patients who are not included or not well represented in clinical trials	HRS/ACC/AHA	2014[28]
Expert consensus statement on ventricular arrhythmias	EHRA/HRS/APHRS	2014[29]
Expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes	HRS/EHRA/APHRS	2013[25]
Guidelines for the diagnosis and management of syncope	ESC	2009[30]

*Revisions to the current documents are being prepared, with publication expected in 2017.

AATS indicates American Association for Thoracic Surgeons; ACC, American College of Cardiology; ACCF, American College of Cardiology Foundation; ACP, American College of Physicians; AHA, American Heart Association; APHRS, Asia Pacific Heart Rhythm Society; EHRA, European Heart Rhythm Association; ESC, European Society of Cardiology; HRS, Heart Rhythm Society; PACES, Pediatric and Congenital Electrophysiology Society; PCNA, Preventive Cardiovascular Nurses Association; SCAI, Society for Cardiovascular Angiography and Interventions; and STS, Society of Thoracic Surgery.

agreed to make Class IIa recommendations because of the paucity of outcome data. The definition of older populations has been evolving. Age >75 years is used to define older populations or older adults in this document, unless otherwise specified. If a study has defined older adults by a different age cutoff, the relevant age is noted in those specific cases. Finally, the guideline addresses the management of syncope with the patient as a focus, rather than larger aspects of health services, such as syncope management units. The goals of the present guideline are:

- To define syncope as a symptom, with different causes, in different populations and circumstances.
- To provide guidance and recommendations on the evaluation and management of patients with suspected syncope in the context of different clinical settings, specific causes, or selected circumstances.
- To identify key areas in which knowledge is lacking, to foster future collaborative research opportunities and efforts.

In developing this guideline, the writing committee reviewed the evidence to support recommendations in the relevant ACC/AHA guidelines noted in Table 2 and affirms the ongoing validity of the related recommendations in the context of syncope, thus obviating the need to repeat existing guideline recommendations in

Table 3. Relevant Terms and Definitions*

Term	Definition/Comments and References
Syncope	A symptom that presents with an abrupt, transient, complete loss of consciousness, associated with inability to maintain postural tone, with rapid and spontaneous recovery. The presumed mechanism is cerebral hypoperfusion.[24,30] There should not be clinical features of other nonsyncope causes of loss of consciousness, such as seizure, antecedent head trauma, or apparent loss of consciousness (ie, pseudosyncope).[24,30]
Loss of consciousness	A cognitive state in which one lacks awareness of oneself and one's situation, with an inability to respond to stimuli.
Transient loss of consciousness	Self-limited loss of consciousness[30] can be divided into syncope and nonsyncope conditions. Nonsyncope conditions include but are not limited to seizures, hypoglycemia, metabolic conditions, drug or alcohol intoxication, and concussion due to head trauma. The underlying mechanism of syncope is presumed to be cerebral hypoperfusion, whereas nonsyncope conditions are attributed to different mechanisms.
Presyncope (near-syncope)	The symptoms before syncope. These symptoms could include extreme lightheadedness; visual sensations, such as "tunnel vision" or "graying out"; and variable degrees of altered consciousness without complete loss of consciousness. Presyncope could progress to syncope, or it could abort without syncope.
Unexplained syncope (syncope of undetermined etiology)	Syncope for which a cause is undetermined after an initial evaluation that is deemed appropriate by the experienced healthcare provider. The initial evaluation includes but is not limited to a thorough history, physical examination, and ECG.
Orthostatic intolerance	A syndrome consisting of a constellation of symptoms that include frequent, recurrent, or persistent lightheadedness, palpitations, tremulousness, generalized weakness, blurred vision, exercise intolerance, and fatigue upon standing. These symptoms can occur with or without orthostatic tachycardia, OH, or syncope.[24] Individuals with orthostatic intolerance have ≥1 of these symptoms associated with reduced ability to maintain upright posture.
Orthostatic tachycardia	A sustained increase in heart rate of ≥30 bpm within 10 min of moving from a recumbent to a quiet (nonexertional) standing position (or ≥40 bpm in individuals 12–19 y of age).[24,30,31]
Orthostatic hypotension (OH)	A drop in systolic BP of ≥20 mm Hg or diastolic BP of ≥10 mm Hg with assumption of an upright posture.[31]
Initial (immediate) OH	A transient BP decrease within 15 s after standing, with presyncope or syncope.[31,32]
Classic OH	A sustained reduction of systolic BP of ≥20 mm Hg or diastolic BP of ≥10 mm Hg within 3 min of assuming upright posture.[31]
Delayed OH	A sustained reduction of systolic BP of ≥20 mm Hg (or 30 mm Hg in patients with supine hypertension) or diastolic BP of ≥10 mm Hg that takes >3 min of upright posture to develop. The fall in BP is usually gradual until reaching the threshold.[31]
Neurogenic OH	A subtype of OH that is due to dysfunction of the autonomic nervous system and not solely due to environmental triggers (eg, dehydration or drugs).[33,34] Neurogenic OH is due to lesions involving the central or peripheral autonomic nerves.
Cardiac (cardiovascular) syncope	Syncope caused by bradycardia, tachycardia, or hypotension due to low cardiac index, blood flow obstruction, vasodilatation, or acute vascular dissection.[35,36]
Noncardiac syncope	Syncope due to noncardiac causes, which include reflex syncope, OH, volume depletion, dehydration, and blood loss.[35]
Reflex (neurally mediated) syncope	Syncope due to a reflex that causes vasodilation, bradycardia, or both.[24,30,31]
Vasovagal syncope (VVS)	The most common form of reflex syncope mediated by the vasovagal reflex. VVS: 1) may occur with upright posture (standing or seated or with exposure to emotional stress, pain, or medical settings; 2) typically is characterized by diaphoresis, warmth, nausea, and pallor; 3) is associated with vasodepressor hypotension and/or inappropriate bradycardia; and 4) is often followed by fatigue. Typical features may be absent in older patients.[24] VVS is often preceded by identifiable triggers and/or by a characteristic prodrome. The diagnosis is made primarily on the basis of a thorough history, physical examination, and eyewitness observation, if available.
Carotid sinus syndrome	Reflex syncope associated with carotid sinus hypersensitivity.[30] Carotid sinus hypersensitivity is present when a pause ≥3 s and/or a decrease of systolic pressure ≥50 mm Hg occurs upon stimulation of the carotid sinus. It occurs more frequently in older patients. Carotid sinus hypersensitivity can be associated with varying degrees of symptoms. Carotid sinus syndrome is defined when syncope occurs in the presence of carotid sinus hypersensitivity.
Situational syncope	Reflex syncope associated with a specific action, such as coughing, laughing, swallowing, micturition, or defecation. These syncope events are closely associated with specific physical functions.
Postural (orthostatic) tachycardia syndrome (POTS)	A clinical syndrome usually characterized by all of the following: 1) frequent symptoms that occur with standing (eg, lightheadedness, palpitations, tremulousness, generalized weakness, blurred vision, exercise intolerance, and fatigue); and 2) an increase in heart rate of ≥30 bpm during a positional change from supine to standing (or ≥40 bpm in those 12–19 y of age); and 3) the absence of OH (>20 mm Hg reduction in systolic BP). Symptoms associated with POTS include those that occur with standing (eg, lightheadedness, palpitations); those not associated with particular postures (eg, bloating, nausea, diarrhea, abdominal pain); and those that are systemic (eg, fatigue, sleep disturbance, migraine headaches).[37] The standing heart rate is often >120 bpm.[31,38–42]
Psychogenic pseudosyncope	A syndrome of apparent but not true loss of consciousness that may occur in the absence of identifiable cardiac, reflex, neurological, or metabolic causes.[30]

*These definitions are derived from previously published definitions from scientific investigations, guidelines, expert consensus statements, and Webster dictionary after obtaining consensus from the WC.

BP indicates blood pressure; ECG, electrocardiogram; OH, orthostatic hypotension; POTS, postural tachycardia syndrome; and VVS, vasovagal syncope.

the present guideline when applicable or when appropriate. Table 2 also contains a list of other statements that may be of interest to the reader.

2. GENERAL PRINCIPLES

2.1. Definitions: Terms and Classification

For the purpose of this guideline, definitions of syncope and relevant terms are provided in Table 3.

2.2. Epidemiology and Demographics

Syncope has many causes and clinical presentations; the incidence depends on the population being evaluated. Estimates of isolated or recurrent syncope may be inaccurate and underestimated because epidemiological data have not been collected in a consistent fashion or because a consistent definition has not been used. Interpretation of the symptoms varies among the patients, observers, and healthcare providers. The evaluation is further obscured by inaccuracy of data collection and by improper diagnosis.

Studies of syncope report prevalence rates as high as 41%, with recurrent syncope occurring in 13.5%.[43] In a cross section of 1925 randomly selected residents of Olmsted County, Minnesota, with a median age of 62 years (all age >45 years), 364 reported an episode of syncope in their lifetime; the estimated prevalence of syncope was 19%. Females reported a higher prevalence of syncope (22% versus 15%, $P<0.001$).[44] The incidence follows a trimodal distribution in both sexes, with the first episode common around 20, 60, or 80 years of age and the third peak occurring 5 to 7 years earlier in males.[45] Predictors of recurrent syncope in older adults are aortic stenosis, impaired renal function, atrioventricular (AV) or left bundle-branch block, male sex, chronic obstructive pulmonary disorder, heart failure (HF), atrial fibrillation (AF), advancing age, and orthostatic medications,[45] with a sharp increase in incidence after 70 years of age.[35] Reflex syncope was most common (21%), followed by cardiac syncope (9%) and orthostatic hypotension (OH) (9%), with the cause of syncope unknown in 37%.[35] In patients with New York Heart Association class III–IV HF, syncope is present in 12% to 14% of patients.[46,47]

In older adults, there is a greater risk of hospitalization and death related to syncope. The National Hospital Ambulatory Medical Care Survey reported 6.7 million episodes of syncope in the emergency department (ED), or 0.77% of all ED patients. Among patients >80 years of age, 58% were admitted to hospital.[48] The prevalence of syncope as a presenting symptom to the ED ranged from 0.8% to 2.4% in multiple studies in both academic and community settings.[49–55]

Older institutionalized patients have a 7% annual incidence of syncope, a 23% overall prevalence, and a 30% 2-year recurrence rate.[56] The incidence of syncope in older adults may overlap with falls, so it may be difficult to distinguish one from the other. Older adults are predisposed to falls when syncope occurs, with a 1-year fall rate of 38% among fainters versus 18.3% among nonfainters.[57]

2.3. Initial Evaluation of Patients With Syncope: Recommendations

The time interval between the index syncopal event and the initial evaluation can vary significantly according to the medical necessity for evaluation and the patient's effort in seeking evaluation. The clinical setting in which the initial evaluation takes place also varies. The patient could seek evaluation in an outpatient setting with a generalist or a specialist or in the ED at a hospital. The recommendations in the present section are intended for consideration under the general principles of what constitutes GDMT during initial evaluation, regardless of the clinical setting. These general principles for the initial evaluation are shown in Figure 1. Additional evaluation is discussed in subsequent sections according to the outcomes of initial evaluation or in the presence of specific disease conditions.

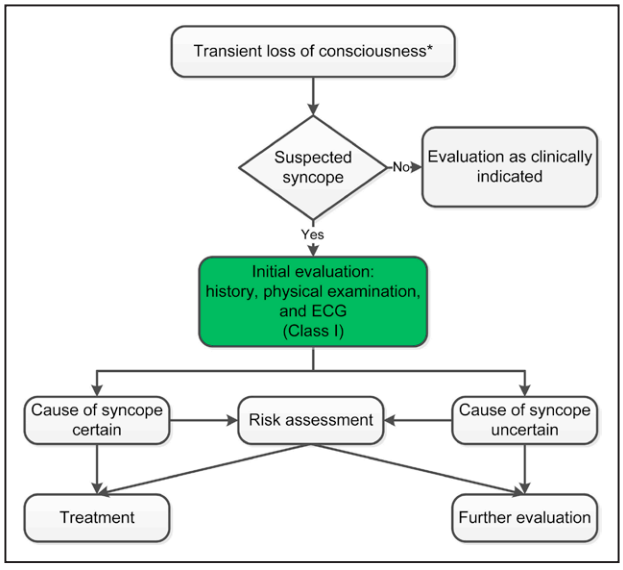

Figure 1. Syncope Initial Evaluation.
*See relevant terms and definitions in Table 3. Colors correspond to Class of Recommendation in Table 1. This figure shows the general principles for initial evaluation of all patients after an episode of syncope. ECG indicates electrocardiogram.

2.3.1. History and Physical Examination: Recommendation

Recommendation for History and Physical Examination		
COR	**LOE**	**Recommendation**
I	**B-NR**	**A detailed history and physical examination should be performed in patients with syncope.[58–66]**
See Online Data Supplement 1.		The history should aim to identify the prognosis, diagnosis, reversible or ameliorable factors, comorbidities, medication use, and patient and family needs. Cardiac syncope carries a significantly worse prognosis than does neurally mediated syncope. Prognostic factors generally separate neurally mediated from cardiac syncope and are described in Section 2.3.3. The diagnostic history focuses on the situations in which syncope occurs, prodromal symptoms that provide physiological insight, patient's self-report, bystander observations of the event and vital signs, and post-event symptoms. Video recordings are helpful when available. Time relationship to meals and physical activities and duration of the prodrome are helpful in differentiating neurally mediated syncope from cardiac syncope. Comorbidities and medication use are particularly important factors in older patients. A history of past medical conditions should be obtained, particularly with regard to the existence of preexisting cardiovascular disease.[58–66] A family history should be obtained, with particular emphasis on histories of syncope or sudden unexplained death (or drowning). Historical characteristics associated with, though not diagnostic of, cardiac and noncardiac syncope are summarized in Table 4. The physical examination should include determination of orthostatic blood pressure and heart rate changes in lying and sitting positions, on immediate standing, and after 3 minutes of upright posture.[31] Careful attention should be paid to heart rate and rhythm, as well the presence of murmurs, gallops, or rubs that would indicate the presence of structural heart disease. A basic neurological examination should be performed, looking for focal defects or other abnormalities that would suggest need for further neurological evaluation or referral.

2.3.2. Electrocardiography: Recommendation

Recommendation for Electrocardiography		
COR	**LOE**	**Recommendation**
I	**B-NR**	**In the initial evaluation of patients with syncope, a resting 12-lead electrocardiogram (ECG) is useful.[76]**
See Online Data Supplement 2.		ECG is widely available and inexpensive and can provide information about the potential and specific cause of the syncope episode (eg, bradyarrhythmia with sinus pauses or high-grade conduction block; ventricular tachyarrhythmia). It may demonstrate an underlying arrhythmogenic substrate for syncope or SCD. Subsets of patients with Wolff-Parkinson-White syndrome, Brugada syndrome, long-QT syndrome (LQTS), hypertrophic cardiomyopathy (HCM), or arrhythmogenic right ventricular cardiomyopathy (ARVC) have characteristic ECG features, which can prompt the decision to pursue further evaluation. Despite the benefit of identifying a likely cause or potential clue about the cause of syncope from the ECG, prospective studies did not conclude that ECG findings significantly affected subsequent management.[73,77–80] The prognostic value of an abnormal ECG in patients with syncope has been questioned, as well.[69,81] However, a multicenter, prospective, observational study[76] concluded that the presence of AF, intraventricular conduction disturbances, voltage criteria for left ventricular (LV) hypertrophy, and ventricular pacing were associated with increased risk of death from all causes at 1 year.

2.3.3. Risk Assessment: Recommendations

Syncope is a symptom that can be due to various causes, ranging from benign to life-threatening conditions. Risk stratification during initial evaluation is important for guiding the treatment and preventing long-term morbidity and mortality. However, risk stratification schemes for short- and long-term clinical outcomes are limited by the inclusion of all patients with syncope, without regard to the presence or absence of underlying medical conditions associated with syncope. For example, outcomes would not be expected to be similar for patients with vasovagal syncope (VVS), heart block with preserved ejection fraction, advanced cardiomyopathy and HF, acute gastric bleeding, or aortic dissection. The short-term prognosis of patients presenting with syncope is mainly related to the cause of syncope and the acute reversibility of the underlying condition; long-term prognosis is related to the effectiveness of therapy and the severity and progression of underlying diseases, especially cardiac or terminal illnesses.

Recommendations for Risk Assessment		
COR	**LOE**	**Recommendations**
I	**B-NR**	**Evaluation of the cause and assessment for the short- and long-term morbidity and mortality risk of syncope are recommended (Table 5).[68,82,83,100]**
See Online Data Supplements 3 and 4.		Syncope may be an acute result of major hemodynamic abnormalities or a manifestation of serious underlying disease. Thus, assessment of the cause of syncope and underlying comorbidities is necessary. Short-term adverse events and deaths are determined largely by the cause of syncope and the effectiveness of the treatment. In patients without a presumptive cause of syncope, risk stratification for potential short-term outcomes is necessary for immediate decision making in the acute setting. Potential predictors of increased short-term risk of death and serious outcomes are listed in Table 5. Long-term adverse events and deaths are more likely determined by the underlying medical comorbidities, many of which are cardiac. The evaluation of patients with syncope should include a full assessment of the long-term risk factors, including those listed in Table 5.[69,70,72–74,84–93,95,97]
IIb	**B-NR**	**Use of risk stratification scores may be reasonable in the management of patients with syncope.[67,68,72,73,75,87,89,100,101]**
See Online Data Supplements 3 and 4.		Investigators have reported numerous risk scores to predict adverse outcomes after syncope (examples in Table 6). This literature has important limitations, including inconsistent definitions of syncope, outcomes, outcome time frames, and predictors; inclusion of patients with serious outcomes already identified in the ED, which biases risk scores toward identifying "obvious" events; the use of composite outcomes that combine events with different pathophysiologies; small samples that limited model reliability; and limited external validation. Risk scores have not performed better than unstructured clinical judgment.[64,67–75,96,98]

Although having precise definitions for high-, intermediate-, and low-risk patient groups after an episode of syncope would be useful for managing these patients, evidence from current clinical studies renders this proposal challenging because of a large number of confounders. Risk markers from history, physical examination, laboratory investigations, study endpoints, adverse event rates, and time intervals between these events are variable from study to study. Current data are best grouped into short-term risk (associated with outcomes in the ED and up to 30 days after syncope) and long-term risk (up to 12 months of follow-up). Risk markers are summarized in Table 5.[64,67–70,72–75,82–98] The types of events, event rates, and study durations from investigations that estimated risk scores are summarized in Table 6.[64,65,76,81,87,89,92,97,99]

2.3.4. Disposition After Initial Evaluation: Recommendations

The evaluating provider must decide whether further workup can continue in an outpatient setting or whether hospital-based evaluation is required. The purpose of hospital-based evaluation is to expedite the treatment of identified serious conditions or to continue the diagnostic evaluation in the absence of a presumptive cause of syncope.[105,106]

The disposition decision is complicated by varying resources available for immediate testing, a lack of consensus on acceptable short-term risk of serious outcomes, varying availability and expertise of outpatient diagnostic clinics, and the lack of data demonstrating that hospital-based evaluation improves outcomes. In patients with a presumptive cause of reflex-mediated syncope and no other dangerous medical conditions identified, hospital-based evaluation is unlikely to provide benefit.[35] In patients with perceived higher risk, the healthcare provider may recommend a hospital-based evaluation. In this setting, a structured ED protocol can be effective as an alternative to inpatient admission.[107–110]

Decision support algorithms may reduce health service use in the evaluation of syncope (Figures 1 and 2),[105,111–113] although there are currently insufficient data to advocate the use of specific decision support algorithms for making disposition decisions.

Specialized syncope evaluation units may lead to reduced health service use and increased diagnostic rates.[114–119] However, the logistical and financial feasibility of specialized syncope units in North American settings is unknown. A wider acceptance of syncope units requires further evidence of improvement in clinical outcomes. Individual risk factors (Table 5) and risk scores (Table 6) are correlated with short- and long-term clinical outcomes, but they are not primary determinants for admission to hospital. Presence of ≥1 serious medical condition, summarized in Table 7, is the key determinant for further in-hospital management of patients after syncope.[90,98]

Recommendations for Disposition After Initial Evaluation

COR	LOE	Recommendations
I	B-NR	**Hospital evaluation and treatment are recommended for patients presenting with syncope who have a serious medical condition potentially relevant to the cause of syncope identified during initial evaluation.[105,106,120]**
See Online Data Supplements 5 and 6.		Table 7 provides examples of serious conditions associated with syncope that may require inpatient evaluation and "treatment." Arrhythmic causes may require consideration of pacemaker/implantable cardioverter-defibrillator (ICD) placement or revision and/or medication modification. Cardiac causes require treatment of the underlying condition (eg, medication management and consideration of surgical intervention for critical aortic stenosis). Finally, a large spectrum of noncardiac serious conditions may be associated with syncope and require management of the underlying problem (eg, severe anemia from a gastrointestinal bleed).
IIa	C-LD	**It is reasonable to manage patients with presumptive reflex-mediated syncope in the outpatient setting in the absence of serious medical conditions.[35]**
See Online Data Supplements 5 and 6.		Patients with presumptive VVS have a long-term risk of death similar to that of risk-matched patients without syncope.[35] Hospital-based evaluation for presumptive VVS is unlikely to improve long-term outcomes. Possible exceptions that might require hospital-based evaluation include frequent recurrent syncope with risk of injury or identified injury related to syncope.
IIa	B-R	**In intermediate-risk patients with an unclear cause of syncope, use of a structured ED observation protocol can be effective in reducing hospital admission.[107–110]**
See Online Data Supplements 5 and 6.		Two small RCTs suggest that structured ED-based protocols, consisting of time-limited observation and expedited access to cardiac testing/consultation, result in reduced health service use without adverse impact on clinical outcomes when compared with unstructured hospital admission. "Intermediate" risk factors included the following: ≥50 years of age; prior history of cardiac disease, cardiac device without evidence of dysfunction, concerning ECG findings, or family history of early SCD; and symptoms not consistent with reflex-mediated syncope. Both trials also allowed unstructured physician judgment to identify intermediate-risk patients.[107–110]
IIb	C-LD	**It may be reasonable to manage selected patients with suspected cardiac syncope in the outpatient setting in the absence of serious medical conditions.[106,121–123]**
See Online Data Supplements 5 and 6.		Hospital-based evaluation of syncope of unclear cause, in the absence of other serious identified medical conditions, has not demonstrated an improvement in patient-relevant outcomes. Several observational studies suggest modest diagnostic yield of hospital admission.[121–123] Patients evaluated for suspected cardiac syncope in outpatient settings are seldom admitted for diagnostic purposes, and it may be reasonable to extend a similar approach to EDs after initial evaluation is completed in the ED. Primary providers can consider expedited referral to specialists with expertise in syncope, as indicated by availability of resources and provider's assessment of short-term risk of serious outcomes, as an alternative to extended hospital-based evaluation.

Table 4. Historical Characteristics Associated with Increased Probability of Cardiac and Noncardiac Causes of Syncope[60,67–75]

More Often Associated With Cardiac Causes of Syncope
Older age (>60 y)
Male sex
Presence of known ischemic heart disease, structural heart disease, previous arrhythmias, or reduced ventricular function
Brief prodrome, such as palpitations, or sudden loss of consciousness without prodrome
Syncope during exertion
Syncope in the supine position
Low number of syncope episodes (1 or 2)
Abnormal cardiac examination
Family history of inheritable conditions or premature SCD (<50 y of age)
Presence of known congenital heart disease
More Often Associated With Noncardiac Causes of Syncope
Younger age
No known cardiac disease
Syncope only in the standing position
Positional change from supine or sitting to standing
Presence of prodrome: nausea, vomiting, feeling warmth
Presence of specific triggers: dehydration, pain, distressful stimulus, medical environment
Situational triggers: cough, laugh, micturition, defecation, deglutition
Frequent recurrence and prolonged history of syncope with similar characteristics

SCD indicates sudden cardiac death.

Table 5. Short- and Long-Term Risk Factors*

Short-Term Risk Factors (≤30 d)	Long-Term Risk Factors (>30 d)
History: Outpatient Clinic or ED Evaluation	
Male sex[74,85,101,102]	Male sex[68,90]
Older age (>60 y)[88]	Older age[67,74,75,90]
No prodrome[68]	Absence of nausea/vomiting preceding syncopal event[93]
Palpitations preceding loss of consciousness[83]	VA[68,90]
Exertional syncope[83]	Cancer[68]
Structural heart disease[70,83,88,101,103]	Structural heart disease[68,103]
HF[74,83,85,88]	HF[90]
Cerebrovascular disease[70]	Cerebrovascular disease[68]
Family history of SCD[70]	Diabetes mellitus[104]
Trauma[68,101]	High CHADS-2 score[95]
Physical Examination or Laboratory Investigation	
Evidence of bleeding[83]	Abnormal ECG[84,90,93]
Persistent abnormal vital signs[70]	Lower GFR
Abnormal ECG[68,72,74,75,105]	
Positive troponin[75]	

*Definitions for clinical endpoints or serious outcomes vary by study. The specific endpoints for the individual studies in this table are defined in Online Data Supplements 3 and 4 and summarized in Table 6 for selected studies. This table includes individual risk predictors from history, physical examination, and laboratory studies associated with adverse outcomes from selected studies.

CHADS-2 indicates congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, and stroke or transient ischemic attack; ECG, electrocardiogram; ED, emergency department; GFR, glomerular filtration rate; HF, heart failure; SCD, sudden cardiac death; and VA, ventricular arrhythmias.

3. ADDITIONAL EVALUATION AND DIAGNOSIS

The selection of a given diagnostic test, after the initial history, physical examination, and baseline ECG, is a clinical decision based on the patient's clinical presentation, risk stratification, and a clear understanding of diagnostic and prognostic value of any further testing. A broad-based use of additional testing is costly and often ineffective. This section provides recommendations for the most appropriate use of additional testing for syncope evaluation. See Figure 3 for the algorithm for additional evaluation and diagnosis for syncope.

3.1. Blood Testing: Recommendations

The availability of simple and accurate biomarkers might streamline risk stratification and diagnosis of the cause of syncope. This section reviews circulating biomarkers, which are being evaluated as markers either of hypotension or underlying disease processes. None have met with strong success.

Recommendations for Blood Testing		
COR	**LOE**	**Recommendations**
IIa	**B-NR**	**Targeted blood tests are reasonable in the evaluation of selected patients with syncope identified on the basis of clinical assessment from history, physical examination, and ECG.[124]**
See Online Data Supplements 7 and 8.		Although broad-panel testing is common in clinical practice at the point of triage, there are no data on the utility of this approach. Data to support specific blood testing are largely descriptive data from case series and registries. Complete blood count and electrolyte panel are frequently obtained during syncope evaluation. The diagnostic yield is low when these are used routinely; however, when these blood tests are conducted in patients with a suspected related diagnosis (eg, history of peptic ulcer disease, or tarry stools associated with OH on physical examination), test results can be diagnostic and useful for guiding therapy. Thus, specific testing should stem from the assessment by history and physical examination when the nature of the syncope presentation or associated comorbidities suggests a diagnostic or more likely prognostic role for laboratory testing. Results have not been linked to clinical decision making or outcomes.[125–128]

Recommendations for Blood Testing (Continued)		
COR	**LOE**	**Recommendations**
IIb	**C-LD**	**Usefulness of brain natriuretic peptide and high-sensitivity troponin measurement is uncertain in patients for whom a cardiac cause of syncope is suspected.**[125,127,129,130]
See Online Data Supplements 7 and 8.		Although data to support biomarker testing are in general relatively weak, there are sufficient data to suggest that natriuretic peptide is elevated in patients whose subsequent cause for syncope is determined to be cardiac. A systematic review of biomarkers found little value in contemporary troponin measurement unless acute myocardial infarction is suspected, and there is modest predictive value for high-sensitivity troponin and natriuretic peptides for major adverse cardiovascular events. The ability of troponin and natriuretic peptide measurement to influence clinical decision making or patient outcome is unknown.[129]
III: No Benefit	**B-NR**	**Routine and comprehensive laboratory testing is not useful in the evaluation of patients with syncope.**[126,131]
See Online Data Supplements 7 and 8.		There are no data on the utility of a standardized broad panel of laboratory testing in patients with syncope. Specific cardiac biomarkers may play a limited role when directed by clinical suspicion from the baseline assessment. There is little biological plausibility linking the remaining elements of broad-panel laboratory testing to the presentation or mechanism of syncope.

3.2. Cardiovascular Testing: Recommendations

Cardiovascular causes of syncope are common. The presence of significant cardiovascular diseases, often associated with the cardiovascular causes of syncope, portends a poor prognosis.[35,132] As such, cardiovascular testing can be a critical element in the evaluation and management of selected patients with syncope. It is important also to recognize that the abnormalities found during cardiovascular testing may not have a causal relationship to syncope itself. Determining the significance of such abnormalities, their causality, and whether subsequent treatment is merited requires clinical judgment and appropriate selection of cardiovascular testing.

3.2.1. Cardiac Imaging: Recommendations

Recommendations for Cardiac Imaging		
COR	**LOE**	**Recommendations**
IIa	**B-NR**	**Transthoracic echocardiography can be useful in selected patients presenting with syncope if structural heart disease is suspected.**[80,99,124]
See Online Data Supplement 9.		Cardiac imaging is often used to identify a structural cardiac abnormality, and imaging with transthoracic echocardiography is widely used for this purpose because it is noninvasive and low risk. Transthoracic echocardiography can be useful when healthcare providers are concerned about the presence of valvular disease (eg, aortic stenosis), HCM, or LV dysfunction.[124,133] In a retrospective study of patients presenting with syncope and suspected cardiac disease after history, physical examination, or ECG, the echocardiogram suggested a diagnosis of cardiac syncope in 48% of the study cohort.[99] In a prospective evaluation of 650 patients referred for syncope of unknown origin, 88 patients had an abnormal history or ECG; an echocardiogram showed systolic dysfunction (LV ejection fraction ≥40%) in 24 patients[80]; and 50% of patients with LV systolic dysfunction had manifest arrhythmias, compared with 9% with minor, incidental abnormalities (P<0.01). Although an echocardiogram may not be able to establish the immediate cause of syncope, it provides information for a potential disease substrate related to prognosis.
IIb	**B-NR**	**Computed tomography (CT) or magnetic resonance imaging (MRI) may be useful in selected patients presenting with syncope of suspected cardiac etiology.**[134]
See Online Data Supplement 9.		Imaging modalities, including CT and MRI, are usually reserved for selected patients presenting with syncope, especially when other noninvasive means are inadequate or inconclusive. These modalities offer superior spatial resolution in delineating cardiovascular anatomy (eg, in patients with structural, infiltrative, or congenital heart disease [CHD]).[135,136] The use of CT and MRI in contemporary cardiology is increasing.[137,138] Their role in the evaluation of syncope has been investigated.[139] The use of CT or MRI increased from 21% in 2001 to 45% in 2010, as reported in a series of patients evaluated for syncope in the ED.[134] MRI is useful when there is a suspicion of ARVC or cardiac sarcoidosis.[140,141] When pulmonary embolism is suspected in patients presenting with syncope to the hospital, CT can confirm the diagnosis in selected patients.[128] CT or MRI may not provide answers about the cause of syncope. They provide information on the structural disease substrate relevant to the overall diagnosis and subsequent evaluation and follow-up in selected patients presenting with syncope.
III: No Benefit	**B-NR**	**Routine cardiac imaging is not useful in the evaluation of patients with syncope unless cardiac etiology is suspected on the basis of an initial evaluation, including history, physical examination, or ECG.**[77,99]
See Online Data Supplement 9.		Although some investigators have advocated for cardiac imaging—particularly transthoracic echocardiography—as a routine screening examination for patients with syncope who lack clear signs or symptoms of cardiovascular disease,[133] clinical evidence does not support such practice. Unexpected findings on echocardiograms to explain syncope are uncommon; a "screening" echocardiogram is of low utility.[142] In 1 evaluation of 2106 inpatients with syncope, a battery of testing, including cardiac enzymes, CT scans, echocardiography, carotid ultrasonography, and electroencephalography, contributed to the diagnosis or management in <5% of cases and helped determine the etiology of syncope <2% of the time.[77] Similarly, in another retrospective series of 128 inpatients with syncope, it was found that echocardiograms in patients with no clinical evidence of heart disease according to history, physical examination, or ECG either were normal (63%) or provided no useful additional information for arriving at a diagnosis (37%).[99] Finally, radionuclide imaging and cardiac catheterization have little role in the evaluation of syncope.

3.2.2. Stress Testing: Recommendation

Recommendation for Stress Testing		
COR	**LOE**	**Recommendation**
IIa	**C-LD**	**Exercise stress testing can be useful to establish the cause of syncope in selected patients who experience syncope or presyncope during exertion.[132,143]**
See Online Data Supplement 10.		Exertion can result in syncope in a variety of conditions, including structural lesions, such as hypertrophic obstructive cardiomyopathy and aortic stenosis; interarterial anomalous coronary artery and pulmonary arterial hypertension; and channelopathies, such as LQTS (type 1) and catecholaminergic polymorphic ventricular tachycardia (CPVT). Subjecting a patient to a treadmill exercise test to reproduce the symptoms or evaluate the hemodynamic response to exertion (eg, hypotension) must be done with extreme caution and in an environment with proper advanced life support. In a prospective evaluation of 433 patients in which tachyarrhythmia was studied as the etiology for exertional syncope,[132] an ECG stress evaluation was felt to be the sole test useful in identifying a presumptive cause of syncope in only 2 patients. However, bradyarrhythmia may ultimately be responsible for exertional syncope as well, and may only be elicited during stress testing. In rare instances, exercise-induced ischemia[143–146] or coronary vasospasm[147] may lead to high-grade/infranodal AV block in patients with underlying coronary disease.

3.2.3. Cardiac Monitoring: Recommendations

Although cardiac monitoring is often used in the evaluation of palpitations or intermittent arrhythmias, the following recommendations and discussion are focused primarily on the use of monitoring for the evaluation of patients with syncope. The choice of monitoring system and duration should be appropriate to the likelihood that a spontaneous event will be detected and the patient may be incapacitated and unable to voluntarily trigger the recording system.

Recommendations for Cardiac Monitoring		
COR	**LOE**	**Recommendations**
I	**C-EO**	**The choice of a specific cardiac monitor should be determined on the basis of the frequency and nature of syncope events.**
N/A		The technology of cardiac rhythm monitoring is dynamic and advancing at rapid speed. Several types of ambulatory cardiac rhythm monitoring are summarized in Table 8. Their selection and usefulness are highly dependent on patient characteristics with regard to the frequency of syncope and the likelihood of an arrhythmic cause of syncope.[148]
IIa	**B-NR**	**To evaluate selected ambulatory patients with syncope of suspected arrhythmic etiology, the following external cardiac monitoring approaches can be useful:** **1. Holter monitor[149–153]** **2. Transtelephonic monitor[150,154,155]** **3. External loop recorder[150,154–156]** **4. Patch recorder[157–159]** **5. Mobile cardiac outpatient telemetry[160,161]**
See Online Data Supplements 11 and 12.		The types of external monitoring devices are summarized in Table 8. The effectiveness of any external cardiac monitoring device for syncope evaluation is related to the duration of monitoring, continuous versus intermittent monitoring, frequency of syncope, duration of prodrome, and suddenness of incapacitation. The patient activation, before or after an event, allows for symptom rhythm correlation; however, some external loop recorders are of limited use in patients who are temporarily incapacitated around the time of syncope. External loop recorders are also limited by infrequent syncopal events. The advantage of an external loop recorder over Holter monitoring stems from a longer monitoring period, which confers a higher yield than Holter monitoring[149,153] and may offer a diagnosis after a negative Holter evaluation.[150] Although the diagnostic yield of an external loop recordermay be lower than that of an implantable cardiac monitor (ICM), the noninvasive strategy is reasonable as a first approach. One prospective, multicenter study of 392 patients (28% with syncope) reported a 4-week diagnostic yield of 24.5%, with recurrent events and previous history of supraventricular arrhythmias being strong predictors of diagnostic events.[156] The advances of new patch-based devices offer another and often less cumbersome means of identifying an arrhythmic cause for syncope.[157–159] The duration of monitoring (2 to 14 days) is often shorter than for the external loop recorder or mobile continuous outpatient telemetry. Some practices offer mobile continuous outpatient telemetry devices, which provide real-time arrhythmia monitoring and analysis. An RCT[161] of 266 patients with suspected intermittent arrhythmias demonstrated that an arrhythmia was diagnosed in 88% of mobile continuous outpatient telemetry patients versus 75% of external loop recorder patients (*P*=0.008). Importantly, therewas a similar result in the subgroup of patients presenting with syncope or presyncope, with a significantly higher diagnostic yield in the mobile continuous outpatient telemetry group (89% versus 69%; *P*=0.008).
IIa	**B-R**	**To evaluate selected ambulatory patients with syncope of suspected arrhythmic etiology, an ICM can be useful.[149,150,153,161–175]**
See Online Data Supplements 11 and 12.		Several RCTs and observational studies have demonstrated a benefit of the ICM in establishing a diagnosis in syncope of unclear etiology. In a prospective study of 60 patients with syncope of unknown origin, the diagnosis (primarily bradyarrhythmia) was made in 55% with ICM, compared with a 19% diagnostic yield with conventional testing (external loop recorder, followed by tilt-table testing and electrophysiological study [EPS]) (*P*=0.0014).[162] These findings are consistent with other studies, which generally have shown that patients who underwent the ICM approach experienced higher rates of diagnosis than those of patients who underwent the conventional approach.[164,176,177] A study on cost-effectiveness of the ICM strategy reported that the mean cost per participant was higher but the cost per diagnosis was lower in patients who received ICM than in patients who underwent conventional approaches.[162,164,178] Key confounders in cost assessment include differences in healthcare settings, heterogeneity of patient populations, pricing of devices and healthcare delivery, and changing technology.

3.2.4. In-Hospital Telemetry: Recommendation

Recommendation for In-Hospital Telemetry		
COR	**LOE**	**Recommendation**
I	**B-NR**	**Continuous ECG monitoring is useful for hospitalized patients admitted for syncope evaluation with suspected cardiac etiology.**[77,182,183]
See Online Data Supplement 13.		Given that patients with syncope and structural heart disease are at high risk of death or significant arrhythmia,[184] inpatient telemetry could be a valuable diagnostic modality. However, the diagnostic yield of inpatient telemetry is low in the absence of high suspicion about an arrhythmic cause.[183] One study of 172 patients with syncope presenting to the ED and admitted to a telemetry unit revealed a diagnostic yield in 18% of patients, with 15% demonstrating bradyarrhythmias.[182] The yield was highest in older patients with HF. No deaths occurred within an average monitoring time of 4.8±2.7 days. In 1 prospective study of 2240 patients admitted to a telemetry unit, patients admitted for syncope (10%) had low rates of unexpected intensive care transfer, and most were unrelated to arrhythmic conditions.[185] Furthermore, in another prospective evaluation of 205 patients admitted to telemetry, significant arrhythmias were seen in only 12 patients with known or suspected coronary artery disease or in those with previously documented arrhythmias.[183] No arrhythmias or interventions occurred in the 7% of patients who were assigned to telemetry because of syncope. A large, prospective evaluation of 2106 patients admitted with syncope demonstrated high telemetry use (95%) but a diagnostic yield of only 5%.[77] Continuous telemetry in the hospital for patients presenting with syncope not suspected of a cardiac etiology is not cost-effective.[186,187]

Table 6. Examples of Syncope Risk Scores

Study/ Reference	Year	Sample N	Events N (%)	Outcome Definition	ED Events*	Predictors	NPV (%)†
Martin[90]	1997	252	104 (41%)	1-y death/arrhythmia	Yes	Abnormal ECG‡; >45 y of age; VA; HF	93
Sarasin[74]	2003	175	30 (17%)	Inpatient arrhythmia	Yes	Abnormal ECG‡; >65 y of age; HF	98
OESIL[67]	2003	270	31 (11%)	1-y death	N/A	Abnormal ECG‡; >65 y of age; no prodrome; cardiac history	100
SFSR[72]	2004	684	79 (12%)	7-d serious events§	Yes	Abnormal ECG‡; dyspnea; hematocrit; systolic BP <90 mm Hg; HF	99
Boston Syncope Rule[70]	2007	293	68 (23%)	30-d serious events‖	Yes	Symptoms of acute coronary syndrome; worrisome cardiac history; family history of SCD; VHD; signs of conduction disease; volume depletion; persistent abnormal vital signs; primary central nervous event	100
Del Rosso[69]	2008	260	44 (17%)	Cardiac etiology	N/A	Abnormal ECG‡/cardiac history; palpitations; exertional; supine; precipitant (a low-risk factor); autonomic prodrome (low-risk factors)	99
STePS[68]	2008	676	41 (6%)	10-d serious events¶	Yes	Abnormal ECG‡; trauma; no prodrome; male sex	–
Syncope Risk Score[75]	2009	2584	173 (7%)	30-d serious events#	No	Abnormal ECG‡; >90 y of age; male sex; positive troponin; history of arrhythmia; systolic BP >160 mm Hg; near-syncope (a low-risk factor)	97
ROSE[73]	2010	550	40 (7%)	30-d serious events#	Yes	Abnormal ECG‡; B-natriuretic peptide; hemoglobin; O_2Sat; fecal occult blood	98

*Did the study include events diagnosed during the ED evaluation?

†NPV: negative predictive value for lowest-risk group for the specific events defined by the study.

‡Abnormal ECG is defined variably in these studies. In the context of syncope evaluation, an abnormal ECG is any rhythm other than normal sinus rhythm, conduction delays (BBB, type-2 second-degree AVB or third-degree AVB), presence of Q waves, ST abnormalities, or prolonged QT interval.

§Events: death, MI, arrhythmia, pulmonary embolism, stroke, hemorrhage, or readmission.

‖Events: death, major therapeutic procedure, MI, arrhythmia, pulmonary embolism, stroke, sepsis, hemorrhage, or life-threatening sequelae of syncope.

¶Events: death, major therapeutic procedure, or readmission.

#Events: death, arrhythmia, MI, new diagnosis of severe structural heart disease, pulmonary embolism, aortic dissection, stroke/TIA, cerebral hemorrhage, or significant anemia requiring blood transfusion.

AVB indicates atrioventricular block; BBB, bundle-branch block; BP, blood pressure; ECG, electrocardiogram; ED, emergency department; HF, heart failure; MI, myocardial infarction; N/A, not available; NPV, negative predictive value; O_2Sat, oxygen saturation; OESIL, Osservatorio Epidemiologico sulla Sincope nel Lazio; ROSE, Risk Stratification of Syncope in the ED; SCD, sudden cardiac death; SFSR, San Francisco Syncope Rule; STePS, Short-Term Prognosis of Syncope Study; TIA, transient ischemic attack; VA, ventricular arrhythmias; and VHD, valvular heart disease.

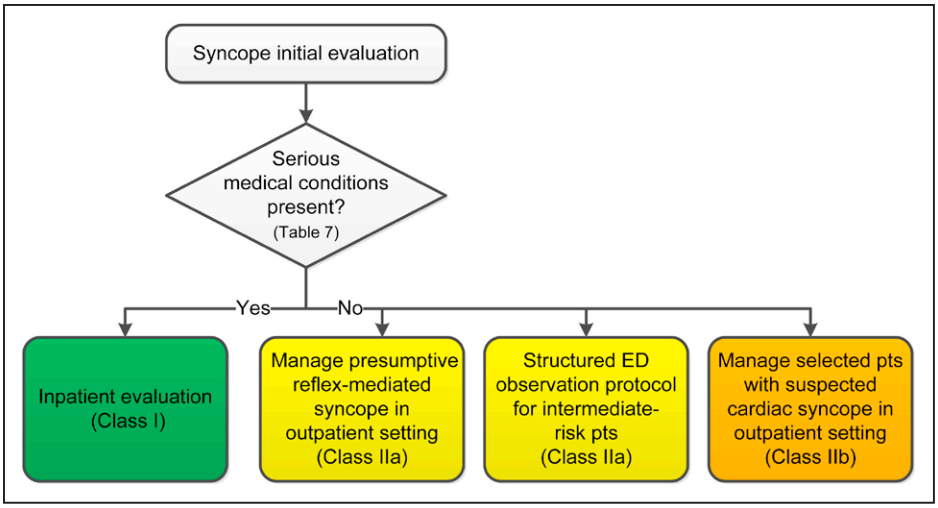

Figure 2. Patient Disposition After Initial Evaluation for Syncope.
Colors correspond to Class of Recommendation in Table 1. ED indicates emergency department; and pts, patients.

3.2.5. Electrophysiological Study: Recommendations

The EPS can identify a substrate for clinical bradyarrhythmia or tachyarrhythmia as a potential cause of syncope after a nondiagnostic initial evaluation. Despite these purported benefits, EPS has a limited role in the evaluation of syncope, especially in patients without known heart disease or with low suspicion of an arrhythmic etiology.[117,187,188] The sensitivity and specificity of EPS to assess sinus node dysfunction and AV conduction disease in patients with syncope are variable, depending on patient selection and pretest probability of a bradycardia substrate.[189–191]

Inducible ventricular tachycardia (VT) in patients with syncope, ischemic heart disease, and a prior history of myocardial infarction is predictive of spontaneous VT and prognosis. The causal relationship between the inducible VT during EPS and syncope requires clinical correlation. The lack of an inducible sustained monomorphic VT predicts lower risk of spontaneous VT and better prognosis.[192] The overall role of EPS in the evaluation of ventricular arrhythmias (VA) in patients with syncope has diminished in the past 2 decades. This is primarily due to the use of ICD as a Class I indication for the primary prevention of SCD in patients with ischemic or nonischemic cardiomyopathy and significant LV dysfunction (ejection fraction ≤35%). An EPS is no longer required in patients with syncope before consideration of ICD therapy. However, although ICDs may reduce risk of death, they may not prevent syncope. The role of EPS in patients with syncope suspected to be due to VA and acquired nonischemic heart disease is unproven.[193–198]

Recommendations for EPS

COR	LOE	Recommendations
IIa	B-NR	**EPS can be useful for evaluation of selected patients with syncope of suspected arrhythmic etiology.[91,151,199–205]**
See Online Data Supplement 14.		Diagnostic results detected during EPS occur predominantly in patients who have cardiac disease (eg, conduction system delay, coronary artery disease, cardiomyopathy, and valvular heart disease). Most of the literature evaluating EPS as a means to diagnose syncope is relatively old, and the data were obtained in referral centers where there was a high pretest probability of an arrhythmia. Eight of these small retrospective studies[91,199–205] (total n=625) found that, of the 406 patients with cardiac disease or an abnormal ECG, 41% had a positive result (of these, 21% had VT and 34% had a bradycardia).[151] Of 219 patients without evidence of heart disease, only 5% had a positive result (1% with VT and 10% with evidence of substrate for symptomatic bradycardia). Overall, the diagnostic yield of EPS was approximately 50% and 10% in patients with and without structural heart disease, respectively.
II: No Benefit	B-NR	**EPS is not recommended for syncope evaluation in patients with a normal ECG and normal cardiac structure and function, unless an arrhythmic etiology is suspected.[205–207]**
See Online Data Supplement 14.		One prospective evaluation of 247 patients with syncope of undetermined etiology who underwent EPS found that the diagnostic yield was significantly higher in patients with an abnormal ECG than in those with a normal ECG (22% versus 3.7%) and that the diagnostic yield was low in patients with a normal ECG and without cardiac disease (2.6%).[206] In another small series of 34 patients with unexplained syncope who had normal ECGs and normal testing otherwise and who underwent EPS,[205] the results were diagnostic in only 4 patients; the results were abnormal but not diagnostic in 2 patients and were normal in the remaining 28 patients. In another evaluation of 421 patients with undiagnosed syncope who underwent noninvasive testing as a means of predicting abnormal EPS findings, a normal ECG and ambulatory monitor were associated with a lower risk of EPS abnormalities than were an abnormal ECG and ambulatory monitor (9% versus 82%).[207]

3.2.6. Tilt-Table Testing: Recommendations

Recommendations for Tilt-Table Testing		
COR	**LOE**	**Recommendations**
IIa	**B-R**	**If the diagnosis is unclear after initial evaluation, tilt-table testing can be useful for patients with suspected VVS.[208–213]**
See Online Data Supplement 15.		Tilt-table testing has been used to evaluate patients with syncope for nearly 3 decades.[208] It is an orthostatic stress test to assess the susceptibility of a vasovagal response to a postural change from a supine to an upright position. A positive response is defined as inducible presyncope or syncope associated with hypotension, with or without bradycardia (less commonly asystole). The hemodynamic response to the tilt maneuver determines whether there is a cardioinhibitory, vasodepressor, or mixed response.[214] There is general consensus that a tilt-table angle of 70 degrees for 30 to 40 minutes would provide optimal yield.[211,213,215] Adjunctive agents, such as a low dose of isoproterenol infusion or sublingual nitrates, may improve sensitivity but decrease specificity.[210,212,216,217] A positive tilt-table test suggests a tendency or predisposition to VVS induced in the laboratory. This observation during tilt-table testing cannot necessarily define a causal etiology or be entirely conclusive of a reflex mechanism for syncope in the clinical setting. Correlation of tilt-table–induced findings to patients' clinical presentation is critically important to prevent consequences of false-positive results from tilt-table testing. The utility of tilt-table testing is highest in patients with a suspected VVS when syncope is recurrent. Several factors have reduced the role of tilt-table testing in the evaluation of syncope: the overall moderate sensitivity, specificity, and reproducibility of tilt-table testing; the presence of false-positive response in controls; the increasing recognition of VVS from a structured history taking; and the availability of long-term cardiac monitoring.[24,211,213]
IIa	**B-NR**	**Tilt-table testing can be useful for patients with syncope and suspected delayed OH when initial evaluation is not diagnostic.[218,219]**
See Online Data Supplement 15.		OH with standing, or a similar fall in blood pressure within 3 minutes of upright tilt-table testing to 60 degrees,[220] is distinct from delayed OH, characterized by a sustained decrease in blood pressure occurring beyond 3 minutes of standing or upright tilt-table testing.[220,221] Delayed OH may be responsible for syncopal episodes or symptoms of orthostatic intolerance only after prolonged standing. In 1 retrospective study of 230 patients with OH, only 46% had OH within 3 minutes of head-up tilt; 15% had OH between 3 and 10 minutes; and 39% had OH only after 10 minutes of tilt-table testing.[218] In 10-year follow-up data from 165 of these patients, 54% of individuals with delayed OH progressed to classic OH.[219] The 10-year death rate in individuals with delayed OH was 29%, compared with 64% and 9% in individuals with baseline OH and controls, respectively.
IIa	**B-NR**	**Tilt-table testing is reasonable to distinguish convulsive syncope from epilepsy in selected patients.[222–225]**
See Online Data Supplement 15.		Convulsive syncope is a term that can be used to describe any form of syncope manifesting with convulsive movements (eg, myoclonus). Prolonged convulsions and marked postictal confusion are uncommon in patients with syncope associated with convulsive movements,[226] and fatigue is frequent after reflex syncope and may be confused with a postictal state.[226] Tilt-table testing has been shown to be of value in this clinical setting when a detailed history cannot clearly determine whether the convulsive movements were secondary to syncope, given the need for objective evidence to help distinguish this entity from true epileptic seizures. In a prospective study of 15 patients with recurrent unexplained seizure-like episodes who were unresponsive to antiepileptic therapy,[223] 67% had convulsive movements associated with hypotension and bradycardia during tilt-table testing. In another study of 74 patients with a questionable diagnosis of epilepsy (because of drug-refractory seizures or clinically suspected not to be true epilepsy), a cardiac diagnosis was established in 42% of patients, with >25% developing profound hypotension or bradycardia during the head-up tilt-table test, confirming the diagnosis of VVS.[225] Taken together, it can be estimated from these studies that approximately 50% of patients with either questionable or drug-refractory epilepsy have positive tilt-table tests suggestive of a vasovagal etiology.[226]
IIa	**B-NR**	**Tilt-table testing is reasonable to establish a diagnosis of pseudosyncope.[227–229]**
See Online Data Supplement 15.		Psychogenic pseudosyncope should be suspected when patients present with frequent (even daily) symptoms that mimic VVS (and, in some cases, with a history of true VVS). It is often challenging to differentiate psychogenic syncope from true syncope. However, tilt-table testing may help to elucidate the diagnosis. During tilt-table testing, the apparent unconsciousness with loss of motor control, combined with normal blood pressure and heart rate (and a normal electroencephalogram [EEG] if such a recording is obtained), rules out true syncope and most forms of epilepsy.[227–229] In 1 study of 800 patients who underwent tilt-table testing, approximately 5% were diagnosed with pseudosyncope. Compared with patients with VVS, eye closure during the event, long periods of apparent transient loss of consciousness, and increased heart rate and blood pressure are highly specific for pseudosyncope. One study of 21 patients with suspected pseudosyncope who were subjected to tilt-table testing with continuous monitoring of the ECG, EEG, and blood pressure revealed 17 patients with non-epileptiform limb shaking without significant changes on an EEG or hemodynamic changes.[227]
III: No Benefit	**B-R**	**Tilt-table testing is not recommended to predict a response to medical treatments for VVS.[230,231]**
See Online Data Supplement 15.		One of the purported advantages of tilt-table testing, in addition to suggesting a diagnosis of VVS, is the ability to assess the efficacy of pharmacological therapeutics in suppressing a vasovagal response to postural stress by evaluating the effectiveness of a therapy during repeated testing.[230,231] Several small studies suggested a possible benefit, but these data were limited by the lack of reproducibility of tilt-table testing.[232–235]

Table 7. Examples of Serious Medical Conditions That Might Warrant Consideration of Further Evaluation and Therapy in a Hospital Setting

Cardiac Arrhythmic Conditions	Cardiac or Vascular Nonarrhythmic Conditions	Noncardiac Conditions
Sustained or symptomatic VT	Cardiac ischemia	Severe anemia/gastrointestinal bleeding
Symptomatic conduction system disease or Mobitz II or third-degree heart block	Severe aortic stenosis	Major traumatic injury due to syncope
Symptomatic bradycardia or sinus pauses not related to neurally mediated syncope	Cardiac tamponade	Persistent vital sign abnormalities
Symptomatic SVT	HCM	
Pacemaker/ICD malfunction	Severe prosthetic valve dysfunction	
Inheritable cardiovascular conditions predisposing to arrhythmias	Pulmonary embolism	
	Aortic dissection	
	Acute HF	
	Moderate-to-severe LV dysfunction	

HCM indicates hypertrophic cardiomyopathy; HF, heart failure; ICD, implantable cardioverter-defibrillator; LV, left ventricular; SVT, supraventricular tachycardia; and VT, ventricular tachycardia.

3.3. Neurological Testing: Recommendations

3.3.1. Autonomic Evaluation: Recommendation

Syncope due to neurogenic OH is common in patients with central or peripheral autonomic nervous system damage or dysfunction. Its causes should be sought so as to provide efficient, accurate, and effective management. Some symptoms of neurogenic OH may differ from those due to dehydration, drugs, and cardiac and reflex syncope; these include persistent and often progressive generalized weakness, fatigue, visual blurring, cognitive slowing, leg buckling, and the "coat hanger" headache (a triangular headache at the base of the neck due to trapezius ischemia). These symptoms may be provoked or exacerbated by exertion, prolonged standing, meals, or increased ambient temperature. Confirmation of specific neurogenic OH conditions causing syncope often requires additional autonomic evaluation.

Recommendation for Autonomic Evaluation		
COR	**LOE**	**Recommendation**
IIa	**C-LD**	**Referral for autonomic evaluation can be useful to improve diagnostic and prognostic accuracy in selected patients with syncope and known or suspected neurodegenerative disease.[219,236–239]**
See Online Data Supplement 16.		The care of patients with neurogenic OH is complex, especially in individuals with neurodegenerative disease. Care providers must be knowledgeable in the pathophysiology of the autonomic nervous system and the pharmacology of treatments for neurodegenerative disease.[33,240] Many symptomatic treatments for neurodegenerative disease will increase the risk of syncope due to worsening OH; selection of these treatments needs to be balanced against the increased morbidity of not treating the symptoms of the neurodegenerative disease. Such care may be provided by a neurologist, cardiologist, internist, or other physician who has sufficient training to treat these complicated patients. Syncope due to neurogenic OH is caused by either central or peripheral autonomic nervous system damage or dysfunction. Central autonomic degenerative disorders include multiple system atrophy,[241] Parkinson's disease,[242] and Lewy Body dementia.[238] Peripheral autonomic dysfunction may be due to a selective degeneration of peripheral autonomic neurons, known as pure autonomic failure,[243] or may accompany autonomic peripheral neuropathies, such as neuropathies due to diabetes amyloidosis, immune-mediated neuropathies, hereditary sensory and autonomic neuropathies, and inflammatory neuropathies. Peripheral neuropathies due to vitamin B_{12} deficiency, neurotoxic exposure, HIV and other infections, and porphyria are less common causes of neurogenic OH.[240] It can be useful to consider referring patients with the following characteristics for autonomic evaluation: Parkinsonism[241,244–246] or other central nervous system features,[247,248] peripheral neuropathies,[240] underlying diseases known to be associated with a peripheral neuropathy,[240,248] progressive autonomic dysfunction without central or peripheral nervous system features,[243,248] postprandial hypotension,[248,249] and known or suspected neuropathic postural tachycardia syndrome (POTS).[37,248,250] Autonomic evaluation may: 1) determine the underlying cause of neurogenic OH; 2) provide prognostic information; and 3) have therapeutic implications.

3.3.2. Neurological and Imaging Diagnostics: Recommendations

Many patients undergo extensive neurological investigation after an uncomplicated syncope event, despite the absence of neurological features on history or examination. A systematic review found that EEG, CT, MRI, and carotid ultrasound were ordered in 11% to 58% of patients with a presentation of syncope.[78] The evidence suggests that routine neurological testing is of very limited value in the context of syncope evaluation and management; the diagnostic yield is low, with very high cost per diagnosis.[36,77,78,251–260] The recommendations pertain to the use of these investigations in patients with syncope and not in patients in the wider category of transient loss of consciousness.

Recommendations for Neurological Diagnostics		
COR	**LOE**	**Recommendations**
IIa	**C-LD**	**Simultaneous monitoring of an EEG and hemodynamic parameters during tilt-table testing can be useful to distinguish among syncope, pseudosyncope, and epilepsy.**[229,261–263]
See Online Data Supplement 16.		Although a thoughtful and detailed history usually suffices to distinguish among convulsive syncope, epileptic convulsions, and pseudosyncope, an EEG is particularly important when a diagnosis cannot be established after a thorough initial evaluation. EEG findings are characteristic if an episode can be induced during the tilt-table testing.[261–263] Epileptiform discharges are recorded during epileptic convulsions whereas, during syncope, an EEG generally shows diffuse brainwave slowing with delta waves and a flat line pattern.[263] Pseudosyncope and psychogenic nonepileptic seizures are associated with a normal EEG.[229]
III: No Benefit	**B-NR**	**MRI and CT of the head are not recommended in the routine evaluation of patients with syncope in the absence of focal neurological findings or head injury that support further evaluation.**[78,260]
See Online Data Supplement 16.		Syncope is due to global cerebral hypoperfusion, and brain structural abnormalities are rare. Nonetheless, MRI and CT are frequently used and infrequently helpful. In 5 studies investigating patients with syncope, MRI was used in 11% of 397 patients and established a diagnosis in only 0.24%. Similarly, in 10 studies of investigation of syncope, CT was used in 57% of 2728 patients and established a diagnosis in only 1%.[77,78,256,257,260] Given the cost and impact on health service facilities, MRI and CT should not be routinely used in the assessment of syncope. Neurological imaging may be indicated if significant head injury as a result of syncope is suspected. Although there is general concern about potential radiation-mediated harm from CT, there are very limited data on the actual harm from CT for syncope evaluation.
III: No Benefit	**B-NR**	**Carotid artery imaging is not recommended in the routine evaluation of patients with syncope in the absence of focal neurological findings that support further evaluation.**[77,78,256,257,260]
See Online Data Supplement 16.		Syncope is due to global cerebral hypoperfusion and therefore not to unilateral ischemia. A review of 5 studies of carotid artery ultrasound and Doppler use in patients with syncope found that these modalities were used in 58% of 551 patients and established a diagnosis in 0.5%.[77,78,256,257,260] Carotid artery ultrasound should not be routinely used in the assessment of syncope.
III: No Benefit	**B-NR**	**Routine recording of an EEG is not recommended in the evaluation of patients with syncope in the absence of specific neurological features suggestive of a seizure.**[36,77,254–258]
See Online Data Supplement 16.		EEGs are ordered frequently for the evaluation of syncope. A review of 7 studies of use of an EEG in patients with syncope found that it was used in 52% of 2084 patients and established a diagnosis in 0.7%.[36,77,254–258] EEGs should not be routinely used in the assessment of syncope.

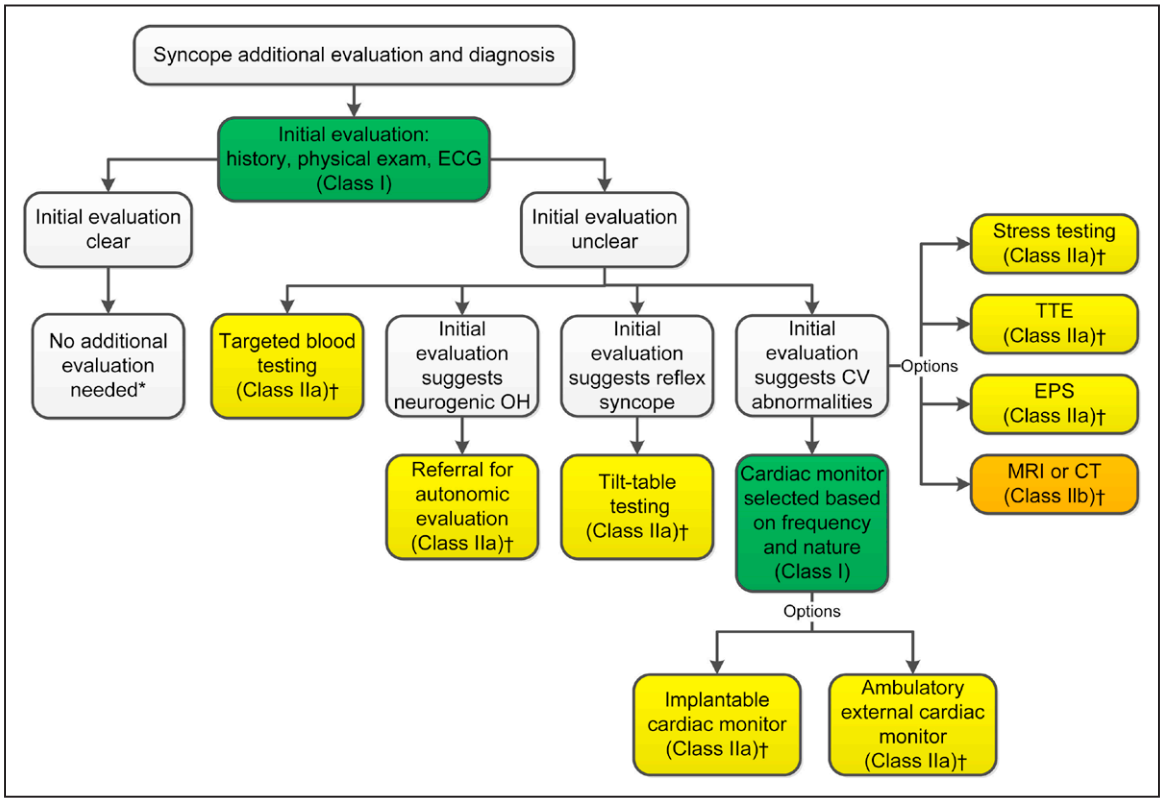

Figure 3. Additional Evaluation and Diagnosis for Syncope. Colors correspond to Class of Recommendation in Table 1. *Applies to patients after a normal initial evaluation without significant injury or cardiovascular morbidities; patients followed up by primary care physician as needed. †In selected patients (see Section 1.4). CT indicates computed tomography; CV, cardiovascular; ECG, electrocardiogram; EPS, electrophysiological study; MRI, magnetic resonance imaging; OH, orthostatic hypotension; and TTE, transthoracic echocardiography.

Table 8. Cardiac Rhythm Monitors

Types of Monitor	Device Description	Patient Selection
Holter monitor[151–153]	A portable, battery-operated device Continuous recording for 24–72 h; up to 2 wk with newer models Symptom rhythm correlation can be achieved through a patient event diary and patient-activated annotations	Symptoms frequent enough to be detected within a short period (24–72 h) of monitoring*
Patient-activated, transtelephonic monitor (event monitor)[150,154,155]	A recording device that transmits patient-activated data (live or stored) via an analog phone line to a central remote monitoring station (eg, physician office)	Frequent, spontaneous symptoms likely to recur within 2–6 wk Limited use in patients with frank syncope associated with sudden incapacitation
External loop recorder (patient or auto triggered)†[150,154,155]	A device that continuously records and stores rhythm data over weeks to months Patient activated, or auto triggered (eg, to record asymptomatic arrhythmias) to provide a recording of events antecedent to (3–14 min), during, and after (1–4 min) the triggered event Newer models are equipped with a cellular phone, which transmits triggered data automatically over a wireless network to a remote monitoring system	Frequent, spontaneous symptoms related to syncope, likely to recur within 2–6 wk
External patch recorders[157–159]	Patch device that continuously records and stores rhythm data, with patient-trigger capability to allow for symptom-rhythm correlation No leads or wires, and adhesive to chest wall/sternum Various models record from 2–14 d Offers accurate means of assessing burden of atrial fibrillation Patient activated, or auto triggered (eg, to record asymptomatic arrhythmias) to provide a recording of events antecedent to, during, and after the triggered event	Can be considered as an alternative to external loop recorder Given that it is leadless, can be accurately self-applied, and is largely water resistant, it may be more comfortable and less cumbersome than an external loop recorder, potentially improving compliance Unlike Holter monitors and other external monitors, it offers only 1-lead recording
Mobile cardiac outpatient telemetry[160,161]	Device that records and transmits data (up to 30 d) from preprogrammed arrhythmias or patient activation to a communication hub at the patient's home Significant arrhythmias are detected; the monitor automatically transmits the patient's ECG data through a wireless network to the central monitoring station, which is attended by trained technicians 24 h/d This offers the potential for real-time, immediate feedback to a healthcare provider for evaluation	Spontaneous symptoms related to syncope and rhythm correlation In high-risk patients whose rhythm requires real-time monitoring
Implantable cardiac monitor[162,167,179–181]	Subcutaneously implanted device, with a battery life of 2–3 y Triggered by the patient (or often family member witness) to store the event Models allow for transtelephonic transmission, as well as automatic detection of significant arrhythmias with remote monitoring	Recurrent, infrequent, unexplained syncope (or suspected atypical reflex syncope) of suspected arrhythmic cause after a nondiagnostic initial workup, with or without structural heart disease

*Includes history, physical examination, and 12-lead ECG; may include nondiagnostic tilt-table test or electrophysiological study.
†Higher yield in patients who are able to record a diary to correlate with possible arrhythmia.
ECG indicates electrocardiogram.

4. MANAGEMENT OF CARDIOVASCULAR CONDITIONS

The writing committee reviewed the evidence to support recommendations in the relevant ACC/AHA guidelines and affirms the ongoing validity of the related recommendations in the context of syncope, thus obviating the need to repeat existing guideline recommendations in the present guideline, except for the specific cardiac conditions in Sections 4.2.4, 4.2.5, and 4.3 for which ACC/AHA guidelines are not available. The relevant guidelines are noted in Table 2.

It is pertinent to note that the principles of evaluation and management of syncope in patients with various cardiac conditions are the same as for other noncardiac conditions. A thorough history, physical examination, and baseline ECG are recommended in all patients. The determination of the immediate cause of syncope may be related, indirectly related, or unrelated to the underlying cardiac condition. Management of

patients with syncope and heart disease would include treating the immediate cause of syncope and further assessing long-term management strategies to improve prognosis. The recommendations stated in this section focus on syncope relevant to and within the context of the specific stated cardiac condition.

4.1. Arrhythmic Conditions: Recommendations

Cardiac arrhythmia is a common cause of syncope, and the prompt identification of an arrhythmic etiology has diagnostic and prognostic implications. When bradyarrhythmias and tachyarrhythmias are discovered in patients with syncope, determining their causal relationship to syncope often poses challenges for the practitioner. The baseline presence of an arrhythmia does not necessarily represent the etiology of syncope (eg, marked resting bradycardia in a young patient with syncope). Furthermore, determining the significance of atrial tachyarrhythmias and VT—which are often paroxysmal and occult on initial evaluation—poses additional challenges and may warrant a more extensive evaluation (Section 3.2). Section 4.1 broadly outlines strategies to guide the practitioner when evaluating patients with bradycardia, supraventricular arrhythmias (including AF), and VT.

4.1.1. Bradycardia: Recommendation

Recommendation for Bradycardia		
COR	**LOE**	**Recommendation**
I	**C-EO**	**In patients with syncope associated with bradycardia, GDMT is recommended.[12]**
N/A		A search and review of papers on syncope and bradycardia has been performed since the last updated guidelines were published in 2012.[12] The writing committee supports the previous recommendations pertaining to syncope in patients with sinus node dysfunction and AV conduction diseases. In adult patients presenting with syncope and chronic bifascicular block but without documented high-degree AV block, for whom other causes have been excluded, an RCT[265] showed that a dual-chamber pacemaker reduced recurrent syncope. The evidence continues to support, without change from the previous recommendation, the notion that permanent pacemaker implantation is reasonable for syncope in patients with chronic bifascicular block when other causes have been excluded. The use of adenosine triphosphate in the evaluation of syncope in older patients continues to evolve. In a small, single-blind trial of older patients (mean age 75 years) randomized to active pacing or back-up pacing with documented adenosine triphosphate–sensitive sinoatrial or AV block, there was a 75% risk reduction in syncope recurrence with dual-chamber pacing.[266] Adenosine triphosphate is not available in the United States. The writing committee has reached a consensus not to make a new recommendation on its use for syncope evaluation because of the limited data at this time.

4.1.2. Supraventricular Tachycardia: Recommendations

Recommendations for Supraventricular Tachycardia (SVT)		
COR	**LOE**	**Recommendations**
I	**C-EO**	**In patients with syncope and SVT, GDMT is recommended.[10]**
N/A		Although patients with SVT frequently manifest palpitations and lightheadedness, syncope is uncommon. Of note, older patients with paroxysmal SVT are more prone to syncope or near-syncope than are younger patients; these symptoms appear to be independent of the rate of tachycardia, which is generally slower in older adult patients than in younger patients.[267,268] Younger patients with SVT causing syncope generally have a very rapid tachycardia. Evaluation of syncope in patients with Wolff-Parkinson-White syndrome with preexcitation on ECG requires a thorough history to differentiate an arrhythmic syncope from a nonarrhythmic syncope, such as VVS, in younger patients.[269] When a patient with syncope reports antecedent palpitations and lightheadedness, VT should be more strongly suspected than SVT. EPS may be useful to distinguish a VT from an SVT responsible for syncope associated with these antecedent symptoms. It should be noted that palpitations can also precede vasovagal faints due to sinus tachycardia, so not all palpitations are necessarily due to paroxysmal SVT or VT.
I	**C-EO**	**In patients with AF, GDMT is recommended.[16]**
N/A		AF can be associated with syncope. As with other forms of SVT, syncope from a rapid ventricular response (in the absence of preexcitation) is relatively unusual. Patients with chronic AF merit control of the ventricular response or maintenance of sinus rhythm with appropriate antiarrhythmic therapy (in carefully selected patients).[16] Patients with paroxysmal AF are predisposed to an abnormal neural response during both sinus rhythm and arrhythmia, and the onset of AF may trigger VVS.[270] In patients with sinus node dysfunction, syncope could occur upon termination of AF when prolonged pauses are present.

4.1.3. Ventricular Arrhythmia: Recommendation

Recommendation for VA		
COR	**LOE**	**Recommendation**
I	C-EO	**In patients with syncope and VA, GDMT is recommended.**[12,13,220,264,271]
N/A		Patients with VA (monomorphic or polymorphic) can present with syncope, whether it is nonsustained or sustained. The mechanism of syncope from VA is multifactorial, including: rapid rate, abrupt change in rate, abnormal atrial and ventricular activation relationships, dyssynchrony of ventricular activation, changes in autonomic tone, and body position during the VA.[272] One study of 113 patients with sustained VA showed that patients who had a mean VA rate of ≥200 bpm had a 65% incidence of syncope or near-syncope, compared with only 15% among patients with a rate <200 bpm.[273] Of the patients with VA ≥200 bpm, 34% did not experience syncope or presyncope. The risk of recurrent syncope and the overall long-term prognosis of patients with VA depend on the severity of the underlying cardiac disease substrates. Indications for ICDs in patients with syncope and suspected VA are predicated on the documentation of or the risk of developing lethal VA.[12]

4.2. Structural Conditions: Recommendations

Syncope occurs not infrequently in patients with underlying heart diseases. Comprehensive guidelines exist for diagnosis and management of many of these diseases, including sections on syncope. In this section, management of syncope is discussed in patients with underlying structural heart disease. The disease-specific ACC/AHA guidelines were assessed first, and then a comprehensive review of literature published since publication of these disease-specific guidelines was performed to ensure that prior recommendations about syncope remained current. If new published data were available, they were incorporated into the present document.

4.2.1. Ischemic and Nonischemic Cardiomyopathy: Recommendation

Recommendation for Ischemic and Nonischemic Cardiomyopathy		
COR	**LOE**	**Recommendation**
I	C-EO	**In patients with syncope associated with ischemic and nonischemic cardiomyopathy, GDMT is recommended.**[12,13]
N/A		Evaluation of syncope in patients with ischemic and nonischemic cardiomyopathy encompasses diagnosis and prognosis. Treatment of syncope is based on the specific cause of syncope, whereas treatment for the underlying cardiomyopathy impacts the long-term prognosis. A review of evidence supports previously published recommendations for patients with syncope in the presence of underlying cardiomyopathy. An ICD is recommended in patients with syncope of undetermined origin with clinically relevant and significant VA induced at the time of an EPS.[28] ICD therapy is also reasonable for patients with unexplained syncope and nonischemic dilated cardiomyopathy with significant LV dysfunction.[12,13,28]

4.2.2. Valvular Heart Disease: Recommendation

Recommendation for Valvular Heart Disease		
COR	**LOE**	**Recommendation**
I	C-EO	**In patients with syncope associated with valvular heart disease, GDMT is recommended.**[11]
N/A		Patients with aortic stenosis may experience syncope during exertion. The mechanism is often hemodynamic, as opposed to arrhythmic, because of inability to augment and sustain cardiac output. In patients with valvular heart disease causing syncope, treatment is recommended by the latest guidelines.[11] Specifically, aortic valve replacement is recommended in patients with severe aortic stenosis and syncope after other causes of syncope are also considered and excluded.

4.2.3. Hypertrophic Cardiomyopathy: Recommendation

Recommendation for HCM		
COR	**LOE**	**Recommendation**
I	C-EO	**In patients with syncope associated with HCM, GDMT is recommended.**[20]
N/A		A MEDLINE search and review of papers on syncope and HCM has been performed since the last guideline was published in 2011.[20] There are no new data that would alter the 2011 recommendations. Thus, the writing committee supports the previous recommendations pertaining to syncope in patients with HCM. Although there are no randomized trials, data from registries have shown consistently that unexplained syncope is an independent predictor for SCD and appropriate ICD discharges. The present writing committee concurs that ICD implantation is reasonable in patients with HCM presenting with ≥1 recent episodes of syncope suspected to be of arrhythmic nature.

4.2.4. Arrhythmogenic Right Ventricular Cardiomyopathy: Recommendations

Recommendations for ARVC		
COR	**LOE**	**Recommendations**
I	**B-NR**	**ICD implantation is recommended in patients with ARVC who present with syncope and have a documented sustained VA.[274–278]**
See Online Data Supplement 17.		ICD indications in patients with ARVC and sustained VA are no different than guidelines-based indications for secondary prevention of SCD in other diseases.[12]
IIa	**B-NR**	**ICD implantation is reasonable in patients with ARVC who present with syncope of suspected arrhythmic etiology.[274,275,277–279]**
See Online Data Supplement 17.		Unexplained or arrhythmic-appearing syncope in patients with ARVC has consistently been associated with increased risk of SCD or appropriate therapy after ICD implantation in multiple observational studies.[274–279]

4.2.5. Cardiac Sarcoidosis: Recommendations

Recommendations for Cardiac Sarcoidosis		
COR	**LOE**	**Recommendations**
I	**B-NR**	**ICD implantation is recommended in patients with cardiac sarcoidosis presenting with syncope and documented spontaneous sustained VA.[12,280–286]**
See Online Data Supplement 18.		ICD indications in patients with cardiac sarcoidosis and sustained VA are no different than guidelines- or consensus-based indications for secondary prevention of SCD.[12,286] Macroreentry around the granulomas is the most common mechanism of VA in patients with cardiac sarcoidosis.[280,281] Other mechanisms include triggered activity and abnormal automaticity due to myocardial inflammation.[282] Unlike AV block, the results of immunosuppression in patients with VA are controversial. Some studies have shown improvement with immunosuppression,[283] whereas others have shown no benefit and even harm due to worsening VA and aneurysm formation.[284,285]
I	**C-EO**	**In patients with cardiac sarcoidosis presenting with syncope and conduction abnormalities, GDMT is recommended.[12,286–289]**
See Online Data Supplement 18.		Patients with cardiac sarcoidosis and conduction abnormalities should be treated according to the most recent guidelines for cardiac pacing.[12] Patients with cardiac sarcoidosis and conduction abnormalities have a worse prognosis than that of patients with idiopathic AV block.[286,287] Immunosuppression can result in transient reversal of AV block; however, the reversibility is unpredictable.[287–289] As such, it is recommended to proceed with pacing according to the most recent guidelines regardless of AV block reversibility.
IIa	**B-NR**	**ICD implantation is reasonable in patients with cardiac sarcoidosis and syncope of suspected arrhythmic origin, particularly with LV dysfunction or pacing indication.[290–293]**
See Online Data Supplement 18.		The presence of myocardial noncaseating granulomas and inflammation puts patients at risk of having both AV block and VA, particularly in the presence of LV dysfunction. Patients with cardiac sarcoidosis and mild-to-moderate LV dysfunction have a substantial risk of developing VA.[290–293] In a multicenter study including 235 patients with cardiac sarcoidosis who received ICD therapy for primary or secondary prevention, including patients with syncope, 36% of patients received appropriate ICD therapy. Patients who received appropriate ICD therapies were more likely to be male and to have a history of syncope, lower LV ejection fraction, ventricular pacing on baseline ECG, and a secondary prevention indication than were those who did not receive appropriate ICD therapies.[292] Therefore, given the presence of a substrate for VA in patients with cardiac sarcoidosis, ICD implantation is reasonable in patients presenting with syncope suspected to be of arrhythmic origin.
IIa	**B-NR**	**EPS is reasonable in patients with cardiac sarcoidosis and syncope of suspected arrhythmic etiology.[294]**
See Online Data Supplement 18.		In patients with cardiac sarcoidosis, programmed electrical stimulation may help identify patients at risk of having VA. According to a study of 76 patients with cardiac sarcoidosis and no cardiac symptoms, 8 (11%) had inducible sustained VA. During a median follow-up of 5 years, 6 of 8 had VA or died, versus 1 of 68 in the noninducible group.[294]

4.3. Inheritable Arrhythmic Conditions: Recommendations

The prevalence of inherited arrhythmic conditions is low, rendering the clinical significance of an abnormal test a challenge. Few syncope-specific studies exist. Most studies of patients with inherited arrhythmias are open label or not randomized and often are uncontrolled. Most of the publications included other cardiac events, such as cardiac arrest and death, either at enrollment or as an outcome. Syncope of suspected arrhythmic cause has been correlated with increased risk of SCD, cardiac arrest, or overall cardiac death. Although ICD is effective in aborting cardiac arrest and presumably reducing risk of death in the patients with inheritable rhythm disorders, its impact on syncope recurrence is unknown.[25,26,220]

4.3.1. Brugada Syndrome: Recommendations

Brugada syndrome is defined as a genetic disease characterized by an increased risk of SCD and ST elevation with type 1 morphology ≥2 mm in ≥1 lead among the right precordial leads V1 and V2, occurring either spontaneously or after intravenous administration of Class I antiarrhythmic drugs. The prevalence is higher in Asian countries than in North America or Western Europe, ranging from 0.01% to 1.00%, with a significant male predominance.[295]

Recommendations for Brugada ECG Pattern and Syncope		
COR	**LOE**	**Recommendations**
IIa	**B-NR**	**ICD implantation is reasonable in patients with Brugada ECG pattern and syncope of suspected arrhythmic etiology.[296–300]**
See Online Data Supplement 19.		Syncope is a risk factor for cardiac arrhythmic events in patients with Brugada syndrome.[296,297] ICD implantation is reasonable in these patients; however, the benefit seems to be limited to patients with suspected arrhythmic syncope.[298] Patients with syncope consistent with a reflex-mediated mechanism should not undergo the implantation of an ICD. In a meta-analysis, the relative risk of cardiac events (SCD, syncope, or ICD shock) among patients with a history of syncope or SCD was approximately 3 times higher than among patients without a prior history of syncope or SCD.[296] Data from an international registry showed that the cardiac event rate per year was 7.7% in patients with aborted SCD, 1.9% in patients with syncope, and 0.5% in asymptomatic patients.[297] In a cohort including 203 patients with Brugada, VA occurred only in patients with syncope suspected to be arrhythmic in origin, at a rate of 5.5% per year. No SCD occurred in patients with nonarrhythmic syncope or with syncope of doubtful origin.[298]
IIb	**B-NR**	**Invasive EPS may be considered in patients with Brugada ECG pattern and syncope of suspected arrhythmic etiology.[297,301,302]**
See Online Data Supplement 19.		The value of EPS in assessing the mechanism of syncope in patients with Brugada is unknown. In large registries of patients with Brugada (PRELUDE and FINGER),[297,301] inducibility of VA was higher among patients with a prior history of syncope or SCD. However, the value of EPS in predicting prognosis in patients with Brugada is essentially unknown in patients with syncope. The role of inducibility of VA in identifying high-risk patients remains controversial.[301,302] Therefore, EPS may be considered only in patients with syncope suspected to be due to an arrhythmia and is not recommended in patients with reflex syncope.
III: No Benefit	**B-NR**	**ICD implantation is not recommended in patients with Brugada ECG pattern and reflex-mediated syncope in the absence of other risk factors.[303,304]**
See Online Data Supplement 19.		In a retrospective multicenter study, appropriate ICD therapy was limited to survivors of cardiac arrest, whereas none of the other patients with syncope and/or inducible ventricular fibrillation (VF) suffered an arrhythmic event.[303,304] Given the lack of benefit of ICD therapy in patients with reflex syncope and the known rate of inappropriate shocks and ICD complications in patients who receive an ICD,[51] ICD implantation is not recommended when the syncope mechanism is believed to be reflex mediated.

4.3.2. Short-QT Syndrome: Recommendation

Short-QT syndrome is a genetic disease characterized by palpitations, syncope, and increased risk of SCD, associated with a QTc interval ≤340 ms.[25,26] It is a rare condition. Limited data are available about its prognostic significance, particularly in the absence of documented VA. Invasive EPS has shown increased vulnerability to VF induction in most patients, yet the clinical significance of this finding remains unknown.[305] Quinidine therapy might provide some protection against VA; however, there are insufficient data to make any recommendations.[305,306]

Recommendation for Short-QT Syndrome		
COR	**LOE**	**Recommendation**
IIb	**C-EO**	**ICD implantation may be considered in patients with short-QT pattern and syncope of suspected arrhythmic etiology.**
See Online Data Supplement 20.		The prevalence of short-QT syndrome is very low, ranging from 0.02% to 1.63%.[305,307–312] There is no evidence that syncope in patients with short-QT pattern is a risk factor for cardiac arrest in the absence of documented VT or VF. Therefore, ICD implantation may be limited to patients with suspected arrhythmic syncope, particularly in the presence of a family history of SCD.[306]

4.3.3. Long-QT Syndrome: Recommendations

LQTS is diagnosed in the presence of QTc ≥500 ms or LQTS risk score ≥3.5 when secondary causes have been excluded or in the presence of a pathogenic mutation in 1 of the LQTS genes. It can also be diagnosed when the QTc is 480 to 499 ms in a patient presenting with syncope.[25] There are several genetic forms of LQTS, which affect presentation and response to therapy. Given that syncope is often the result of an arrhythmic event in patients with LQTS, early recognition and treatment are needed to avoid recurrences, which could present as cardiac arrest or SCD. This is particularly true in the pediatric population, where significant overlap exists in the clinical presentation of patients with VVS and arrhythmic syncope.[313,314] Attention to the triggers and presence of palpitations preceding syncope onset have been helpful in diagnosing an arrhythmic etiology.[315]

Patients with LQTS and syncope should adhere to the lifestyle changes previously published, including avoidance of strenuous activity in LQTS1, and drugs known to prolong QT interval in all patients with LQTS.[25]

Recommendations for LQTS		
COR	**LOE**	**Recommendations**
I	B-NR	**Beta-blocker therapy, in the absence of contraindications, is indicated as a first-line therapy in patients with LQTS and suspected arrhythmic syncope.[316–318]**
See Online Data Supplement 21.		In the International Long QT Registry, patients who experienced ≥1 episode of syncope had a 6- to 12-fold increase in the risk of subsequent fatal/near-fatal events, independent of QTc duration. Beta-blocker therapy was associated with a significant reduction in the risk of recurrent syncope and subsequent fatal/near-fatal events. The response to beta blockers depends on the genotype, and not all beta blockers are the same.[316,319] Patients with LQTS1 appear to respond better than patients with LQTS2 and LQTS3.[316,320]
IIa	B-NR	**ICD implantation is reasonable in patients with LQTS and suspected arrhythmic syncope who are on beta-blocker therapy or are intolerant to beta-blocker therapy.[317,320–324]**
See Online Data Supplement 21.		Cardiac events can occur in patients receiving beta-blocker therapy, with a prevalence ranging from 10% to 32%, depending on the genotype.[316,317] Many patients who appear to not respond to beta blockers are poorly compliant or do not tolerate the medication.[317] Therefore, ICD implantation is reasonable in patients with LQTS who continue to have syncope despite beta-blocker therapy and in those who cannot tolerate beta-blocker therapy. In a study of 459 patients with genetically confirmed LQTS who received an ICD, syncope was a predictor of appropriate therapy.[322]
IIa	C-LD	**Left cardiac sympathetic denervation (LCSD) is reasonable in patients with LQTS and recurrent syncope of suspected arrhythmic mechanism who are intolerant to beta-blocker therapy or for whom beta-blocker therapy has failed.[325–327]**
See Online Data Supplement 21.		LCSD has been shown to be associated with a large and significant clinical benefit in patients with symptomatic LQTS who are either refractory or intolerant to beta-blocker therapy.[325,326] LCSD also reduces shocks in patients with an ICD during arrhythmia storms. Therefore, LCSD can be beneficial in patients with recurrent syncope despite beta blockade, in those who cannot tolerate beta-blocker therapy, and in those with frequent shocks from their ICD. However, LCSD alone does not completely prevent cardiac events, including SCD, during long-term follow-up.

4.3.4. Catecholaminergic Polymorphic Ventricular Tachycardia: Recommendations

CPVT is characterized by the presence of catecholamine-induced (often exertional) bidirectional VT or polymorphic VT in the setting of a structurally normal heart and normal resting ECG.[328,329] In patients with CPVT, 60% have a mutation in either the gene encoding the cardiac ryanodine receptor (*RyR2*) (autosomal dominant) or in the cardiac calsequestrin gene (*CASQ2*) (autosomal recessive).[330–333] The prevalence of the disease is estimated to be around 0.1 per 1000 patients. Patients usually present in the first or second decade of life with stress-induced syncope.[25]

Recommendations for CPVT		
COR	**LOE**	**Recommendations**
I	C-LD	**Exercise restriction is recommended in patients with CPVT presenting with syncope of suspected arrhythmic etiology.[328,334,335]**
See Online Data Supplements 22 and 23.		The presence of VA in patients with CPVT has been shown to correlate with increases in heart rate, highlighting the role of the sympathetic nervous system in arrhythmogenesis.[328,334] Therefore, exercise restriction, including avoidance of heavy exercise and competitive sports, is recommended in all patients with CPVT.[335]
I	C-LD	**Beta blockers lacking intrinsic sympathomimetic activity are recommended in patients with CPVT and stress-induced syncope.[329,334,336–339]**
See Online Data Supplements 22 and 23.		Beta blockers should be first-line therapy in patients with CPVT, as they have been shown to suppress exercise-induced arrhythmias. However, they are not always completely protective.[329,334,336] The variability in outcome with beta-blocker therapy is due to multiple factors, including dosing and compliance.[337,338] Repeat exercise testing and cardiac monitoring to document arrhythmia suppression can be reassuring.[334,339]
IIa	C-LD	**Flecainide is reasonable in patients with CPVT who continue to have syncope of suspected VA despite beta-blocker therapy.[319,320]**
See Online Data Supplements 22 and 23.		Despite beta-blocker therapy, breakthrough arrhythmias occur in patients with CPVT because of treatment failure, noncompliance, and subtherapeutic dosing. The addition of flecainide to conventional therapy has been shown to partly or completely suppress exercise-induced VA.[340] In patients intolerant of beta-blocker therapy, flecainide is useful as monotherapy.[341]
IIa	B-NR	**ICD therapy is reasonable in patients with CPVT and a history of exercise- or stress-induced syncope despite use of optimal medical therapy or LCSD.[271,342,343]**
See Online Data Supplements 22 and 23.		ICD therapy appears to reduce mortality rate in patients with CPVT and syncope or VA refractory to medical therapy. However, VT storms in patients with CPVT may not always respond to ICD shocks,[344] and shocks may precipitate early recurrence of arrhythmia because of their painful nature with resultant adrenergic state. Furthermore, the effectiveness of ICD shock therapy in CPVT depends on the mechanism of the VA, with greater success noted when shocks are delivered for VF.[345] ICD implantation should be performed in conjunction with beta-blocker therapy or LCSD when available.[342] Careful programming, including long detection intervals with high cutoff rate, is recommended to decrease the prevalence of inappropriate shocks.[342,343]
IIb	C-LD	**In patients with CPVT who continue to experience syncope or VA, verapamil with or without beta-blocker therapy may be considered.[346,347]**
See Online Data Supplements 22 and 23.		Verapamil alone or in combination with beta blockers helps suppress arrhythmias in patients with CPVT,[347] including delaying the onset of exercise-induced ventricular ectopy.[346,347]

Recommendations for CPVT (Continued)		
COR	LOE	Recommendations
IIb	C-LD	**LCSD may be reasonable in patients with CPVT, syncope, and symptomatic VA despite optimal medical therapy.[348–350]**
See Online Data Supplements 22 and 23.		When syncope occurs despite optimal medical therapy, LCSD may be a reasonable therapy.[348–350] In a worldwide cohort study, the percentage of patients with major cardiac events despite optimal medical therapy was reduced 68% after LCSD.[349]

4.3.5. Early Repolarization Pattern: Recommendations

Early repolarization pattern is characterized by a distinct J point and ST elevation in the lateral or inferolateral leads. The pattern is more prevalent in young athletes, particularly African Americans, with 70% of the subjects being male.[351] Early repolarization ECG pattern (>1 mm) in the inferior/lateral leads occurs in 1% to 13% of the general population and in 15% to 70% of idiopathic VF cases.[352–354] Furthermore, it has been shown in population-based studies to be associated with increased risk of cardiac death.[352,353,355–357] One study showed that the presence of a J wave increased the risk of VF from 3.4/100 000 to 11.0/100 000.[353] However, given the low incidence of VF in the general population, the absolute risk in patients with early repolarization remains low. In patients with syncope, the clinical significance of the early repolarization pattern is unknown.

Recommendations for Early Repolarization Pattern		
COR	LOE	Recommendations
IIb	C-EO	**ICD implantation may be considered in patients with early repolarization pattern and suspected arrhythmic syncope in the presence of a family history of early repolarization pattern with cardiac arrest.**
N/A		ICD implantation may be considered in patients with early repolarization pattern and suspected cardiac syncope if they have a family history of unexplained SCD, VF, or polymorphic VT with documented early repolarization pattern in the affected family member.[358,359]
III: Harm	B-NR	**EPS should not be performed in patients with early repolarization pattern and history of syncope in the absence of other indications.[359]**
See Online Data Supplement 24.		In a multicenter study including 81 patients with early repolarization syndrome and aborted SCD who underwent EPS, VF was inducible in only 22% of cases. The VF recurrence rate was similar in patients who were inducible and in those who were noninducible.[359] Given the high prevalence of early repolarization, the possibility of inducing VF in healthy individuals, and the limited value of ventricular programmed stimulation in risk stratification, EPS is not recommended in patients with early repolarization and syncope in the absence of other cardiac indications.[352,353,360]

5. REFLEX CONDITIONS: RECOMMENDATIONS

5.1. Vasovagal Syncope: Recommendations

VVS is the most common cause of syncope and a frequent reason for ED visits.[66] The underlying pathophysiology of VVS results from a reflex causing hypotension and bradycardia, triggered by prolonged standing or exposure to emotional stress, pain, or medical procedures.[361–365] An episode of VVS is typically associated with a prodrome of diaphoresis, warmth, and pallor, with fatigue after the event. Given the benign nature of VVS and its frequent remissions, medical treatment is usually not required unless conservative measures are unsatisfactory. In some patients, effective treatment is needed, as syncopal events may result in injury and an impaired quality of life (QoL).[366–368] Despite the need and substantial efforts by investigators, there are limited evidence-based therapeutic options.[369] Preliminary data from cardiac ganglia plexi ablation in treating selected patients with VVS are encouraging but still insufficient to make recommendations at this time.[370–372] See Figure 4 for the algorithm for treatment of VVS.

Recommendations for VVS		
COR	LOE	Recommendations
I	C-EO	**Patient education on the diagnosis and prognosis of VVS is recommended.**
See Online Data Supplements 25 and 26.		In all patients with the common faint or VVS, an explanation of the diagnosis, education targeting awareness of and possible avoidance of triggers (eg, prolonged standing, warm environments, coping with dental and medical settings), and reassurance about the benign nature of the condition should be provided.
IIa	B-R	**Physical counter-pressure maneuvers can be useful in patients with VVS who have a sufficiently long prodromal period.[373–375]**
See Online Data Supplements 25 and 26.		Patients with a syncope prodrome should be instructed to assume a supine position to prevent a faint and minimize possible injury. In patients with a sufficiently long prodrome, physical counter-maneuvers (eg, leg crossing, limb and/or abdominal contraction, squatting) are a core management strategy. In a randomized, parallel, open-label trial, leg crossing with conventional therapy (ie, fluid, salt intake, counseling, and avoidance) was superior to conventional therapy in preventing syncope recurrence.[375]

Recommendations for VVS (Continued)		
COR	**LOE**	**Recommendations**
IIa	**B-R**	**Midodrine is reasonable in patients with recurrent VVS with no history of hypertension, HF, or urinary retention.[376–380]**
See Online Data Supplements 25 and 26.		Midodrine is a prodrug that is metabolized to desglymidodrine, which is a peripherally active alpha-agonist used to ameliorate the reduction in peripheral sympathetic neural outflow responsible for venous pooling and vasodepression in VVS. Studies on the efficacy of midodrine support its use. In a meta-analysis of 5 RCTs in adults and children, midodrine was associated with a 43% reduction in syncope recurrence.[318,376,378,379,381]
IIb	**B-R**	**The usefulness of orthostatic training is uncertain in patients with frequent VVS.[382–386]**
See Online Data Supplements 25 and 26.		There are 2 main methods of orthostatic training. Patients undergo repetitive tilt-table tests in a monitored setting until a negative tilt-table test occurs and then are encouraged to stand quietly against a wall for 30 to 60 minutes daily, or patients simply standing quietly against a wall at home for a prolonged period of time daily. RCTs have not shown a sustained benefit in reducing episodes of syncope recurrence with either option.[382,383,385,387]
IIb	**B-R**	**Fludrocortisone might be reasonable for patients with recurrent VVS and inadequate response to salt and fluid intake, unless contraindicated.[388,389]**
See Online Data Supplements 25 and 26.		Fludrocortisone has mineralocorticoid activity resulting in sodium and water retention and potassium excretion, which results in increased blood volume. In a pediatric population, an RCT found more recurrent symptoms in the fludrocortisone arm than in the placebo arm.[389] Serum potassium level should be monitored because of potential drug-induced hypokalemia. POST II (Prevention of Syncope Trial II) reported a marginally insignificant 31% risk reduction in adults with moderately frequent VVS, which was significant in patients after a 2-week dose stabilization period.[388]
IIb	**B-NR**	**Beta blockers might be reasonable in patients 42 years of age or older with recurrent VVS.[390–393]**
See Online Data Supplements 25 and 26.		RCTs on the efficacy and effectiveness of beta blockers for the prevention of syncope have been negative.[64,390–393] However, in a meta-analysis of a prespecified, prestratified substudy of POST I and a large observational study, an age-dependent benefit of beta blockers among patients ≥42 years of age was found, compared with those of younger age.[394,395]
IIb	**C-LD**	**Encouraging increased salt and fluid intake may be reasonable in selected patients with VVS, unless contraindicated.[396–399]**
N/A		Evidence for the effectiveness of salt and fluid intake for patients with VVS is limited. Nonetheless, in patients with recurrent VVS and no clear contraindication, such as a history of hypertension, renal disease, HF, or cardiac dysfunction, it may be reasonable to encourage ingestion of 2 to 3 L of fluid per day and a total of 6 to 9 g (100 to 150 mmol) of salt per day, or about 1 to 2 heaping teaspoonfuls. The long-term balance of risks and benefits of a strategy of increasing salt and water intake is unknown.
IIb	**C-LD**	**In selected patients with VVS, it may be reasonable to reduce or withdraw medications that cause hypotension when appropriate.[400]**
N/A		A careful examination of the patient's history for medications that may lower blood pressure (hypotensive agents) should be performed. Care should be taken to withdraw or reduce medications only where safe to do so and in conjunction with the prescribing healthcare provider.
IIb	**C-LD**	**In patients with recurrent VVS, a selective serotonin reuptake inhibitor might be considered.[393,401,402]**
See Online Data Supplements 25 and 26.		Serotonin has central neurophysiological effects on blood pressure and heart rate and acutely induces syncope during tilt-table testing.[403] Three small RCTs on selective serotonin reuptake inhibitors have been conducted on the effectiveness of fluoxetine and paroxetine in preventing syncope, with contradictory evidence of effectiveness.[393,401,402]

5.2. Pacemakers in Vasovagal Syncope: Recommendation

Pacemakers might seem to be an obvious therapy for VVS, given that bradycardia and asystole are present during some spells. Numerous observational studies and RCTs have assessed whether pacemakers are efficacious in preventing syncope.[404–409] It is becoming clear that strict patient selection on the basis of documented asystole during clinical syncope is important, and that observation combined with a tilt-table test that induces minimal or no vasodepressor response may increase the likelihood of a response to pacing. This is because a positive tilt-table test might identify patients who are likely to also have a vasodepressor response during VVS and therefore not respond as well to permanent pacing. As noted in Section 1.1, the recommendation in this section was based on a separately commissioned systematic review of the available evidence, the results of which were used to frame our decision making. Full details are provided in the ERC's systematic review report.[9]

Recommendation for Pacemakers in VVS		
COR	**LOE**	**Recommendation**
IIb	**B-R[SR]**	**Dual-chamber pacing might be reasonable in a select population of patients 40 years of age or older with recurrent VVS and prolonged spontaneous pauses.[404–408,410]**
See Online Data Supplements 27 and 28.		Among patients with a positive tilt-table test, a benefit of pacing for treatment of recurrent syncope was evident as compared with medical or no therapy in open-label trials,[52,404,406,410–412] but this result must be interpreted with caution because of the possibility of outcome ascertainment bias. In 2 RCTs, there was no statistically significant benefit seen with active pacing.[407,408] However, in a select population of patients >40 years of age with recurrent syncope and documented spontaneous pauses ≥3 seconds correlated with syncope or an asymptomatic pause ≥6 seconds, dual-chamber pacing reduced syncope recurrence. There was less benefit in patients with a positive tilt-table test that induced a vasodepressor response.[405]

SR indicates systematic review.

5.3. Carotid Sinus Syndrome: Recommendations

Carotid sinus syndrome is associated with mechanical manipulation of the carotid sinus, either spontaneously or with carotid sinus massage. It is diagnosed by the reproduction of clinical syncope during carotid sinus massage, with a cardioinhibitory response if asystole is >3 seconds or if there is AV block, or a significant vasodepressor response if there is ≥50 mm Hg drop in systolic blood pressure, or a mixed cardioinhibitory and vasodepressor response. It occurs more commonly in men >40 years of age[413,414] and is due to an abnormal reflex attributed to baroreceptor and possibly medulla dysfunction.[415,416] Carotid sinus massage should be performed sequentially over the right and left carotid artery sinus in both the supine and upright positions for 5 seconds each, with continuous beat-to-beat heart rate monitoring and blood pressure measurement.[417] Contraindications to performing carotid sinus massage include auscultation of carotid bruit and transient ischemic attack, stroke, or myocardial infarction within the prior 3 months, except if carotid Doppler excludes significant stenosis.[418]

Recommendations for Carotid Sinus Syndrome

COR	LOE	Recommendations
IIa	B-R	**Permanent cardiac pacing is reasonable in patients with carotid sinus syndrome that is cardioinhibitory or mixed.**[413,419–426]
See Online Data Supplements 29–32.		Syncope recurred in fewer patients treated with pacing than in untreated patients, with observation periods up to 5 years.[420,423] In 3 controlled, open-label trials, the relative risk reduction of syncope recurrence with pacemaker implantation was 76%.[409,427–429] There are no large RCTs.
IIb	B-R	**It may be reasonable to implant a dual-chamber pacemaker in patients with carotid sinus syndrome who require permanent pacing.**[427–430]
See Online Data Supplements 29–32.		Evidence for dual-chamber pacing versus single-chamber pacing in carotid sinus hypersensitivity is limited to a few small RCTs and limited observational data.[409,418,427–429] Although mixed, the data suggest dual-chamber pacing may prevent hemodynamic compromise and improve symptom recurrence in older adults who may have concomitant sinus node dysfunction or conduction system disease.

5.4. Other Reflex Conditions

Situational syncope is defined as syncope occurring only in certain distinct and usually memorable circumstances, including micturition syncope, defecation syncope, cough syncope, laugh syncope, and swallow syncope.[431–437] Appropriate investigations should be undertaken to determine an underlying etiology, including causes that may be reversible.[431,433–436] Evidence for treatment is limited mainly to case reports, small case series, and small observational studies.[431,433–436] Treatment of most types of situational syncope relies heavily on avoidance or elimination of a triggering event. This may not always be possible, so increased fluid and salt consumption and reduction or removal of hypotensive drugs and diuretics are encouraged where appropriate and safe.[436]

6. ORTHOSTATIC HYPOTENSION: RECOMMENDATIONS

6.1. Neurogenic Orthostatic Hypotension: Recommendations

OH involves excessive pooling of blood volume in the splanchnic and leg circulations. With standing, venous

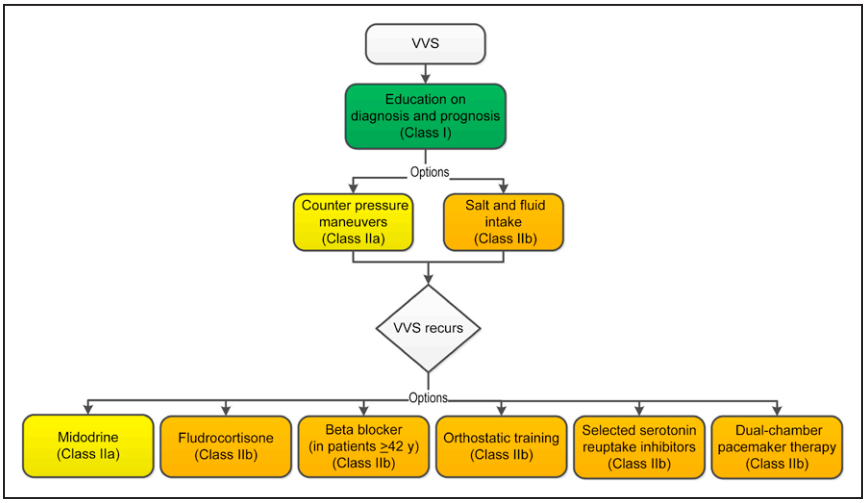

Figure 4. Vasovagal Syncope. Colors correspond to Class of Recommendation in Table 1. VVS indicates vasovagal syncope.

return to the heart drops, with a resultant decrease in cardiac output.[31] Normally, the autonomic nervous system provides compensatory changes in vascular tone, heart rate, and cardiac contractility. In some individuals, this response may be defective or inadequate.[31] In neurogenic OH, the vasoconstrictor mechanisms of vascular tone may be inadequate because of neurodegenerative disorders, such as multiple system atrophy, pure autonomic failure, Parkinson's disease, and autonomic peripheral neuropathies, such as those due to diabetes mellitus and other systemic diseases.[31] Neurogenic OH may present clinically as classic or delayed OH. Most commonly, OH is due to dehydration or medications, such as diuretics and vasodilators. Syncope caused by OH conditions occurs in the upright position. See Figure 5 for the algorithm for treatment of OH.

Recommendations for Neurogenic OH

COR	LOE	Recommendations
I	B-R	**Acute water ingestion is recommended in patients with syncope caused by neurogenic OH for occasional, temporary relief.[438,439]**
See Online Data Supplements 33–35.		In neurogenic OH, acute water ingestion can temporarily restore orthostatic tolerance.[438–444] The pressor effect of water is most likely sympathetically driven, with the peak effect occurring 30 minutes after ingestion of ≥240 mL and additional benefit seen with ≥480 mL.[398,441,442] The presence of glucose or salt may reduce this effect by splanchnic vasodilatation or a decreased osmopressor response, respectively.[397,439] Acute water ingestion for temporary relief of OH is not intended for routine or long-term use.[24]
IIa	C-LD	**Physical counter-pressure maneuvers can be beneficial in patients with neurogenic OH with syncope.[374,445–450]**
See Online Data Supplements 33–35.		Isometric contraction, such as by leg crossing, lower body muscle tensing, and maximal force handgrip, can increase blood pressure, with the largest effect occurring with squatting versus other counter-pressure maneuvers.[374,445–450] Leg crossing increases cardiac output in patients with neurogenic hypotension.[447] Similar or larger benefit would be expected with squatting and other isometric contraction.[449] The benefit is limited to patients with sufficient prodrome and the ability to perform these maneuvers adequately and safely.[449]
IIa	C-LD	**Compression garments can be beneficial in patients with syncope and OH.[451–455]**
See Online Data Supplements 33–35.		In patients with OH, including older adult patients and those with neurogenic etiologies, compression garments can improve orthostatic symptoms and blunt associated decreases in blood pressure.[451–456] The garments should be at least thigh high and preferably include the abdomen, as shorter garments have not been proved to be beneficial.[457]
IIa	B-R	**Midodrine can be beneficial in patients with syncope due to neurogenic OH.[458–467]**
See Online Data Supplements 33–35.		Midodrine improves symptoms of OH in patients with neurogenic OH.[458–467] There is a dose-dependent effect, usually corresponding to an increase in standing blood pressure.[459,460,462,463,466,467] Its use may be limited by supine hypertension, and other common side effects include scalp tingling, piloerection, and urinary retention.[459,460,463,467]
IIa	B-R	**Droxidopa can be beneficial in patients with syncope due to neurogenic OH.[380,468–471]**
See Online Data Supplements 33–35.		Droxidopa improves symptoms of neurogenic OH due to Parkinson disease, pure autonomic failure, and multiple system atrophy.[380,468,470,471] Droxidopa might reduce falls, according to small studies.[472] Use of carbidopa in patients with Parkinson disease may decrease the effectiveness of droxidopa.[380] Use and titration of droxidopa may be limited by supine hypertension,[380,469] headache, dizziness, and nausea.[468,470–472]
IIa	C-LD	**Fludrocortisone can be beneficial in patients with syncope due to neurogenic OH.[473–476]**
See Online Data Supplements 33–35.		Fludrocortisone increases plasma volume, with a resultant improvement in symptoms of OH.[473,477,478] When taken regularly, fludrocortisone may prevent OH, at least in astronauts after space flight.[476] Supine hypertension may be a limiting factor. When supine hypertension is present, other medications should be used before fludrocortisone. Other side effects commonly seen include edema, hypokalemia, and headache, but more serious adverse reactions, such as adrenal suppression and immunosuppression, can also occur with doses >0.3 mg daily.[479,480]
IIb	C-LD	**Encouraging increased salt and fluid intake may be reasonable in selected patients with neurogenic OH.[396,398,441,443,444]**
See Online Data Supplements 33–35.		Although the data are limited for salt and fluid supplementation in patients with OH, these 2 treatments may improve blood pressure while decreasing symptoms from OH.[396,398,439–444] Salt supplementation (eg, 6 to 9 g [100 to 150 mmol; about 1 to 2 teaspoons] of salt per day) increases plasma volume, with limited benefit in patients with already high salt intake.[396] Water ingestion increases the blood pressure via a pressor effect, most likely mediated by sympathetic activation, with a peak effect approximately 30 minutes after ingestion.[398,439,441–443] This additional salt and fluid intake may not be beneficial in patients with history of hypertension, renal disease, HF, or cardiac dysfunction, and the long-term effects of these treatments, including the benefits and risks, is unknown.
IIb	C-LD	**Pyridostigmine may be beneficial in patients with syncope due to neurogenic OH who are refractory to other treatments.[466,481,482]**
See Online Data Supplements 33–35.		In patients with autonomic failure and neurogenic OH, pyridostigmine is able to improve orthostatic tolerance through increases in peripheral vascular resistance and blood pressure.[481,482] Side effects include nausea, vomiting, abdominal cramping, sweating, salivation, and urinary incontinence.[483]
IIb	C-LD	**Octreotide may be beneficial in patients with syncope and refractory recurrent postprandial or neurogenic OH.[484–487]**
See Online Data Supplements 33–35.		Splanchnic circulation pooling can contribute to OH, and this pooling can worsen in the postprandial period.[484–487] Octreotide reduces splanchnic blood flow by approximately 20%,[486] which prevents postprandial hypotension, increases blood pressure, and improves orthostatic tolerance.[484–487]

6.2. Dehydration and Drugs: Recommendations

Syncope related to medication becomes prevalent particularly in older adults, who frequently have multiple comorbidities requiring treatment and are prone to polypharmacy effects.[488–490] Cessation of offending medications is usually key for symptomatic improvement, but often feasibility of cessation of medications is limited by the necessity of the treatments.[491–493] Dehydration may manifest along a spectrum of symptoms, ranging from tachycardia to shock, depending on whether a person has compensated or uncompensated hypovolemia.[494] Orthostatic tolerance worsens with dehydration and is exacerbated by heat stress, which promotes vasodilation.[495–497] Rehydration, whether by intravenous or oral formulation, should include sodium supplementation for more rapid recovery.[21,498–501]

Recommendations for Dehydration and Drugs

COR	LOE	Recommendations
I	C-LD	**Fluid resuscitation via oral or intravenous bolus is recommended in patients with syncope due to acute dehydration.[438,499,501–504]**
See Online Data Supplements 36 and 37.		Fluid resuscitation is recommended for syncope secondary to both dehydration and exercise-associated hypotension. The latter is likely due to peripheral vasodilation and vasovagal physiology.[438,495,504,505] Both dehydration and heat stress worsen orthostatic tolerance.[495–497] Oral fluid bolus may require less volume than intravenous fluid infusion to have a similar treatment effect because oral fluid loading has a pressor effect.[398,438,440–444,502] Beverages with increased sodium concentration (closer to normal body osmolality) rehydrate faster than beverages with lower sodium concentration or increased osmolality (eg, because of glucose content).[498–501,503,506]
IIa	B-NR	**Reducing or withdrawing medications that may cause hypotension can be beneficial in selected patients with syncope.[488–490,492,507–510]**
See Online Data Supplements 36 and 37.		Syncope is a commonly reported adverse drug reaction, often resulting in hospital admission.[488,489] The prevalence of medication-related syncope appears higher in older patients.[491,492,507,510] Several drug classes have been implicated in syncope, including diuretics, vasodilators, venodilators, negative chronotropes, and sedatives.[488–490,492,507–510] Close supervision during adjustment of medications is frequently required because of potential worsening of preexisting supine hypertension or cardiac arrhythmias.[491–493,511] Other factors to consider include frailty, HF and/or cardiac dysfunction, and the use of a large number of medications causing adverse effects because of drug-drug interactions.[488,507,511–513]
IIa	C-LD	**In selected patients with syncope due to dehydration, it is reasonable to encourage increased salt and fluid intake.[396,498–501,503]**
See Online Data Supplements 36 and 37.		In patients with dehydration, sodium supplementation improves plasma volume and improves orthostatic tolerance.[396,499,503] This additional dietary sodium may be provided as sodium tablets or sodium already dissolved in beverages.[396,498–500,503] Higher-sodium-content beverages with osmolality comparable to normal body osmolality may rehydrate faster than lower-sodium-content beverages.[498–501,503] This treatment option is not appropriate for patients with cardiac dysfunction or HF, uncontrolled hypertension, or chronic kidney disease.[19]

7. ORTHOSTATIC INTOLERANCE

Orthostatic intolerance is a general term referring to frequent, recurrent, or persistent symptoms that develop upon standing (usually with a change in position from sitting or lying to an upright position) and are relieved by sitting or lying.[38] Most commonly, the symptoms include lightheadedness, palpitations, tremulousness, generalized weakness, blurred vision, exercise intolerance, and fatigue. These symptoms may be accompanied by hemodynamic disturbances, including blood pressure decrease, which may or may not meet criteria for OH, and heart rate increase, which may be inadequate or compensatory.[38] The pathophysiology is quite varied. One condition of note is POTS, in which upright posture results in an apparently inappropriate tachycardia, usually with heart rates >120 bpm.[24]

Although syncope occurs in patients with POTS, it is relatively infrequent, and there is little evidence that the syncope is due to POTS.[24,514] Treatments that improve symptoms of POTS might decrease the occurrence of syncope, although this is unknown.[24,514–523] For further guidance on the management of POTS, we refer readers to the HRS consensus statement.[24]

8. PSEUDOSYNCOPE: RECOMMENDATIONS

Psychogenic pseudosyncope is a syndrome of apparent loss of consciousness occurring in the absence of impaired cerebral perfusion or function. Psychogenic pseudosyncope is believed to be a conversion disorder—in essence, an external somatic manifestation or response to internal psychological stresses. It is an involuntary response and should not be confused with malingering or Munchausen syndrome. Psychogenic pseudosyncope and pseudoseizures may be the same condition. The clinical distinction between the two is based on whether prominent jerky muscle movements simulating seizure activity are reported by witnesses. In the absence of associated jerky movements, the patient is likely to be referred for evaluation of syncope.[30,229,524] Psychogenic pseudosyncope does not

Circulation. 2017;136:e60–e122. DOI: 10.1161/CIR.0000000000000499

result in a true loss of consciousness, but it is included in the present document because patients appear to exhibit syncope and therefore are referred for evaluation of syncope.

Several key clinical features are suggestive of the diagnosis of psychogenic pseudosyncope. None alone, however, provides a definitive diagnosis. Patients with psychogenic pseudosyncope are often young females with a higher prevalence of preexisting VVS or a history of physical and/or sexual abuse.[229,525] The apparent duration of loss of consciousness is often long (5 to 20 minutes), and episodes are frequent.[525] Some common characteristics include closed eyes, lack of pallor and diaphoresis, and usually little physical harm.[526] A normal pulse, blood pressure, or EEG during a psychogenic pseudosyncope episode can be documented.[229] Although many patients with pseudosyncope can be diagnosed with a careful history, occasionally tilt-table testing with or without transcranial Doppler and monitoring of an EEG is helpful.

Recommendations for the Treatment of Pseudosyncope

COR	LOE	Recommendations
IIb	C-LD	**In patients with suspected pseudosyncope, a candid discussion with the patient about the diagnosis may be reasonable.[30,527–529]**
See Online Data Supplements 38 and 39.		Some reports suggest that patients benefit from being informed of the suspected diagnosis in a clear but sympathetic manner that also acknowledges the involuntary nature of the attacks.[30,527,528]
IIb	C-LD	**Cognitive behavioral therapy may be beneficial in patients with pseudosyncope.[530–532]**
See Online Data Supplements 38 and 39.		Uncontrolled studies suggest that psychotherapy, particularly cognitive behavioral therapy, may be beneficial in conversion disorders.[530–532] One RCT reported that cognitive behavioral therapy provided a non–statistically significant trend toward improvement in pseudosyncope at 3 months.[530] There are no data that support significant benefit from pharmacotherapy.[529]

9. UNCOMMON CONDITIONS ASSOCIATED WITH SYNCOPE

Syncope has been reported in many uncommon diseases, according to case reports. However, specific conditions may predispose the patient to various types of syncope. Table 9 provides a list of less common conditions associated with syncope. It is not intended as a reference for differential diagnosis or a complete synopsis of all conditions associated with syncope. Furthermore, it is not necessary to fully evaluate for all these causes when the etiology remains elusive. Most of these presentations rarely cause syncope, and data are sparse. If the cause for syncope is unclear, these conditions could be included in the differential diagnosis on the basis of other clinical characteristics and/or historical features.

10. AGE, LIFESTYLE, AND SPECIAL POPULATIONS: RECOMMENDATIONS

10.1. Pediatric Syncope: Recommendations

Syncope is common in the pediatric population. By 18 years of age, it is estimated that 30% to 50% of children experience at least 1 fainting episode, and syncope accounts for 3% of all pediatric ED visits.[617–622] The incidence is higher in females and peaks between 15 to 19 years of age.[617] Neurally mediated syncope accounts for 75% of pediatric syncope, followed by psychogenic or unexplained syncope in 8% to 15% of cases.[623] Breath-holding spells are a form of syncope unique to the pediatric population. Cyanotic breath-holding spells typically occur from age 6 months to age 5 years and may be due to desaturation caused by forced expiration during crying. Pallid breath-holding spells are seen in the first 1 to 2 years of age and may be an early form of VVS. The latter episodes are associated with significant bradycardia and prolonged asystole. Pediatric cardiac syncope may result from obstruction to blood flow (HCM, aortic stenosis, pulmonary hypertension), myocardial dysfunction (myocarditis, cardiomyopathy, congenital coronary anomaly, or post–Kawasaki disease) or a primary arrhythmic etiology (LQTS, CPVT, Brugada syndrome, ARVC, or Wolff-Parkinson-White syndrome).

A detailed history with careful attention to the events leading up to the syncope and a complete physical examination can guide practitioners in differentiating the life-threatening causes of syncope (with potential for injury or SCD) from the more common and benign neurally mediated syncope. A detailed family history, with particular attention to premature SCD among first- and second-degree relatives and the manner in which those deaths occurred, is helpful. Given that many of the causes of non-CHD cardiac syncope in children who do not have a form of CHD are similar to those experienced in an adult cohort (LQTS, HCM, Wolff-Parkinson-White, Brugada, and ARVC), interventions recommended for adults with similar conditions presenting with syncope can be applied in children.

Recommendations for Pediatric Syncope		
COR	**LOE**	**Recommendations**
I	**C-LD**	**VVS evaluation, including a detailed medical history, physical examination, family history, and a 12-lead ECG, should be performed in all pediatric patients presenting with syncope.**[315,618,620,624–630]
See Online Data Supplement 40.		Although VVS is the most common cause of pediatric syncope, cardiac syncope does represent 1.5% to 6% of pediatric cases (usually defined as up to 18 years of age).[617,619,620,629,631,632] Characteristics of presenting signs and symptoms differentiating VVS from cardiac causes of syncope are generally similar to those in adults. A family history of VVS and early SCD should be sought. VVS occurs in 33% to 80% of children with syncope.[624,628] Risk factors that raise suspicion of a cardiac etiology include the absence of prodromal symptoms, presence of preceding palpitations within seconds of loss of consciousness, lack of a prolonged upright posture, syncope during exercise or in response to auditory or emotional triggers, family history of SCD, abnormal physical examination, and abnormal ECG,[626,627] although the specificity is modest.[618,627,630,633] It should be remembered that children may not be able to clearly communicate specific symptoms. Exertional syncope has been associated with LQTS and CPVT.[315,318,337,630,634] Regardless of symptoms, exertional syncope, especially mid-exertional syncope, should result in a high index of suspicion for a cardiac etiology.[633]
I	**C-LD**	**Noninvasive diagnostic testing should be performed in pediatric patients presenting with syncope and suspected CHD, cardiomyopathy, or primary rhythm disorder.**[315,318,618,625,627,630,633]
See Online Data Supplement 40.		Channelopathies are major causes of cardiac-related syncope in young people. They may be associated with a family history of SCD, and they increase the risk of SCD in these patients.[315,337,630,632,634,635] Exercise stress testing may be helpful in the diagnosis of channelopathies, such as LQTS and CPVT, which have adrenergically mediated arrhythmias. Extended monitoring is reasonable when an arrhythmia diagnosis is suspected. The types of monitoring devices, their clinical utility, and their limitations are available in Table 8. Prolonged heart rhythm monitoring can often provide a correlation between symptoms and an arrhythmia. In 5 retrospective studies of prolonged monitoring in 87 children with either syncope or presyncope, the mean diagnostic yield was 43%.[636–640] Bradyarrhythmias and high-grade AV block or asystole, as well as tachyarrhythmias, SVT, and polymorphic VT, were documented.[636–640] The diagnostic yield of an ICM is higher if the clinical indication was exertional syncope or the patient had underlying CHD.[637,639,640]
I	**C-EO**	**Education on symptom awareness of prodromes and reassurance are indicated in pediatric patients with VVS.**
See Online Data Supplement 40.		Management of children with VVS should include reassurance about the generally benign nature of this condition.[641,642] Treatment should emphasize symptom awareness and avoidance of precipitating factors that might worsen the condition, such as dehydration, standing for prolonged periods of time, hot crowded environments, and diuretic intake.
IIa	**C-LD**	**Tilt-table testing can be useful for pediatric patients with suspected VVS when the diagnosis is unclear.**[624,629,643–650]
See Online Data Supplement 40.		Tilt-table testing has a diminishing role in the diagnosis of children with unexplained syncope. The sensitivity of tilt-table testing ranges from 20% to 90%,[624,629,643,644,647,648,651,652] and the specificity ranges from 83% to 100%.[624,643,652] Pediatric patients with episodes of VVS may exhibit convulsive movements during loss of consciousness that mimic epileptic seizures. In children with syncope and convulsions on tilt-table testing, 64% exhibited cardiac asystole with pauses >3 seconds.[645] Upright tilt-table testing combined with a graded isoproterenol infusion identified 42% to 67% of patients previously thought to have a primary seizure disorder.[223,649] A combined cardiology and neurology evaluation may be warranted in this group of patients with syncope and seizure-like activity.
IIa	**B-R**	**In pediatric patients with VVS not responding to lifestyle measures, it is reasonable to prescribe midodrine.**[381,620,653]
See Online Data Supplement 40.		In a single-center prospective case series, pseudoephedrine reduced clinical symptoms in 94% of children with recurrent neurally mediated syncope.[653] In an RCT comparing patients receiving conventional therapy (health education, tilt-table training, and salt) and midodrine with patients receiving conventional therapy alone, the recurrence rate of syncope decreased from 80% to 22%.[381] In 2 prospective studies, side effects from midodrine were rare.[381,653]
IIb	**B-R**	**Encouraging increased salt and fluid intake may be reasonable in selected pediatric patients with VVS.**[642]
See Online Data Supplement 40.		In an RCT, conventional therapy and oral rehydration salts resulted in no further recurrence of syncope in 56% of patients, versus 39% in the placebo arm ($P<0.05$).[642]
IIb	**C-LD**	**The effectiveness of fludrocortisone is uncertain in pediatric patients with OH associated with syncope.**[389,654,655]
See Online Data Supplement 40.		In 2 single-center prospective case series of 0.1 mg of fludrocortisone, 83% of subjects demonstrated improvement or resolution of symptoms.[654,655] In the only pediatric RCT, children with recurrent syncope did better on placebo than on fludrocortisone.[389]
IIb	**B-NR**	**Cardiac pacing may be considered in pediatric patients with severe neurally mediated syncope secondary to pallid breath-holding spells.**[656,657]
See Online Data Supplement 40.		In 2 separate studies of 22 predominantly infants and toddlers with reflex anoxic seizures, pallid breath-holding spells, and documented prolonged asystole (pauses >4 seconds), 86% had either complete resolution or a significant reduction in the number of syncopal events with pacing.[656,657] Although the studies were not powered to address the specifics of pacing programming, either single- or dual-chamber pacing significantly reduced the number of syncopal episodes compared with a sensing-only strategy.[656,657] Single-chamber pacing with hysteresis appears as effective as dual-chamber pacing with rate drop response for the prevention of syncope and seizures. The beneficial response to pacing in these studies cannot exclude a placebo effect from pacemaker implantation itself; however, the young age of the patients with pallid breath-holding spells makes placebo effect less likely. The long-term outcome with pacing in this population has not been reported. Finally, it is important to remember that pallid breath-holding syncope does end, although some patients do present again at a later age with classic VVS. This should be balanced against the known complications of permanent cardiac pacing.
III: No Benefit	**B-R**	**Beta blockers are not beneficial in pediatric patients with VVS.**[655,658]
See Online Data Supplement 40.		In an RCT comparing metoprolol and conventional therapy, the treatment group actually had a higher recurrence rate. Side effects of beta blockers occur frequently in children.[655,659]

10.2. Adult Congenital Heart Disease: Recommendations

Recommendations for ACHD		
COR	**LOE**	**Recommendations**
IIa	**C-EO**	**For evaluation of patients with ACHD and syncope, referral to a specialist with expertise in ACHD can be beneficial.**
N/A		The care of the expanding population of ACHD survivors is complex, especially in patients with moderate-to-severe ACHD. Care providers must be knowledgeable in the anatomy and repair; be vigilant in the recognition and management of HF, arrhythmias, and pulmonary hypertension; and have a deep understanding of noncardiac comorbidities. Delivery of ACHD care in highly specialized centers has been shown to reduce mortality rate.[663] In a population-based retrospective study of 71 467 patients with ACHD from Quebec, Canada, between 1990 and 2005, care in a specialized referral center for ACHD care, compared with other care, was independently associated with reduced mortality rate, particularly in those with severe ACHD.[663]
IIa	**B-NR**	**EPS is reasonable in patients with moderate or severe ACHD and unexplained syncope.[664,665]**
See Online Data Supplement 40.		SCD is a leading cause of death in the patient with ACHD. Unexplained syncope is a concerning event. In a cohort of 252 patients with repaired tetralogy of Fallot undergoing risk stratification with programmed ventricular stimulation, induction of either monomorphic or polymorphic VT predicted future clinical VT and SCD.[664] Patients with tetralogy of Fallot and inducible monomorphic or polymorphic VT were more likely to have a history of syncope (42.9%) than were those without inducible VT (13.4%).[664] In a cohort study of ICD recipients with transposition of the great arteries after an atrial baffle procedure, 35% of patients with primary-prevention ICDs presented with syncope. In 50% of patients receiving appropriate ICD shocks, atrial tachyarrhythmias preceded or coexisted with VT.[665] It is reasonable to exclude atrial arrhythmias in patients with syncope and a CHD substrate at risk of atrial arrhythmias (eg, Mustard, Senning, Fontan, Ebstein anomaly, and tetralogy of Fallot).[665]

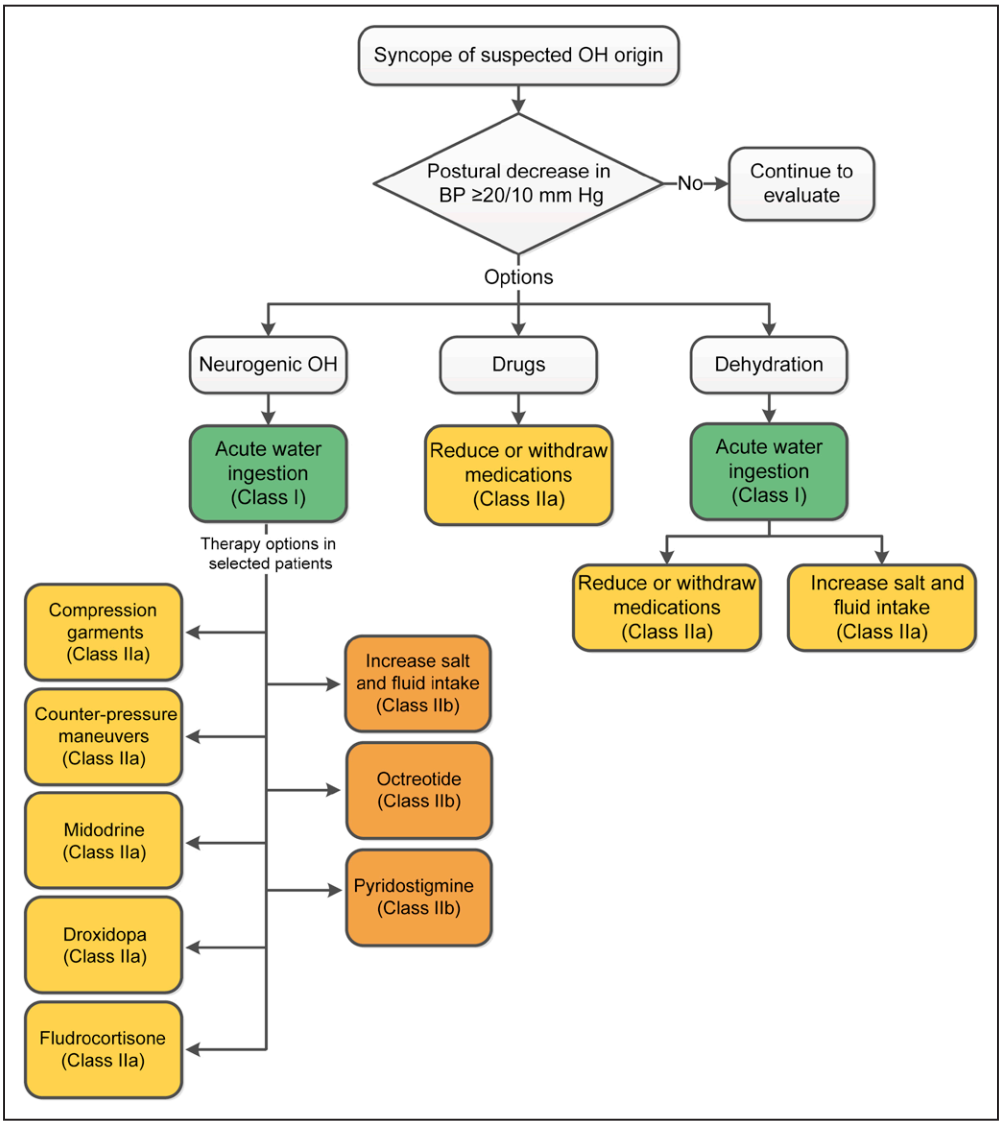

Figure 5. Orthostatic Hypotension.
Colors correspond to Class of Recommendation in Table 1. BP indicates blood pressure; and OH, orthostatic hypotension.

Patients with ACHD are at risk for syncope as a result not only of the underlying structural disease, but also as a result of a previous palliative or corrective surgery. These patients may present with syncope of both hemodynamic and either bradycardic or tachycardic origin. Care by a physician with experience in management of CHD can be beneficial. The entire spectrum of arrhythmias may be seen in adults with CHD, including bradyarrhythmias secondary to sinus or AV nodal disease, atrial arrhythmias, and VA. By age 50 years, approximately 38% of patients with ACHD will develop an atrial arrhythmia, and by age 65 years, >50% of patients with severe CHD will develop atrial arrhythmias.[660] The prevalence of VT after tetralogy of Fallot repair is 3% to 14%.[661,662]

10.3. Geriatric Patients: Recommendations

The management of syncope in older adults is particularly challenging: The incidence is high; the differential diagnosis is broad; the diagnosis is imprecise because of amnesia, falls, lack of witnesses, and polypharmacy; and secondary morbidity is high because of comorbidities, physical injury, and frailty.[35,45,666–675] The vulnerability of older adults to syncope increases because of age-associated cardiovascular and autonomic changes, decreased fluid conservation,[45,671,676–678] and an increased probability of developing multiple concurrent morbidities (with their associated pharmacological treatments) that can overwhelm homeostasis. In many instances, a syncopal event in an older adult is multifactorial, with many predisposing factors present simultaneously.

Older patients (>75 years of age) who present with syncope tend to have poor outcomes, both fatal and nonfatal.[109,679,680] Although some of the risk is attributable to the aspects of syncope described in this guideline, among older adults such risks are usually compounded by multiple morbidities and frailty, which add to age-related vulnerability to syncope,[671,681,682] and by the physical injuries associated with falls, collisions, or trauma, which more commonly result from syncope in old age.[670] Furthermore, recurrent syncope can lead to nursing home admission and a devastating loss of independence.[683] Given the multifactorial etiologies and high risks associated with syncope, a comprehensive and multidisciplinary approach is often necessary to assess for multiple morbidities, frailty, trauma, and other dimensions of health (including cognition and medications) pertinent to diagnosis and management.[77,188,684,685] A thorough history and physical examination, including orthostatic vital signs, is particularly important in older patients.[77]

Recommendations for Geriatric Patients

COR	LOE	Recommendations
IIa	C-EO	**For the assessment and management of older adults with syncope, a comprehensive approach in collaboration with an expert in geriatric care can be beneficial.**
N/A		A multidisciplinary approach helps to facilitate diagnosis of frailty and other factors that predispose to syncope and poor outcome in older adults. The goal is to make management decisions in which older patients are well informed, therapeutic choices are tailored to each patient's needs and goals of care, and decision making is successfully shared between patients and providers. Diagnostic and therapeutic approaches to syncope should incorporate considerations of age, comorbid illness, physical and cognitive functions, patient preferences, and severity of symptoms. Assessment is required of underlying cardiovascular and noncardiovascular diseases; use of medications (eg, polypharmacy, drug-drug interaction, age-related reduction in hepatic and renal clearance); the potential to reduce medications that might lower blood pressure; and circumstantial factors, such as dehydration, infection, or fever. Consideration of frailty is particularly relevant. Characteristics of frailty include weight loss, weakness, exhaustion, reduced physical activity, physical slowing, and cognitive decline, with cumulative severity and impact that typically vary between patients and even in 1 patient over time.
IIa	B-NR	**It is reasonable to consider syncope as a cause of nonaccidental falls in older adults.[666–669,686]**
See Online Data Supplement 41.		Approximately 30% of older adults who present with nonaccidental falls may have had syncope.[687] Amnesia is commonly associated with both falls and loss of consciousness, which diminishes the effectiveness of the history. Cognitive impairment is also frequently present in older adults, even in those without a formal diagnosis of dementia,[688–690] and this too can reduce the accuracy of recall of the clinical event.[666–669,673,686]

10.4. Driving and Syncope: Recommendation

The assessment of medical fitness to drive is a common issue for practitioners caring for patients with syncope. The main concern is the risk of causing injury or death to the driver or others as a result of recurrent syncope.[691] Factors to consider in assessing the risk of syncope while driving are summarized in a formula developed by the Canadian Cardiovascular Society 25 years ago[692] that estimates the risk that a driver will suddenly become incapacitated. The acceptable level of risk then becomes a societal decision.

Balancing the need to minimize risk from drivers fainting is the need for patients to drive to meet the demands of family and work. Society recognizes that

certain groups, such as younger and older adults, are allowed to drive despite their higher risk of causing harm for reasons other than syncope.[693] The societally acceptable risk of injury and death due to motor vehicle accidents has been quantified from an analysis of accident data collected in the United States, United Kingdom, and Canada.[694] In the general population, the yearly risk of serious injury and death is 0.067%, or 1 in 1500.[694] The 418 patients in POST I and POST II had a median of 3 vasovagal faints in 1 year but had no serious injuries or deaths and only 2 minor accidents in the subsequent year.[694] This provides an estimated yearly risk of serious injury and death in the VVS population of <0.0017%, less than the Risk of Harm formula predicted.[692] However, for patients with other etiologies of syncope or those in whom syncope occurred without prodrome or warning, the risk of causing harm may be higher than for patients with VVS. Public policies, laws, and regulations have not been adapted to these results, and providers caring for patients with syncope should be aware of pertinent local driving laws and restrictions. Although untreated syncope may disqualify patients from driving, effective treatment reduces the risk enough to permit driving after a period of observation has elapsed without recurrent syncope. Regulatory agencies are more likely to disqualify commercial drivers than private drivers because of the amount of driving and the impact of accidents (ie, commercial drivers typically operate vehicles heavier than private automobiles). As the risk of recurrent syncope decreases with treatment or with the natural history of a disease process, the risk of harm may become low enough for private drivers to resuming driving, but not necessarily for commercial drivers because of the higher risk of harm. The suggestions in Table 10 provide general guidance for private drivers. Most suggestions are based on expert opinion and supported by limited data. Commercial driving in the United States is governed by federal law and administered by the US Department of Transportation.[695]

Recommendation for Driving and Syncope

COR	LOE	Recommendation
IIa	C-EO	**It can be beneficial for healthcare providers managing patients with syncope to know the driving laws and restrictions in their regions and discuss implications with the patient.**
N/A		The writing committee encourages healthcare providers who care for patients with syncope to know pertinent driving laws and restrictions in their region (eg, states or provinces), as well as the duty of drivers or physicians to report inability of an individual to drive a motor vehicle. The Risk of Harm formula simply estimates risk and does not supersede local driving regulations.[692] In the United States, private driving is state regulated, but commercial driving requiring a US Department of Transportation commercial driver's license is federally regulated. Recommendations about commercial driving are more a legal than a medical matter, and are not within the purview of this guideline. Physicians providing care to commercial drivers should be familiar with US Department of Transportation policy.[695] Individual states may require reporting of drivers who faint. Many patients do not stop driving despite advice to do so, regardless of the duration of restriction.[696,697] Although physicians have an obligation to maintain confidentiality, if a patient's condition poses a significant risk to others, then this information should be reported as specific laws require.

10.5. Athletes: Recommendations

Syncope occurring in the athlete is predominantly of vasovagal origin, but underlying cardiac conditions may place athletes at undue risk for adverse events.[703] Syncope during exercise is associated with increased probability of cardiac causes of syncope (Table 4). A thorough history, differentiating syncope occurring during exercise from syncope occurring after exercise or at other times, with typical characteristics of dehydration or VVS, is critically important during initial evaluation. The definition of an athlete is imprecise, but *athlete* can be defined as someone who engages in routine vigorous training (eg, >150 minutes per week) and is skilled in exercises, sports, or games requiring physical strength, agility, or stamina.[704] More importantly, cardiac adaptations to high levels of exercise may lead to the "athlete's heart" and thus alter the myocardial substrate.[705] Primary or secondary prevention of syncope, morbidity, and mortality in at-risk athletes is a major consideration, but current strategies are largely inadequate.[706] The current evidence base is insufficient to support general screening with ECG or echocardiography at baseline.[706,707]

Several approved therapeutics, especially macrolide antibiotics and antihistamines/decongestants, have been associated with syncopal episodes.[708] Performance-enhancing agents, such as somatotrophic compounds and amphetamine-like stimulants, are associated with precipitous collapse. A careful history is required in the athlete with syncope to rule out exposure to any of these agents.[709] Similarly, before drugs are prescribed to highly competitive athletes, it is prudent to determine whether the drug or its metabolites are on lists of banned substances.

Recommendations for Athletes		
COR	**LOE**	**Recommendations**
I	**C-EO**	**Cardiovascular assessment by a care provider experienced in treating athletes with syncope is recommended prior to resuming competitive sports.**
N/A		A thorough history and physical examination should be completed by an experienced provider, including an assessment for OH and evidence of underlying cardiovascular disease.[709–711] Cardiovascular causes account for 75% of sport-related deaths in young athletes.[709,710] Syncope that occurs after exercise is often of benign origin and may be due to abdominal venous pooling. However, syncope during exercise is a much more compelling symptom and can be a harbinger of SCD.[712,713] Syncopal episodes first require a personal and family history to evaluate precipitating causes and benign conditions, particularly volume depletion and vasovagal activity. Concomitant illnesses, especially viral infections, should be investigated and an ECG obtained.[709,710]
IIa	**C-LD**	**Assessment by a specialist with disease-specific expertise is reasonable for athletes with syncope and high-risk markers.[706,714]**
N/A		Syncope in the competitive athlete requires an evaluation for potentially fatal causes of syncope, especially when evidence of HCM, LQTS, Wolff-Parkinson-White syndrome, ARVC, ventricular noncompaction, symptomatic mitral valve prolapse, Marfan syndrome, congenital coronary anomalies, or other at-risk conditions is present.[706,709,715,716] Any suspected cardiovascular pathology requires further evaluation, and family counseling and/or genetic testing is advised for those conditions with a known familial tendency.
IIa	**C-LD**	**Extended monitoring can be beneficial for athletes with unexplained exertional syncope after an initial cardiovascular evaluation.[717,718]**
N/A		For those with a suspected cardiovascular etiology of syncope, an evaluation includes an ECG, tilt-table testing, and imaging as clinically indicated (Figure 3).[719] Imaging may include echocardiography or MRI as required. Exercise stress testing, unless contraindicated, can be helpful. For persistent unexplained syncope, extended arrhythmia monitoring can be used, as appropriate. This is a rapidly evolving field, with no firm data on the best device and optimum monitoring period.[720]
III: Harm	**B-NR**	**Participation in competitive sports is not recommended for athletes with syncope and phenotype-positive HCM, CPVT, LQTS1, or ARVC before evaluation by a specialist.[704,721–724]**
See Online Data Supplement 42.		In the absence of vagal mechanisms, VA in patients with HCM, CPVT, LQTS1, or ARVC is catecholamine sensitive. Participation in competitive sports in that circumstance in these patients is not recommended.[704,715,716]

11. QUALITY OF LIFE AND HEALTHCARE COST OF SYNCOPE

11.1. Impact of Syncope on Quality of Life

QoL is reduced with recurrent syncope,[725–733] as demonstrated in studies that compared patients with and without syncope.[727,731] QoL associated with recurrent syncope was equivalent to severe rheumatoid arthritis and chronic low-back pain in an adult population.[728] Similarly, pediatric patients with recurrent syncope reported worse QoL than individuals with diabetes mellitus and equivalent QoL to individuals with asthma, end-stage renal disease, and structural heart disease.[725] In a hospital-based cohort of patients with a prior episode of syncope, 33% reported syncope-related functional impairments with daily activities, such as driving or working.[732] Those with more frequent syncope have reported poorer QoL.[726,729,730,732] There is consistent evidence that syncope is associated with worse function on multiple domains of QoL, such as perceptions of low overall physical health[725,730,734]; perception of mental health, including increased fear, somatization, depression, and anxiety[725,727,728,731,734]; and impairment in activities of daily living, such as driving, working, and attending school.

QoL impairments associated with syncope improve over time.[733] In the Fainting Assessment Study,[733] general and syncope-specific QoL improved over a 1-year period. Predictors of worse QoL over time include advanced age, recurrent syncope, neurological or psychogenic reason for syncope, and greater comorbidity at baseline.[733] Syncope-related QoL can be improved through effective diagnosis and treatment. In 1 study, use of an implantable loop recorder increased diagnostic rate, reduced syncope recurrence, and improved QoL as compared with patients who received a conventional diagnostic workup.[164] In a second study, nonpharmacological treatment of recurrent syncope was associated with reductions in recurrent syncope and improvements in QoL.[729]

11.2. Healthcare Costs Associated with Syncope

High healthcare costs are associated with the evaluation and management of syncope. Costs are defined as the resources needed to produce a set of services and are distinct from charges billed by facilities and healthcare providers.[735] Most studies have focused on facility costs and excluded professional fees and patient copays. These high costs have been estimated both in the United States and abroad. In the US Healthcare Utilization Project, total annual hospital costs exceeded $4.1 billion in 2014 dollars, with a mean cost of $9400 per admission.[736] Total costs and costs per admission for presumptive undiagnosed syncope were $1.6 billion and $7200, respectively.[736] Single-center studies from multiple countries, including Austria, the United Kingdom, Israel, and Spain, confirm similarly high costs associated with the hospital evaluation of syncope.[122,737,738]

Table 9. Conditions Uncommonly Associated with Syncope

Condition	Clinical Characteristics	Notes
Cardiovascular and Cardiopulmonary		
Cardiac tamponade	Hypotension, tachycardia, cardiogenic shock.	Often tachycardia and hypotension; may be hypotensive and bradycardic acutely.
Constrictive pericarditis[533–535]	Severe HF symptoms, including edema, exertional dyspnea, orthopnea.	May be associated with cough syncope.
LV noncompaction[536–539]	Cardiomyopathy characterized by prominent LV trabeculae and deep intertrabecular recesses, due to embryologic perturbation.	Syncope reported in 5%–9% of both adult and pediatric patients. The mechanism may be a tachyarrhythmia.
Takotsubo cardiomyopathy[540,541]	Apical ballooning and basal hypercontractility, often due to stress. Chest pain and ECG changes consistent with ischemia are commonly seen.	Syncope is uncommon and may be multifactorial.
Pulmonary embolus[128,542,543]	Hypoxemia, tachycardia; hypotension and shock leading to pulseless electrical activity cardiac arrest in severe cases.	Syncope due to bradycardia and/or hypotension. One study showed higher prevalence of pulmonary embolus in older patients with first episode of syncope after admission to the hospital. Further confirmation of this finding in the older populations is warranted.
Pulmonary arterial hypertension	Occurs more often during exertion in younger patients.	Syncope due to inability to augment or sustain cardiac output during exertion, followed by vasodilatation.
Infiltrative		
Fabry disease[544,545]	Lysosomal storage disorder with neuropathic pain, renal failure concentric LVH, and HF.	Syncope usually due to AV block.
Amyloidosis[546,547]	Systemic disease due to amyloid deposition. Light chain amyloidosis affects the kidneys, heart, and peripheral and autonomic nervous systems.	Syncope may be due to conduction system disease, arrhythmias, impaired cardiac output from restrictive cardiomyopathy, or neurological involvement. AV block is the likely cause, although VA may occur with myocardial involvement.
Hemochromatosis[548]	Systemic iron deposition causing liver disease, skin pigmentation, diabetes mellitus, arthropathy, impotence, and dilated cardiomyopathy.	Myocardial involvement more common than sick sinus syndrome and AV conduction disease.
Infectious		
Myocarditis[413,549–553]	Chest pain, arrhythmias, or profound LV systolic dysfunction. Hemodynamic collapse may occur.	VT and AV block are the likely causes of syncope; transient hemodynamic collapse is possible.
Lyme disease[554]	Lyme myocarditis with classical features of Lyme disease, including erythema migraines and neurological manifestations.	Syncope may be due to AV block, but many patients manifest VVS.[554,555]
Chagas disease[556–559]	Chagasic cardiomyopathy caused by trypanosomiasis.	Syncope and sudden death associated with ventricular tachyarrhythmias. AV block also occurs.
Neuromuscular		
Myotonic dystrophy[12,560,561]	Autosomal dominant inheritance with multiple organ systems affected. Grip myotonia, weakness, temporal wasting, alopecia, cataracts, glucose intolerance, and daytime somnolence.	Both bradyarrhythmia and tachyarrhythmias.
Friedreich ataxia[562,563]	Autosomal recessive inheritance with limb and gait ataxia, bladder dysfunction, and daytime somnolence. Diffuse interstitial fibrosis and HCM.	Syncope can be bradycardic or tachycardic. SCD is known to occur.
Kearns-Sayre Syndrome[564,565]	Mitochondrial myopathy. Chronic progressive external ophthalmoplegia; pigmentary retinopathy.	Many patients develop significant His-Purkinje disease.
Erb dystrophy[566]	Limb girdle muscular dystrophy, manifesting as scapulohymeral and/or pelvifemoral weakness and atrophy.	AV conduction disease, dilated cardiomyopathy.
Anatomic		
Lenègre-Lev disease[567–571]	Progressive fibrosis and sclerosis of cardiac conduction system, including the cardiac skeleton, including the aortic and mitral rings.	Syncope is usually due to high-grade AV block.
Cardiac tumors[572]	Triad of obstruction, embolic, and systemic signs and symptoms.	Syncope is often due to obstruction to blood flow.
Prosthetic valve thrombosis[573–575]	Ranges from asymptomatic to profound HF.	May have similar presentation to a cardiac tumor, with a high risk of embolic phenomenon and obstruction.
Anomalous coronary artery[576–579]	Common cause of exertional syncope or SCD, classically in young athletes.	Syncope can be due to Bezold Jarisch reflex, hypotension, VT, or AV block.

(*Continued*)

Table 9. Continued

Condition	Clinical Characteristics	Notes
Aortic dissection[580–582]	Aortic dissection may manifest with neurological symptoms, myocardial infarction, and HF. Syncope can occur in as many as 13% of aortic dissections.	The risk of in-hospital death, tamponade, and neurological deficits is higher in patients with syncope. Otherwise, syncope alone does not appear to increase the risk of death.
Subclavian steal[583–587]	The phenomenon of flow reversal in a vertebral artery ipsilateral to a hemodynamically significant stenosis of the subclavian artery. Severe cases resulting in vertebrobasilar ischemia may rarely result in syncope.	Syncope is generally associated with upper-extremity activity.
Coarctation of the aorta[588]	If severe, it can result in HF or aortic dissection.	Associated bicuspid aortic valve stenosis may be considered with syncope.
Rheumatoid arthritis[589]	Chronic, autoimmune inflammatory disorder with systemic manifestations.	Rarely associated with complete heart block and syncope.
Syringomyelia[590–597] Chiari malformation[598]	Arnold Chiari malformations are the most common form of syringomyelia.	Syringomyelia-induced disruption of sympathetic fibers in the thoracic spinal cord is a rare mechanism of syncope.[599]
Neck/vagal tumor[600,601]	Recurrent syncope is an uncommon complication of neck malignancy.	The mechanism may be invasion of the carotid sinus or the afferent nerve fibers of the glossopharyngeal nerve.
Endocrine		
Carcinoid syndrome[602] Pheochromocytoma[602,603] Mastocytosis[602–609] Vasoactive intestinal peptide tumor	These tumors can release vasoactive peptides and cause vasodilation, flushing, pruritus, and gastrointestinal symptoms.	Syncope is usually due to transient hypotension.
Hematologic		
Beta thalassemia major[610]	Severe anemia, multiple organ failure, and dilated cardiomyopathy due to iron overload.	Syncope may be arrhythmic.
Neurological disorders		
Seizure-induced bradycardia/ hypotension[611–614]	Generally due to temporal lobe epilepsy.	Postictal bradyarrhythmia is uncommon and likely originates from the temporal lobe or limbic system.
Migraine[615,616]	Migraine headaches are statistically associated with syncope.	Syncope may be vasovagal or due to orthostatic intolerance.

ACC indicates American College of Cardiology; AHA, American Heart Association; AV, atrioventricular; ECG, electrocardiogram; HCM, hypertrophic cardiomyopathy; HF, heart failure; HRS, Heart Rhythm Society; LV, left ventricular; LVH, left ventricular hypertrophy; SCD, sudden cardiac death; VA, ventricular arrhythmias; VT, ventricular tachycardia; and VVS, vasovagal syncope.

Several investigators have estimated the costs per clinically meaningful test result. Physician reviewers determined whether the results of a diagnostic test affected clinical management at a US tertiary referral hospital after an episode of syncope.[77] The cost per informative diagnosis (as ordered in routine practice) affecting clinical management varied widely by specific diagnostic test, from postural blood pressure ($50) through telemetry ($1100) to EEG ($32 973).[77] Similar high costs per actionable diagnosis occur in children admitted for new-onset syncope. Finally, mean costs per diagnostic result were also high in an outpatient ($19 900) specialty clinic for unexplained recurrent syncope.[163]

12. EMERGING TECHNOLOGY, EVIDENCE GAPS, AND FUTURE DIRECTIONS

The writing committee created a list of key areas in which knowledge gaps are present in the evaluation and management of patients presenting with syncope. These knowledge gaps present opportunities for future research to ultimately improve clinical outcomes and effectiveness of healthcare delivery.

12.1. Definition, Classification, and Epidemiology

Reported incidence and prevalence of syncope vary significantly because of several confounders: variable definitions for syncope versus transient loss of consciousness, different populations, different clinical settings, and different study methodologies. Definition and classification of syncope provided in this document will set the standard for future research. Standardized national registries and large sample databases are needed to gather data on a continuous basis to understand the true incidence and prevalence of syncope, understand patient risk, inform driving policies, improve patient outcomes, and improve and streamline health service delivery.

Circulation. 2017;136:e60–e122. DOI: 10.1161/CIR.0000000000000499

Table 10. Avoidance of Private Driving After an Episode of Syncope: Suggested Symptom-Free Waiting Times for Various Conditions

Condition	Symptom-Free Waiting Time*
OH	1 month
VVS, no syncope in prior year[698]	No restriction
VVS, 1–6 syncope per year[694]	1 month
VVS, >6 syncope per year[694,698]	Not fit to drive until symptoms resolved
Situational syncope other than cough syncope	1 month
Cough syncope, untreated	Not fit to drive
Cough syncope, treated with cough suppression	1 month
Carotid sinus syncope, untreated[698]	Not fit to drive
Carotid sinus syncope, treated with permanent pacemaker[698]	1 week
Syncope due to nonreflex bradycardia, untreated[698]	Not fit to drive
Syncope due to nonreflex bradycardia, treated with permanent pacemaker[12,698]	1 week
Syncope due to SVT, untreated[698]	Not fit to drive
Syncope due to SVT, pharmacologically suppressed[698]	1 month
Syncope due to SVT, treated with ablation[698]	1 week
Syncope with LVEF <35% and a presumed arrhythmic etiology without an ICD[699,700]	Not fit to drive
Syncope with LVEF <35% and presumed arrhythmic etiology with an ICD[701,702]	3 months
Syncope presumed due to VT/VF, structural heart disease, and LVEF ≥35%, untreated	Not fit to drive
Syncope presumed due to VT/VF, structural heart disease, and LVEF ≥35%, treated with an ICD and guideline-directed drug therapy[701,702]	3 months
Syncope presumed due to VT with a genetic cause, untreated	Not fit to drive
Syncope presumed due to VT with a genetic cause, treated with an ICD or guideline-directed drug therapy	3 months
Syncope presumed due to a nonstructural heart disease VT, such as RVOT or LVOT, untreated	Not fit to drive
Syncope presumed due to a nonstructural heart disease VT, such as RVOT or LVOT, treated successfully with ablation or suppressed pharmacologically[698]	3 months
Syncope of undetermined etiology	1 month

*It may be prudent to wait and observe for this time without a syncope spell before resuming driving.

ICD indicates implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; LVOT, left ventricular outflow tract; OH, orthostatic hypotension; RVOT, right ventricular outflow tract; SVT, supraventricular tachycardia; VF, ventricular fibrillation; VT, ventricular tachycardia; and VVS, vasovagal syncope.

12.2. Risk Stratification and Clinical Outcomes

At a patient's presentation, several key questions follow: What is the likely cause of syncope? Does the patient have significant underlying heart disease and/or comorbid medical illnesses? If the cause of syncope is determined, is there an effective therapy to prevent recurrent syncope, prevent syncope-related nonfatal outcomes (injury, diminished healthcare–related QoL, lost workdays), or improve survival? What are the predictors of short- and long-term clinical outcomes? What are the key outcomes relevant to patients with syncope, including recurrent syncope? When the cause of syncope is unknown, what is the standard of care for this group of patients?

- Studies are needed to determine whether syncope is an independent predictor of nonfatal or fatal outcomes in selected patient populations.
- Studies are needed to develop risk scores to be prospectively validated in a given clinical setting with predefined endpoints from short- and long-term follow-up.
- Prospective and well-designed studies are needed to define relevant clinical outcomes with regard to recurrent syncope, nonfatal outcomes such as injury, and fatal outcomes. Future studies should incorporate QoL, work loss, and functional capacity as additional clinical endpoints.
- Prospective studies are needed to differentiate cardiac and noncardiac clinical outcomes in different clinical settings and with different follow-up durations.
- Among patients without identifiable causes of syncope, studies are needed to determine short- and long-term outcomes to guide the overall management of these patients.

12.3. Evaluation and Diagnosis

Because of the concerns that patients presenting with syncope are at higher risk for an impending catastrophic event, overuse and inappropriate use of testing and hospital admission are common. Answers to the following question will improve the effectiveness of patient evaluation: How should the initial evaluation and subsequent follow-up vary by risk (low, intermediate, or high) to assess clinical outcomes?

- Studies are needed to better understand the interaction and relationships among the presenting symptom of syncope, the cause of syncope, the underlying disease condition, and their effect on clinical outcomes.
- Investigations are needed to understand the key components of clinical characteristics during the initial evaluation and to develop standardization tools to guide the evaluation by healthcare team.
- RCTs are needed to develop structured protocols to evaluate patients with syncope who are at intermediate risk without an immediate

presumptive diagnosis. In addition to the endpoints of diagnostic yield and healthcare utilization, relevant clinical endpoints of nonfatal and fatal outcomes and recurrence of syncope are to be included.
- RCTs are needed to determine the features of syncope-specialized facilities that are necessary to achieve beneficial outcomes for patient care and to improve efficiency and effectiveness of healthcare delivery.
- As technology advances, studies are needed to determine the value of new technology in the evaluation and management of patients with syncope.

12.4. Management of Specific Conditions

- Although potential causes of syncope are multiple, a treatment decision is usually fairly straightforward for patients with cardiac causes of syncope or orthostatic causes. VVS is the most common cause of syncope in the general population. Treatment remains challenging in patients who have recurrences despite conservative therapy. Studies are needed to differentiate "arrhythmic syncope" versus "nonarrhythmic syncope" versus "aborted SCD" in patients with inheritable arrhythmic conditions.
- Prospectively designed multicenter or national registries are needed to gather clinical information from patients with reflex syncope to better our understanding on other associated conditions, plausible mechanisms, effectiveness of therapeutic interventions, and natural history of these uncommon conditions.
- RCTs are needed to continue the identification of effective treatment approaches to patients with recurrent reflex syncope.

12.5. Special Populations

- Each population in Section 6 is unique with regard to syncope, and within each of them we identified several key areas that are important for future research considerations.
- Questions and research about risk stratification, evaluation, and management outlined above for the adult population are needed in the pediatric population, geriatric population, and athletes.
- Prospective national registries and big databases are needed to determine risk associated with driving among different populations with syncope.
- Prospective and randomized studies are needed to assess the usefulness of specialized syncope units in different clinical settings.

ACC/AHA TASK FORCE MEMBERS

Glenn N. Levine, MD, FACC, FAHA, Chair; Patrick T. O'Gara, MD, MACC, FAHA, Chair-Elect; Jonathan L. Halperin, MD, FACC, FAHA, Immediate Past Chair*; Sana M. Al-Khatib, MD, MHS, FACC, FAHA; Kim K. Birtcher, MS, PharmD, AACC; Biykem Bozkurt, MD, PhD, FACC, FAHA; Ralph G. Brindis, MD, MPH, MACC*; Joaquin E. Cigarroa, MD, FACC; Lesley H. Curtis, PhD, FAHA; Lee A. Fleisher, MD, FACC, FAHA; Federico Gentile, MD, FACC; Samuel Gidding, MD, FAHA; Mark A. Hlatky, MD, FACC; John Ikonomidis, MD, PhD, FAHA; José Joglar, MD, FACC, FAHA; Susan J. Pressler, PhD, RN, FAHA; Duminda N. Wijeysundera, MD, PhD

PRESIDENTS AND STAFF

American College of Cardiology

Richard A. Chazal, MD, FACC, President
Shalom Jacobovitz, Chief Executive Officer
William J. Oetgen, MD, MBA, FACC, Executive Vice President, Science, Education, Quality, and Publishing
Amelia Scholtz, PhD, Publications Manager, Science, Education, Quality, and Publishing

American College of Cardiology/ American Heart Association

Katherine Sheehan, PhD, Director, Guideline Strategy and Operations
Lisa Bradfield, CAE, Director, Guideline Methodology and Policy
Abdul R. Abdullah, MD, Science and Medicine Advisor
Clara Fitzgerald, Project Manager, Science and Clinical Policy
Allison Rabinowitz, MPH, Project Manager, Science and Clinical Policy

American Heart Association

Steven R. Houser, PhD, FAHA, President
Nancy Brown, Chief Executive Officer
Rose Marie Robertson, MD, FAHA, Chief Science and Medicine Officer
Gayle R. Whitman, PhD, RN, FAHA, FAAN, Senior Vice President, Office of Science Operations
Jody Hundley, Production Manager, Scientific Publications, Office of Science Operations

FOOTNOTES

This document was approved by the American College of Cardiology Clinical Policy Approval Committee on behalf of the Board of Trustees, the American Heart Association Science Advisory and Coordinating Committee, the American Heart Association Executive Committee, and the Heart Rhythm Society Board of Trustees in January 2017.

*Former Task Force member; current member during the writing effort.

Circulation. 2017;136:e60–e122. DOI: 10.1161/CIR.0000000000000499

The online Comprehensive RWI Data Supplement table is available with this article at http://circ.ahajournals.org/lookup/suppl/doi:10.1161/CIR.0000000000000499/-/DC1.

The online Data Supplement is available with this article at http://circ.ahajournals.org/lookup/suppl/doi:10.1161/CIR.0000000000000499/-/DC2.

This article has been copublished in the *Journal of the American College of Cardiology* and **Heart**Rhythm.

Copies: This document is available on the World Wide Web sites of the American College of Cardiology (www.acc.org), the American Heart Association (professional.heart.org), and the Heart Rhythm Society (www.hrsonline.org). A copy of the document is available at http://professional.heart.org/statements by selecting either the "By Topic" link or the "By Publication Date" link. To purchase additional reprints, call 843-216-2533 or e-mail kelle.ramsay@wolterskluwer.com.

Expert peer review of AHA Scientific Statements is conducted by the AHA Office of Science Operations. For more on AHA statements and guidelines development, visit http://professional.heart.org/statements and select the "Policies and Development" link.

Circulation is available at http://circ.ahajournals.org.

REFERENCES

1. Committee on Standards for Developing Trustworthy Clinical Practice Guidelines, Institute of Medicine (U.S.). Clinical Practice Guidelines We Can Trust. Washington, DC: National Academies Press; 2011.
2. Committee on Standards for Systematic Reviews of Comparative Effectiveness Research, Institute of Medicine (U.S.). Finding What Works in Health Care: Standards for Systematic Reviews. Washington, DC: National Academies Press; 2011.
3. Anderson JL, Heidenreich PA, Barnett PG, et al. ACC/AHA statement on cost/value methodology in clinical practice guidelines and performance measures: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures and Task Force on Practice Guidelines. Circulation. 2014;129:2329–45.
4. ACCF/AHA Task Force on Practice Guidelines. Methodology Manual and Policies From the ACCF/AHA Task Force on Practice Guidelines. American College of Cardiology and American Heart Association, 2010. Available at: http://assets.cardiosource.com/Methodology_Manual_for_ACC_AHA_Writing_Committees.pdf and http://my.americanheart.org/idc/groups/ahamah-public/@wcm/@sop/documents/downloadable/ucm_319826.pdf. Accessed January 23, 2015.
5. Halperin JL, Levine GN, Al-Khatib SM, et al. Further evolution of the ACC/AHA clinical practice guideline recommendation classification system: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2016;133:1426–28.
6. Jacobs AK, Kushner FG, Ettinger SM, et al. ACCF/AHA clinical practice guideline methodology summit report: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;127:268–310.
7. Jacobs AK, Anderson JL, Halperin JL. The evolution and future of ACC/AHA clinical practice guidelines: a 30-year journey: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;130:1208–17.
8. Arnett DK, Goodman RA, Halperin JL, et al. AHA/ACC/HHS strategies to enhance application of clinical practice guidelines in patients with cardiovascular disease and comorbid conditions: from the American Heart Association, American College of Cardiology, and U.S. Department of Health and Human Services. Circulation. 2014;130:1662–7.
9. Varosy PD, Chen LY, Miller AL, et al. Pacing as a treatment for reflex-mediated (vasovagal, situational, or carotid sinus hypersensitivity) syncope: a systematic review for the 2017 ACC/AHA/HRS guideline for the evaluation and management of syncope: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Circulation. 2017;136:e123–135.
10. Page RL, Joglar JA, Caldwell MA, et al. 2015 ACC/AHA/HRS guideline for the management of adult patients with supraventricular tachycardia: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Circulation. 2016;133;e506–74.
11. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;129:2440–92.
12. Epstein AE, DiMarco JP, Ellenbogen KA, et al. 2012 ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. Circulation. 2013;127:e283–352.
13. Zipes DP, Camm AJ, Borggrefe M, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death). Circulation. 2006;114:1088–132.
14. Fihn SD, Blankenship JC, Alexander KP, et al. 2014 ACC/AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. Circulation. 2014;130:1749–67.
15. Fihn SD, Gardin JM, Abrams J, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. Circulation. 2012;126:e354–471.
16. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. Circulation 2014;130:e199–267.
17. Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;130:e344–426.
18. Goff DC Jr, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;129[suppl 2]:S49–73.
19. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;128:e240–327.
20. Gersh BJ, Maron BJ, Bonow RO, et al. 2011 ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the American Association for Thoracic Surgery, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiog-

raphy and Interventions, and Society of Thoracic Surgeons. Circulation. 2011;124:e783–831.
21. Greenland P, Alpert JS, Beller GA, et al. 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2010;122:e584–636.
22. Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines on the Management of Adults With Congenital Heart Disease). Developed in collaboration with the American Society of Echocardiography, Heart Rhythm Society, International Society for Adult Congenital Heart Disease, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. Circulation. 2008;118:e714–833.
23. Patton KK, Ellinor PT, Ezekowitz M, et al. Electrocardiographic early repolarization: a scientific statement from the American Heart Association. Circulation. 2016;133:1520–9.
24. Sheldon RS, Grubb BP, Olshansky B, et al. 2015 Heart Rhythm Society expert consensus statement on the diagnosis and treatment of postural tachycardia syndrome, inappropriate sinus tachycardia, and vasovagal syncope. Heart Rhythm. 2015;12:e41–63.
25. Priori SG, Wilde AA, Horie M, et al. HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes: document endorsed by HRS, EHRA, and APHRS in May 2013 and by ACCF, AHA, PACES, and AEPC in June 2013. Heart Rhythm. 2013;10:1932–63.
26. Priori SG, Blomstrom-Lundqvist C, Mazzanti A, et al. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology. G Ital Cardiol (Rome). 2016;17:108–70.
27. Khairy P, Van Hare GF, Balaji S, et al. PACES/HRS expert consensus statement on the recognition and management of arrhythmias in adult congenital heart disease: developed in partnership between the Pediatric and Congenital Electrophysiology Society (PACES) and the Heart Rhythm Society (HRS). Can J Cardiol. 2014;30:e1–e63.
28. Kusumoto FM, Calkins H, Boehmer J, et al. HRS/ACC/AHA expert consensus statement on the use of implantable cardioverter-defibrillator therapy in patients who are not included or not well represented in clinical trials. Circulation. 2014;130:94–125.
29. Pedersen CT, Kay GN, Kalman J, et al. EHRA/HRS/APHRS expert consensus on ventricular arrhythmias. Heart Rhythm. 2014;11:e166–e196.
30. Moya A, Sutton R, Ammirati F, et al. Guidelines for the diagnosis and management of syncope (version 2009). Eur Heart J. 2009;30:2631–71.
31. Freeman R, Wieling W, Axelrod FB, et al. Consensus statement on the definition of orthostatic hypotension, neurally mediated syncope and the postural tachycardia syndrome. Clin Auton Res. 2011;21:69–72.
32. Wieling W, Krediet CT, van DN, et al. Initial orthostatic hypotension: review of a forgotten condition. Clin Sci. 2007;112:157–65.
33. Metzler M, Duerr S, Granata R, et al. Neurogenic orthostatic hypotension: pathophysiology, evaluation, and management. J Neurol. 2013;260:2212–9.
34. Nwazue VC, Raj SR. Confounders of vasovagal syncope: orthostatic hypotension. Cardiol Clin. 2013;31:89–100.
35. Soteriades ES, Evans JC, Larson MG, et al. Incidence and prognosis of syncope. N Engl J Med. 2002;347:878–85.
36. Kapoor WN, Karpf M, Wieand S, et al. A prospective evaluation and follow-up of patients with syncope. N Engl J Med. 1983;309:197–204.
37. Thieben MJ, Sandroni P, Sletten DM, et al. Postural orthostatic tachycardia syndrome: the Mayo Clinic experience. Mayo Clin Proc. 2007;82:308–13.
38. Low PA, Sandroni P, Joyner M, et al. Postural tachycardia syndrome (POTS). J Cardiovasc Electrophysiol. 2009;20:352–8.
39. Low PA, Opfer-Gehrking TL, Textor SC, et al. Postural tachycardia syndrome (POTS). Neurology. 1995;45:S19–25.
40. Schondorf R, Low PA. Idiopathic postural orthostatic tachycardia syndrome: an attenuated form of acute pandysautonomia? Neurology. 1993;43:132–7.
41. Singer W, Sletten DM, Opfer-Gehrking TL, et al. Postural tachycardia in children and adolescents: what is abnormal? J Pediatr. 2012;160:222–6.
42. Garland EM, Raj SR, Black BK, et al. The hemodynamic and neurohumoral phenotype of postural tachycardia syndrome. Neurology. 2007;69:790–8.
43. Lamb LE. Incidence of loss of consciousness in 1,980 Air Force personnel. Aerosp Med. 1960;31:973–88.
44. Chen LY, Shen WK, Mahoney DW, et al. Prevalence of syncope in a population aged more than 45 years. Am J Med. 2006;119:e1–e7.
45. Ruwald MH, Hansen ML, Lamberts M, et al. The relation between age, sex, comorbidity, and pharmacotherapy and the risk of syncope: Danish nationwide study. Europace. 2012;14:1506–14.
46. Olshansky B, Poole JE, Johnson G, et al. Syncope predicts the outcome of cardiomyopathy patients: analysis of the SCD-HeFT study. J Am Coll Cardiol. 2008;51:1277–82.
47. Middlekauff HR, Stevenson WG, Stevenson LW, et al. Syncope in advanced heart failure: high risk of sudden death regardless of origin of syncope. J Am Coll Cardiol. 1993;21:110–6.
48. Sun BC, Emond JA, Camargo CA Jr, Characteristics and admission patterns of patients presenting with syncope to U.S. emergency departments, 1992–2000. Acad Emerg Med. 2004;11:1029–34.
49. Morichetti A, Astorino G. [Epidemiological and clinical findings in 697 syncope events]. Minerva Med. 1998;89:211–20.
50. Ruwald MH, Hansen ML, Lamberts M, et al. Accuracy of the ICD-10 discharge diagnosis for syncope. Europace. 2013;15:595–600.
51. Olde Nordkamp LR.A, van Dijk N, Ganzeboom KS, et al. Syncope prevalence in the ED compared to general practice and population: a strong selection process. Am J Emerg Med. 2009;27:271–9.
52. Ammirati F, Colivicchi F, Minardi G, et al. [The management of syncope in the hospital: the OESIL Study (Osservatorio Epidemiologico della Sincope nel Lazio)]. G Ital Cardiol. 1999;29:533–9.
53. Blanc JJ, L'Her C, Touiza A, et al. Prospective evaluation and outcome of patients admitted for syncope over a 1 year period. Eur Heart J. 2002;23:815–20.
54. Disertori M, Brignole M, Menozzi C, et al. Management of patients with syncope referred urgently to general hospitals. Europace. 2003;5:283–91.
55. Day SC, Cook EF, Funkenstein H, et al. Evaluation and outcome of emergency room patients with transient loss of consciousness. Am J Med. 1982;73:15–23.
56. Lipsitz LA, Wei JY, Rowe JW. Syncope in an elderly, institutionalised population: prevalence, incidence, and associated risk. Q J Med. 1985;55:45–54.
57. Kenny RA, Bhangu J, King-Kallimanis BL. Epidemiology of syncope/collapse in younger and older Western patient populations. Prog Cardiovasc Dis. 2013;55:357–63.
58. Alboni P, Brignole M, Menozzi C, et al. Diagnostic value of history in patients with syncope with or without heart disease. J Am Coll Cardiol. 2001;37:1921–8.
59. Alboni P, Brignole M, Menozzi C, et al. Clinical spectrum of neurally mediated reflex syncopes. Europace. 2004;6:55–62.
60. Berecki-Gisolf J, Sheldon A, Wieling W, et al. Identifying cardiac syncope based on clinical history: a literature-based model tested in four independent datasets. PLoS ONE. 2013;8:e75255
61. Calkins H, Shyr Y, Frumin H, et al. The value of the clinical history in the differentiation of syncope due to ventricular tachycardia, atrioventricular block, and neurocardiogenic syncope. Am J Med. 1995;98:365–73.
62. Romme JJ.M, van Dijk N, Boer KR, et al. Diagnosing vasovagal syncope based on quantitative history-taking: validation of the Calgary Syncope Symptom Score. Eur Heart J. 2009;30:2888–96.
63. Sheldon R, Rose S, Ritchie D, et al. Historical criteria that distinguish syncope from seizures. J Am Coll Cardiol. 2002;40:142–8.
64. Sheldon R, Rose S, Connolly S, et al. Diagnostic criteria for vasovagal syncope based on a quantitative history. Eur Heart J. 2006;27:344–50.
65. Sheldon R, Hersi A, Ritchie D, et al. Syncope and structural heart disease: historical criteria for vasovagal syncope and ventricular tachycardia. J Cardiovasc Electrophysiol. 2010;21:1358–64.
66. Van Dijk N, Boer KR, Colman N, et al. High diagnostic yield and accuracy of history, physical examination, and ECG in patients with transient loss of consciousness in FAST: the Fainting Assessment study. J Cardiovasc Electrophysiol. 2008;19:48–55.
67. Colivicchi F, Ammirati F, Melina D, et al. Development and prospective validation of a risk stratification system for patients with syncope in the emergency department: the OESIL risk score. Eur Heart J. 2003;24:811–9.
68. Costantino G, Perego F, Dipaola F, et al. Short- and long-term prognosis of syncope, risk factors, and role of hospital admission: results from the STePS (Short-Term Prognosis of Syncope) study. J Am Coll Cardiol. 2008;51:276–83.
69. Del Rosso A, Ungar A, Maggi R, et al. Clinical predictors of cardiac syncope at initial evaluation in patients referred urgently to a general hospital: the EGSYS score. Heart. 2008;94:1620–6.

70. Grossman SA, Fischer C, Lipsitz LA, et al. Predicting adverse outcomes in syncope. J Emerg Med. 2007;33:233–9.
71. Martin GJ, Adams SL, Martin HG, et al. Prospective evaluation of syncope. Ann Emerg Med. 1984;13:499–504.
72. Quinn JV, Stiell IG, McDermott DA, et al. Derivation of the San Francisco Syncope Rule to predict patients with short-term serious outcomes. Ann Emerg Med. 2004;43:224–32.
73. Reed MJ, Newby DE, Coull AJ, et al. The ROSE (Risk Stratification of Syncope in the Emergency Department) study. J Am Coll Cardiol. 2010;55:713–21.
74. Sarasin FP, Hanusa BH, Perneger T, et al. A risk score to predict arrhythmias in patients with unexplained syncope. Acad Emerg Med. 2003;10: 1312–7.
75. Sun BC, Derose SF, Liang LJ, et al. Predictors of 30-day serious events in older patients with syncope. Ann Emerg Med. 2009;54:769–78.
76. Pérez-Rodon J, Martínez-Alday J, Baron-Esquivias G, et al. Prognostic value of the electrocardiogram in patients with syncope: data from the group for syncope study in the emergency room (GESINUR). Heart Rhythm. 2014;11:2035–44.
77. Mendu ML, McAvay G, Lampert R, et al. Yield of diagnostic tests in evaluating syncopal episodes in older patients. Arch Intern Med. 2009;169:1299–305.
78. Johnson PC, Ammar H, Zohdy W, et al. Yield of diagnostic tests and its impact on cost in adult patients with syncope presenting to a community hospital. South Med J. 2014;107:707–14.
79. Quinn J, McDermott D. Electrocardiogram findings in emergency department patients with syncope. Acad Emerg Med. 2011;18:714–8.
80. Sarasin FP, Junod AF, Carballo D, et al. Role of echocardiography in the evaluation of syncope: a prospective study. Heart. 2002;88:363–7.
81. Thiruganasambandamoorthy V, Hess EP, Turko E, et al. Defining abnormal electrocardiography in adult emergency department syncope patients: the Ottawa Electrocardiographic Criteria. CJEM. 2012;14:248–58.
82. Costantino G, Casazza G, Reed M, et al. Syncope risk stratification tools vs clinical judgment: an individual patient data meta-analysis. Am J Med. 2014;127:1126.e13–25.
83. D'Ascenzo F, Biondi-Zoccai G, Reed MJ, et al. Incidence, etiology and predictors of adverse outcomes in 43,315 patients presenting to the emergency department with syncope: an international meta-analysis. Int J Cardiol. 2013;167:57–62.
84. Da Costa A, Gulian JL, Romeyer-Bouchard C, et al. Clinical predictors of cardiac events in patients with isolated syncope and negative electrophysiologic study. Int J Cardiol. 2006;109:28–33.
85. Derose SF, Gabayan GZ, Chiu VY, et al. Patterns and preexisting risk factors of 30-day mortality after a primary discharge diagnosis of syncope or near syncope. Acad Emerg Med. 2012;19:488–96.
86. Dipaola F, Costantino G, Perego F, et al. San Francisco Syncope Rule, Osservatorio Epidemiologico sulla Sincope nel Lazio risk score, and clinical judgment in the assessment of short-term outcome of syncope. Am J Emerg Med. 2010;28:432–9.
87. Expósito V, Guzmán JC, Orava M, et al. Usefulness of the Calgary Syncope Symptom Score for the diagnosis of vasovagal syncope in the elderly. Europace. 2013;15:1210–4.
88. Gabayan GZ, Derose SF, Asch SM, et al. Predictors of short-term (seven-day) cardiac outcomes after emergency department visit for syncope. Am J Cardiol. 2010;105:82–6.
89. Kayayurt K, Akoglu H, Limon O, et al. Comparison of existing syncope rules and newly proposed Anatolian syncope rule to predict short-term serious outcomes after syncope in the Turkish population. Int J Emerg Med. 2012;5:17
90. Martin TP, Hanusa BH, Kapoor WN. Risk stratification of patients with syncope. Ann Emerg Med. 1997;29:459–66.
91. Moazez F, Peter T, Simonson J, et al. Syncope of unknown origin: clinical, noninvasive, and electrophysiologic determinants of arrhythmia induction and symptom recurrence during long-term follow-up. Am Heart J. 1991;121:81–8.
92. Numeroso F, Mossini G, Spaggiari E, et al. Syncope in the emergency department of a large northern Italian hospital: incidence, efficacy of a short-stay observation ward and validation of the OESIL risk score. Emerg Med J. 2010;27:653–8.
93. Oh JH, Hanusa BH, Kapoor WN. Do symptoms predict cardiac arrhythmias and mortality in patients with syncope? Arch Intern Med. 1999;159: 375–80.
94. Quinn J, McDermott D, Stiell I, et al. Prospective validation of the San Francisco Syncope Rule to predict patients with serious outcomes. Ann Emerg Med. 2006;47:448–54.
95. Ruwald MH, Ruwald AC, Jons C, et al. Evaluation of the CHADS2 risk score on short- and long-term all-cause and cardiovascular mortality after syncope. Clin Cardiol. 2013;36:262–8.
96. Saccilotto RT, Nickel CH, Bucher HC, et al. San Francisco Syncope Rule to predict short-term serious outcomes: a systematic review. CMAJ. 2011;183:e1116–e1126.
97. Serrano LA, Hess EP, Bellolio MF, et al. Accuracy and quality of clinical decision rules for syncope in the emergency department: a systematic review and meta-analysis. Ann Emerg Med. 2010;56:362–73.
98. Sule S, Palaniswamy C, Aronow WS, et al. Etiology of syncope in patients hospitalized with syncope and predictors of mortality and rehospitalization for syncope at 27-month follow-up. Clin Cardiol. 2011;34:35–8.
99. Recchia D, Barzilai B. Echocardiography in the evaluation of patients with syncope. J Gen Intern Med. 1995;10:649–55.
100. Grossman SA, Babineau M, Burke L, et al. Applying the Boston syncope criteria to near syncope. J Emerg Med. 2012;43:958–63.
101. Ungar A, Del Rosso A, Giada F, et al. Early and late outcome of treated patients referred for syncope to emergency department: the EGSYS 2 follow-up study. Eur Heart J. 2010;31:2021–6.
102. Grossman SA, Chiu D, Lipsitz L, et al. Can elderly patients without risk factors be discharged home when presenting to the emergency department with syncope? Arch Gerontol Geriatr. 2014;58:110–4.
103. Numeroso F, Mossini G, Lippi G, et al. Evaluation of the current prognostic role of heart diseases in the history of patients with syncope. Europace. 2014;16:1379–83.
104. Khera S, Palaniswamy C, Aronow WS, et al. Predictors of mortality, rehospitalization for syncope, and cardiac syncope in 352 consecutive elderly patients with syncope. J Am Med Dir Assoc. 2013;14:326–30.
105. Daccarett M, Jetter TL, Wasmund SL, et al. Syncope in the emergency department: comparison of standardized admission criteria with clinical practice. Europace. 2011;13:1632–8.
106. Sun BC, Thiruganasambandamoorthy V, Cruz JD. Standardized reporting guidelines for emergency department syncope risk-stratification research. Acad Emerg Med. 2012;19:694–702.
107. Shen WK, Decker WW, Smars PA, et al. Syncope Evaluation in the Emergency Department Study (SEEDS): a multidisciplinary approach to syncope management. Circulation. 2004;110:3636–45.
108. Sun BC, McCreath H, Liang LJ, et al. Randomized clinical trial of an emergency department observation syncope protocol versus routine inpatient admission. Ann Emerg Med. 2014;64:167–75.
109. Ungar A, Tesi F, Chisciotti VM, et al. Assessment of a structured management pathway for patients referred to the emergency department for syncope: results in a tertiary hospital. Europace. 2015;18:457–62.
110. Shin TG, Kim JS, Song HG, et al. Standardized approaches to syncope evaluation for reducing hospital admissions and costs in overcrowded emergency departments. Yonsei Med J. 2013;54:1110–8.
111. Parry SW, Frearson R, Steen N, et al. Evidence-based algorithms and the management of falls and syncope presenting to acute medical services. Clin Med (Lond). 2008;8:157–62.
112. Raucci U, Scateni S, Tozzi AE, et al. The availability and the adherence to pediatric guidelines for the management of syncope in the emergency department. J Pediatr. 2014;165:967–72.e1.
113. Sanders NA, Jetter TL, Brignole M, et al. Standardized care pathway versus conventional approach in the management of patients presenting with faint at the University of Utah. Pacing Clin Electrophysiol. 2013;36:152–62.
114. Kenny RA, O'Shea D, Walker HF. Impact of a dedicated syncope and falls facility for older adults on emergency beds. Age Ageing. 2002;31:272–5.
115. Croci F, Brignole M, Alboni P, et al. The application of a standardized strategy of evaluation in patients with syncope referred to three syncope units. Europace. 2002;4:351–5.
116. Brignole M, Disertori M, Menozzi C, et al. Management of syncope referred urgently to general hospitals with and without syncope units. Europace. 2003;5:293–8.
117. Brignole M, Ungar A, Bartoletti A, et al. Standardized-care pathway vs. usual management of syncope patients presenting as emergencies at general hospitals. Europace. 2006;8:644–50.
118. Brignole M, Ungar A, Casagranda I, et al. Prospective multicentre systematic guideline-based management of patients referred to the syncope units of general hospitals. Europace. 2010;12:109–18.
119. Ammirati F, Colaceci R, Cesario A, et al. Management of syncope: clinical and economic impact of a syncope unit. Europace. 2008;10:471–6.
120. Costantino G, Sun BC, Barbic F, et al. Syncope clinical management in the emergency department: a consensus from the first international

workshop on syncope risk stratification in the emergency department. Eur Heart J. 2016;37:1493–8.
121. Morag RM, Murdock LF, Khan ZA, et al. Do patients with a negative emergency department evaluation for syncope require hospital admission? J Emerg Med. 2004;27:339–43.
122. Shiyovich A, Munchak I, Zelingher J, et al. Admission for syncope: evaluation, cost and prognosis according to etiology. Isr Med Assoc J. 2008;10:104–8.
123. Schillinger M, Domanovits H, Müllner M, et al. Admission for syncope: evaluation, cost and prognosis. Wien Klin Wochenschr. 2000;112:835–41.
124. Chiu DT, Shapiro NI, Sun BC, et al. Are echocardiography, telemetry, ambulatory electrocardiography monitoring, and cardiac enzymes in emergency department patients presenting with syncope useful tests? A preliminary investigation. J Emerg Med. 2014;47:113–8.
125. Thiruganasambandamoorthy V, Ramaekers R, Rahman MO, et al. Prognostic value of cardiac biomarkers in the risk stratification of syncope: a systematic review. Intern Emerg Med. 2015;10:1003–14.
126. Pfister R, Diedrichs H, Larbig R, et al. NT-pro-BNP for differential diagnosis in patients with syncope. Int J Cardiol. 2009;133:51–4.
127. Reed MJ, Mills NL, Weir CJ. Sensitive troponin assay predicts outcome in syncope. Emerg Med J. 2012;29:1001–3.
128. Prandoni P, Lensing AWA, Prins MH, et al. Prevalence of pulmonary embolism among patients hospitalized for syncope. N Engl J Med. 2016;375:1524–31.
129. Tanimoto K, Yukiiri K, Mizushige K, et al. Usefulness of brain natriuretic peptide as a marker for separating cardiac and noncardiac causes of syncope. Am J Cardiol. 2004;93:228–30.
130. Costantino G, Solbiati M, Pisano G, et al. NT-pro-BNP for differential diagnosis in patients with syncope. Int J Cardiol. 2009;137:298–9; author reply 9.
131. Fedorowski A, Burri P, Juul-Moller S, et al. A dedicated investigation unit improves management of syncopal attacks (Syncope Study of Unselected Population in Malmo–SYSTEMA I). Europace. 2010;12:1322–8.
132. Kapoor WN. Evaluation and outcome of patients with syncope. Medicine (Baltimore). 1990;69:160–75.
133. Douglas PS, Garcia MJ, Haines DE, et al. ACCF/ASE/AHA/ASNC/HFSA/HRS/SCAI/SCCM/SCCT/SCMR 2011 appropriate use criteria for echocardiography. A report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Society of Echocardiography, American Heart Association, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Critical Care Medicine, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance. J Am Coll Cardiol. 2011;57:1126–66.
134. Probst MA, Kanzaria HK, Gbedemah M, et al. National trends in resource utilization associated with ED visits for syncope. Am J Emerg Med. 2015;33:998–1001.
135. Sparrow PJ, Merchant N, Provost YL, et al. CT and MR imaging findings in patients with acquired heart disease at risk for sudden cardiac death. Radiographics. 2009;29:805–23.
136. Sparrow P, Merchant N, Provost Y, et al. Cardiac MRI and CT features of inheritable and congenital conditions associated with sudden cardiac death. Eur Radiol. 2009;19:259–70.
137. Hulten EA, Carbonaro S, Petrillo SP, et al. Prognostic value of cardiac computed tomography angiography: a systematic review and meta-analysis. J Am Coll Cardiol. 2011;57:1237–47.
138. El Aidi H, Adams A, Moons KG.M, et al. Cardiac magnetic resonance imaging findings and the risk of cardiovascular events in patients with recent myocardial infarction or suspected or known coronary artery disease: a systematic review of prognostic studies. J Am Coll Cardiol. 2014;63:1031–45.
139. Tandri H, Calkins H. MR and CT imaging of arrhythmogenic cardiomyopathy. Card Electrophysiol Clin. 2011;3:269–80.
140. Steckman DA, Schneider PM, Schuller JL, et al. Utility of cardiac magnetic resonance imaging to differentiate cardiac sarcoidosis from arrhythmogenic right ventricular cardiomyopathy. Am J Cardiol. 2012;110:575–9.
141. Janardhanan R. Echocardiography in arrhythmogenic right ventricular dysplasia/cardiomyopathy: can the technology survive in the era of cardiac magnetic resonance imaging? Cardiol J. 2015;22:355–6.
142. Krumholz HM, Douglas PS, Goldman L, et al. Clinical utility of transthoracic two-dimensional and Doppler echocardiography. J Am Coll Cardiol. 1994;24:125–31.
143. Woelfel AK, Simpson RJ Jr, Gettes LS, et al. Exercise-induced distal atrioventricular block. J Am Coll Cardiol. 1983;2:578–81.
144. Rozanski JJ, Castellanos A, Sheps D, et al. Paroxysmal second-degree atrioventricular block induced by exercise. Heart Lung. 1980;9:887–90.
145. Oliveros RA, Seaworth J, Weiland FL, et al. Intermittent left anterior hemiblock during treadmill exercise test. Correlation with coronary arteriogram. Chest. 1977;72:492–4.
146. Bobba P, Salerno JA, Casari A. Transient left posterior hemiblock. Report of four cases induced by exercise test. Circulation. 1972;46:931–8.
147. Bharati S, Dhingra RC, Lev M, et al. Conduction system in a patient with Prinzmetal's angina and transient atrioventricular block. Am J Cardiol. 1977;39:120–5.
148. Subbiah R, Chia PL, Gula LJ, et al. Cardiac monitoring in patients with syncope: making that elusive diagnosis. Curr Cardiol Rev. 2013;9:299–307.
149. Gibson TC, Heitzman MR. Diagnostic efficacy of 24-hour electrocardiographic monitoring for syncope. Am J Cardiol. 1984;53:1013–7.
150. Linzer M, Pritchett EL, Pontinen M, et al. Incremental diagnostic yield of loop electrocardiographic recorders in unexplained syncope. Am J Cardiol. 1990;66:214–9.
151. Linzer M, Yang EH, Estes NA 3rd, et al. Diagnosing syncope. Part 2: unexplained syncope. Clinical Efficacy Assessment Project of the American College of Physicians. Ann Intern Med. 1997;127:76–86.
152. Reiffel JA, Schwarzberg R, Murry M. Comparison of autotriggered memory loop recorders versus standard loop recorders versus 24-hour Holter monitors for arrhythmia detection. Am J Cardiol. 2005;95:1055–9.
153. Sivakumaran S, Krahn AD, Klein GJ, et al. A prospective randomized comparison of loop recorders versus Holter monitors in patients with syncope or presyncope. Am J Med. 2003;115:1–5.
154. Brown AP, Dawkins KD, Davies JG. Detection of arrhythmias: use of a patient-activated ambulatory electrocardiogram device with a solid-state memory loop. Br Heart J. 1987;58:251–3.
155. Cumbee SR, Pryor RE, Linzer M. Cardiac loop ECG recording: a new noninvasive diagnostic test in recurrent syncope. South Med J. 1990;83:39–43.
156. Locati ET, Moya A, Oliveira M, et al. External prolonged electrocardiogram monitoring in unexplained syncope and palpitations: results of the SYNARR-Flash study. Europace. 2016;18:1265–72.
157. Barrett PM, Komatireddy R, Haaser S, et al. Comparison of 24-hour Holter monitoring with 14-day novel adhesive patch electrocardiographic monitoring. Am J Med. 2014;127:95–7.
158. Rosenberg MA, Samuel M, Thosani A, et al. Use of a noninvasive continuous monitoring device in the management of atrial fibrillation: a pilot study. Pacing Clin Electrophysiol. 2013;36:328–33.
159. Turakhia MP, Hoang DD, Zimetbaum P, et al. Diagnostic utility of a novel leadless arrhythmia monitoring device. Am J Cardiol. 2013;112:520–4.
160. Joshi AK, Kowey PR, Prystowsky EN, et al. First experience with a Mobile Cardiac Outpatient Telemetry (MCOT) system for the diagnosis and management of cardiac arrhythmia. Am J Cardiol. 2005;95:878–81.
161. Rothman SA, Laughlin JC, Seltzer J, et al. The diagnosis of cardiac arrhythmias: a prospective multi-center randomized study comparing mobile cardiac outpatient telemetry versus standard loop event monitoring. J Cardiovasc Electrophysiol. 2007;18:241–7.
162. Krahn AD, Klein GJ, Yee R, et al. Randomized assessment of syncope trial: conventional diagnostic testing versus a prolonged monitoring strategy. Circulation. 2001;104:46–51.
163. Krahn AD, Klein GJ, Yee R, et al. Cost implications of testing strategy in patients with syncope: randomized assessment of syncope trial. J Am Coll Cardiol. 2003;42:495–501.
164. Farwell DJ, Freemantle N, Sulke N. The clinical impact of implantable loop recorders in patients with syncope. Eur Heart J. 2006;27:351–6.
165. Da Costa A, Defaye P, Romeyer-Bouchard C, et al. Clinical impact of the implantable loop recorder in patients with isolated syncope, bundle branch block and negative workup: a randomized multicentre prospective study. Arch Cardiovasc Dis. 2013;106:146–54.
166. Krahn AD, Klein GJ, Norris C, et al. The etiology of syncope in patients with negative tilt table and electrophysiological testing. Circulation. 1995;92:1819–24.
167. Krahn AD, Klein GJ, Yee R, et al. Use of an extended monitoring strategy in patients with problematic syncope. Reveal Investigators. Circulation. 1999;99:406–10.
168. Moya A, Brignole M, Menozzi C, et al. Mechanism of syncope in patients with isolated syncope and in patients with tilt-positive syncope. Circulation. 2001;104:1261–7.
169. Brignole M, Menozzi C, Moya A, et al. Mechanism of syncope in patients with bundle branch block and negative electrophysiological test. Circulation. 2001;104:2045–50.

170. Boersma L, Mont L, Sionis A, et al. Value of the implantable loop recorder for the management of patients with unexplained syncope. Europace. 2004;6:70–6.
171. Krahn AD, Klein GJ, Yee R, et al. Detection of asymptomatic arrhythmias in unexplained syncope. Am Heart J. 2004;148:326–32.
172. Pierre B, Fauchier L, Breard G, et al. Implantable loop recorder for recurrent syncope: influence of cardiac conduction abnormalities showing up on resting electrocardiogram and of underlying cardiac disease on follow-up developments. Europace. 2008;10:477–81.
173. Edvardsson N, Frykman V, van Mechelen R, et al. Use of an implantable loop recorder to increase the diagnostic yield in unexplained syncope: results from the PICTURE registry. Europace. 2011;13:262–9.
174. Linker NJ, Voulgaraki D, Garutti C, et al. Early versus delayed implantation of a loop recorder in patients with unexplained syncope—effects on care pathway and diagnostic yield. Int J Cardiol. 2013;170:146–51.
175. Palmisano P, Accogli M, Zaccaria M, et al. Predictive factors for pacemaker implantation in patients receiving an implantable loop recorder for syncope remained unexplained after an extensive cardiac and neurological workup. Int J Cardiol. 2013;168:3450–7.
176. Podoleanu C, DaCosta A, Defaye P, et al. Early use of an implantable loop recorder in syncope evaluation: a randomized study in the context of the French healthcare system (FRESH study). Arch Cardiovasc Dis. 2014;107:546–52.
177. Sulke N, Sugihara C, Hong P, et al. The benefit of a remotely monitored implantable loop recorder as a first line investigation in unexplained syncope: the EaSyAS II trial. Europace. 2016;18:912–8.
178. Solbiati M, Costantino G, Casazza G, et al. Implantable loop recorder versus conventional diagnostic workup for unexplained recurrent syncope. Cochrane Database Syst Rev. 2016;4:CD011637
179. Brignole M, Menozzi C, Maggi R, et al. The usage and diagnostic yield of the implantable loop-recorder in detection of the mechanism of syncope and in guiding effective antiarrhythmic therapy in older people. Europace. 2005;7:273–9.
180. Krahn AD, Klein GJ, Fitzpatrick A, et al. Predicting the outcome of patients with unexplained syncope undergoing prolonged monitoring. Pacing Clin Electrophysiol. 2002;25:37–41.
181. Lombardi F, Calosso E, Mascioli G, et al. Utility of implantable loop recorder (Reveal Plus) in the diagnosis of unexplained syncope. Europace. 2005;7:19–24.
182. Benezet-Mazuecos J, Ibanez B, Rubio JM, et al. Utility of in-hospital cardiac remote telemetry in patients with unexplained syncope. Europace. 2007;9:1196–201.
183. Lipskis DJ, Dannehl KN, Silverman ME. Value of radiotelemetry in a community hospital. Am J Cardiol. 1984;53:1284–7.
184. Kapoor WN. Syncope. N Engl J Med. 2000;343:1856–62.
185. Estrada CA, Rosman HS, Prasad NK, et al. Role of telemetry monitoring in the non-intensive care unit. Am J Cardiol. 1995;76:960–5.
186. Sivaram CA, Summers JH, Ahmed N. Telemetry outside critical care units: patterns of utilization and influence on management decisions. Clin Cardiol. 1998;21:503–5.
187. Ivonye C, Ohuabunwo C, Henriques-Forsythe M, et al. Evaluation of telemetry utilization, policy, and outcomes in an inner-city academic medical center. J Natl Med Assoc. 2010;102:598–604.
188. Ungar A, Mussi C, Del Rosso A, et al. Diagnosis and characteristics of syncope in older patients referred to geriatric departments. J Am Geriatr Soc. 2006;54:1531–6.
189. Fujimura O, Yee R, Klein GJ, et al. The diagnostic sensitivity of electrophysiologic testing in patients with syncope caused by transient bradycardia. N Engl J Med. 1989;321:1703–7.
190. Scheinman MM, Peters RW, Suavé MJ, et al. Value of the H-Q interval in patients with bundle branch block and the role of prophylactic permanent pacing. Am J Cardiol. 1982;50:1316–22.
191. Blanc JJ. Clinical laboratory testing: what is the role of tilt-table testing, active standing test, carotid massage, electrophysiological testing and ATP test in the syncope evaluation? Prog Cardiovasc Dis. 2013;55:418–24.
192. Link MS, Kim KM, Homoud MK, et al. Long-term outcome of patients with syncope associated with coronary artery disease and a nondiagnostic electrophysiologic evaluation. Am J Cardiol. 1999;83:1334–7.
193. Militianu A, Salacata A, Seibert K, et al. Implantable cardioverter defibrillator utilization among device recipients presenting exclusively with syncope or near-syncope. J Cardiovasc Electrophysiol. 1997;8:1087–97.
194. Pezawas T, Stix G, Kastner J, et al. Unexplained syncope in patients with structural heart disease and no documented ventricular arrhythmias: value of electrophysiologically guided implantable cardioverter defibrillator therapy. Europace. 2003;5:305–12.
195. Steinberg JS, Beckman K, Greene HL, et al. Follow-up of patients with unexplained syncope and inducible ventricular tachyarrhythmias: analysis of the AVID registry and an AVID substudy. Antiarrhythmics Versus Implantable Defibrillators. J Cardiovasc Electrophysiol. 2001;12:996–1001.
196. Andrews NP, Fogel RI, Pelargonio G, et al. Implantable defibrillator event rates in patients with unexplained syncope and inducible sustained ventricular tachyarrhythmias: a comparison with patients known to have sustained ventricular tachycardia. J Am Coll Cardiol. 1999;34:2023–30.
197. Bass EB, Elson JJ, Fogoros RN, et al. Long-term prognosis of patients undergoing electrophysiologic studies for syncope of unknown origin. Am J Cardiol. 1988;62:1186–91.
198. Olshansky B, Mazuz M, Martins JB. Significance of inducible tachycardia in patients with syncope of unknown origin: a long-term follow-up. J Am Coll Cardiol. 1985;5:216–23.
199. Denniss AR, Ross DL, Richards DA, et al. Electrophysiologic studies in patients with unexplained syncope. Int J Cardiol. 1992;35:211–7.
200. Lacroix D, Dubuc M, Kus T, et al. Evaluation of arrhythmic causes of syncope: correlation between Holter monitoring, electrophysiologic testing, and body surface potential mapping. Am Heart J. 1991;122:1346–54.
201. Sra JS, Anderson AJ, Sheikh SH, et al. Unexplained syncope evaluated by electrophysiologic studies and head-up tilt testing. Ann Intern Med. 1991;114:1013–9.
202. Click RL, Gersh BJ, Sugrue DD, et al. Role of invasive electrophysiologic testing in patients with symptomatic bundle branch block. Am J Cardiol. 1987;59:817–23.
203. Reiffel JA, Wang P, Bower R, et al. Electrophysiologic testing in patients with recurrent syncope: are results predicted by prior ambulatory monitoring? Am Heart J. 1985;110:1146–53.
204. Morady F, Higgins J, Peters RW, et al. Electrophysiologic testing in bundle branch block and unexplained syncope. Am J Cardiol. 1984;54:587–91.
205. Gulamhusein S, Naccarelli GV, Ko PT, et al. Value and limitations of clinical electrophysiologic study in assessment of patients with unexplained syncope. Am J Med. 1982;73:700–5.
206. Sagristà-Sauleda J, Romero-Ferrer B, Moya A, et al. Variations in diagnostic yield of head-up tilt test and electrophysiology in groups of patients with syncope of unknown origin. Eur Heart J. 2001;22:857–65.
207. Gatzoulis KA, Karystinos G, Gialernios T, et al. Correlation of noninvasive electrocardiography with invasive electrophysiology in syncope of unknown origin: implications from a large syncope database. Ann Noninvasive Electrocardiol. 2009;14:119–27.
208. Kenny RA, Ingram A, Bayliss J, et al. Head-up tilt: a useful test for investigating unexplained syncope. Lancet. 1986;1:1352–5.
209. Fitzpatrick A, Theodorakis G, Vardas P, et al. The incidence of malignant vasovagal syndrome in patients with recurrent syncope. Eur Heart J. 1991;12:389–94.
210. Almquist A, Goldenberg IF, Milstein S, et al. Provocation of bradycardia and hypotension by isoproterenol and upright posture in patients with unexplained syncope. N Engl J Med. 1989;320:346–51.
211. Grubb BP, Kosinski D. Tilt table testing: concepts and limitations. Pacing Clin Electrophysiol. 1997;20:781–7.
212. Morillo CA, Klein GJ, Zandri S, et al. Diagnostic accuracy of a low-dose isoproterenol head-up tilt protocol. Am Heart J. 1995;129:901–6.
213. Natale A, Akhtar M, Jazayeri M, et al. Provocation of hypotension during head-up tilt testing in subjects with no history of syncope or presyncope. Circulation. 1995;92:54–8.
214. Brignole M, Menozzi C, Del Rosso A, et al. New classification of haemodynamics of vasovagal syncope: beyond the VASIS classification. Analysis of the pre-syncopal phase of the tilt test without and with nitroglycerin challenge. Vasovagal Syncope International Study. Europace. 2000;2:66–76.
215. Benditt DG, Ferguson DW, Grubb BP, et al. Tilt table testing for assessing syncope. American College of Cardiology. J Am Coll Cardiol. 1996;28:263–75.
216. Gisolf J, Westerhof BE, van DN, et al. Sublingual nitroglycerin used in routine tilt testing provokes a cardiac output-mediated vasovagal response. J Am Coll Cardiol. 2004;44:588–93.
217. Raviele A, Menozzi C, Brignole M, et al. Value of head-up tilt testing potentiated with sublingual nitroglycerin to assess the origin of unexplained syncope. Am J Cardiol. 1995;76:267–72.
218. Gibbons CH, Freeman R. Delayed orthostatic hypotension: a frequent cause of orthostatic intolerance. Neurology. 2006;67:28–32.
219. Gibbons CH, Freeman R. Clinical implications of delayed orthostatic hypotension: a 10-year follow-up study. Neurology. 2015;85:1362–7.

220. The definition of orthostatic hypotension, pure autonomic failure, and multiple system atrophy. J Auton Nerv Syst. 1996;58:123–4.
221. Streeten DH, Anderson GH Jr, Delayed orthostatic intolerance. Arch Intern Med. 1992;152:1066–72.
222. Passman R, Horvath G, Thomas J, et al. Clinical spectrum and prevalence of neurologic events provoked by tilt table testing. Arch Intern Med. 2003;163:1945–8.
223. Grubb BP, Gerard G, Roush K, et al. Differentiation of convulsive syncope and epilepsy with head-up tilt testing. Ann Intern Med. 1991;115:871–6.
224. Song PS, Kim JS, Park J, et al. Seizure-like activities during head-up tilt test-induced syncope. Yonsei Med J. 2010;51:77–81.
225. Zaidi A, Clough P, Cooper P, et al. Misdiagnosis of epilepsy: many seizure-like attacks have a cardiovascular cause. J Am Coll Cardiol. 2000;36:181–4.
226. Sheldon R. How to differentiate syncope from seizure. Cardiol Clin. 2015;33:377–85.
227. Zaidi A, Crampton S, Clough P, et al. Head-up tilting is a useful provocative test for psychogenic non-epileptic seizures. Seizure. 1999;8:353–5.
228. Luzza F, Pugliatti P, di Rosa S, et al. Tilt-induced pseudosyncope. Int J Clin Pract. 2003;57:373–5.
229. Tannemaat MR, van Niekerk J, Reijntjes RH, et al. The semiology of tilt-induced psychogenic pseudosyncope. Neurology. 2013;81:752–8.
230. Moya A, Permanyer-Miralda G, Sagrista-Sauleda J, et al. Limitations of head-up tilt test for evaluating the efficacy of therapeutic interventions in patients with vasovagal syncope: results of a controlled study of etilefrine versus placebo. J Am Coll Cardiol. 1995;25:65–9.
231. Morillo CA, Leitch JW, Yee R, et al. A placebo-controlled trial of intravenous and oral disopyramide for prevention of neurally mediated syncope induced by head-up tilt. J Am Coll Cardiol. 1993;22:1843–8.
232. Milstein S, Buetikofer J, Dunnigan A, et al. Usefulness of disopyramide for prevention of upright tilt-induced hypotension-bradycardia. Am J Cardiol. 1990;65:1339–44.
233. Raviele A, Gasparini G, Di PF, et al. Usefulness of head-up tilt test in evaluating patients with syncope of unknown origin and negative electrophysiologic study. Am J Cardiol. 1990;65:1322–7.
234. Grubb BP, Wolfe DA, Samoil D, et al. Usefulness of fluoxetine hydrochloride for prevention of resistant upright tilt induced syncope. Pacing Clin Electrophysiol. 1993;16:458–64.
235. Sra JS, Murthy VS, Jazayeri MR, et al. Use of intravenous esmolol to predict efficacy of oral beta-adrenergic blocker therapy in patients with neurocardiogenic syncope. J Am Coll Cardiol. 1992;19:402–8.
236. Low PA, Benrud-Larson LM, Sletten DM, et al. Autonomic symptoms and diabetic neuropathy: a population-based study. Diabetes Care. 2004;27:2942–7.
237. Kim DH, Zeldenrust SR, Low PA, et al. Quantitative sensation and autonomic test abnormalities in transthyretin amyloidosis polyneuropathy. Muscle Nerve. 2009;40:363–70.
238. Thaisetthawatkul P, Boeve BF, Benarroch EE, et al. Autonomic dysfunction in dementia with Lewy bodies. Neurology. 2004;62:1804–9.
239. Iodice V, Lipp A, Ahlskog JE, et al. Autopsy confirmed multiple system atrophy cases: Mayo experience and role of autonomic function tests. J Neurol Neurosurg Psychiatr. 2012;83:453–9.
240. Freeman R. Autonomic peripheral neuropathy. Lancet. 2005;365:1259–70.
241. Fanciulli A, Wenning GK. Multiple-system atrophy. N Engl J Med. 2015;372:1375–6.
242. Cersosimo MG, Benarroch EE. Autonomic involvement in Parkinson's disease: pathology, pathophysiology, clinical features and possible peripheral biomarkers. J Neurol Sci. 2012;313:57–63.
243. Garland EM, Hooper WB, Robertson D. Pure autonomic failure. Handb Clin Neurol. 2013;117:243–57.
244. Cersosimo MG, Benarroch EE. Central control of autonomic function and involvement in neurodegenerative disorders. Handb Clin Neurol. 2013;117:45–57.
245. Fanciulli A, Strano S, Colosimo C, et al. The potential prognostic role of cardiovascular autonomic failure in alpha-synucleinopathies. Eur J Neurol. 2013;20:231–5.
246. Figueroa JJ, Singer W, Parsaik A, et al. Multiple system atrophy: prognostic indicators of survival. Mov Disord. 2014;29:1151–7.
247. Benarroch EE. The clinical approach to autonomic failure in neurological disorders. Nat Rev Neurol. 2014;10:396–407.
248. Low PA, Tomalia VA, Park KJ. Autonomic function tests: some clinical applications. J Clin Neurol. 2013;9:1–8.
249. Jansen RW, Lipsitz LA. Postprandial hypotension: epidemiology, pathophysiology, and clinical management. Ann Intern Med. 1995;122:286–95.
250. Gibbons CH, Bonyhay I, Benson A, et al. Structural and functional small fiber abnormalities in the neuropathic postural tachycardia syndrome. PLoS ONE. 2013;8:e84716
251. Al-Nsoor NM, Mhearat AS. Brain computed tomography in patients with syncope. Neurosciences (Riyadh). 2010;15:105–9.
252. Giglio P, Bednarczyk EM, Weiss K, et al. Syncope and head CT scans in the emergency department. Emerg Radiol. 2005;12:44–6.
253. Goyal N, Donnino MW, Vachhani R, et al. The utility of head computed tomography in the emergency department evaluation of syncope. Intern Emerg Med. 2006;1:148–50.
254. Abubakr A, Wambacq I. The diagnostic value of EEGs in patients with syncope. Epilepsy Behav. 2005;6:433–4.
255. Poliquin-Lasnier L, Moore FGA. EEG in suspected syncope: do EEGs ordered by neurologists give a higher yield? Can J Neurol Sci. 2009;36:769–73.
256. Kang GH, Oh JH, Kim JS, et al. Diagnostic patterns in the evaluation of patients presenting with syncope at the emergency or outpatient department. Yonsei Med J. 2012;53:517–23.
257. Pires LA, Ganji JR, Jarandila R, et al. Diagnostic patterns and temporal trends in the evaluation of adult patients hospitalized with syncope. Arch Intern Med. 2001;161:1889–95.
258. Mecarelli O, Pulitano P, Vicenzini E, et al. Observations on EEG patterns in neurally-mediated syncope: an inspective and quantitative study. Neurophysiol Clin. 2004;34:203–7.
259. Mitsunaga MM, Yoon HC. Journal Club: Head CT scans in the emergency department for syncope and dizziness. AJR Am J Roentgenol. 2015;204:24–8.
260. Sclafani JJ, My J, Zacher LL, et al. Intensive education on evidence-based evaluation of syncope increases sudden death risk stratification but fails to reduce use of neuroimaging. Arch Intern Med. 2010;170:1150–4.
261. Ammirati F, Colivicchi F, Di Battista G, et al. Electroencephalographic correlates of vasovagal syncope induced by head-up tilt testing. Stroke. 1998;29:2347–51.
262. Sheldon RS, Koshman ML, Murphy WF. Electroencephalographic findings during presyncope and syncope induced by tilt table testing. Can J Cardiol. 1998;14:811–6.
263. van Dijk JG, Thijs RD, van Zwet E, et al. The semiology of tilt-induced reflex syncope in relation to electroencephalographic changes. Brain. 2014;137:576–85.
264. Deleted in press.
265. Santini M, Castro A, Giada F, et al. Prevention of syncope through permanent cardiac pacing in patients with bifascicular block and syncope of unexplained origin: the PRESS study. Circ Arrhythm Electrophysiol. 2013;6:101–7.
266. Flammang D, Church TR, De Roy L, et al. Treatment of unexplained syncope: a multicenter, randomized trial of cardiac pacing guided by adenosine 5′-triphosphate testing. Circulation. 2012;125:31–6.
267. Kalusche D, Ott P, Arentz T, et al. AV nodal re-entry tachycardia in elderly patients: clinical presentation and results of radiofrequency catheter ablation therapy. Coron Artery Dis. 1998;9:359–63.
268. Haghjoo M, Arya A, Heidari A, et al. Electrophysiologic characteristics and results of radiofrequency catheter ablation in elderly patients with atrioventricular nodal reentrant tachycardia. J Electrocardiol. 2007;40:208–13.
269. Auricchio A, Klein H, Trappe HJ, et al. Lack of prognostic value of syncope in patients with Wolff-Parkinson-White syndrome. J Am Coll Cardiol. 1991;17:152–8.
270. Brignole M, Gianfranchi L, Menozzi C, et al. Role of autonomic reflexes in syncope associated with paroxysmal atrial fibrillation. J Am Coll Cardiol. 1993;22:1123–9.
271. Russo AM, Stainback RF, Bailey SR, et al. ACCF/HRS/AHA/ASE/HFSA/SCAI/SCCT/SCMR 2013 appropriate use criteria for implantable cardioverter-defibrillators and cardiac resynchronization therapy: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, Heart Rhythm Society, American Heart Association, American Society of Echocardiography, Heart Failure Society of America, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance. J Am Coll Cardiol. 2013;61:1318–68.
272. Huikuri HV, Zaman L, Castellanos A, et al. Changes in spontaneous sinus node rate as an estimate of cardiac autonomic tone during stable and unstable ventricular tachycardia. J Am Coll Cardiol. 1989;13:646–52.

273. Morady F, Shen EN, Bhandari A, et al. Clinical symptoms in patients with sustained ventricular tachycardia. West J Med. 1985;142:341–4.
274. Bhonsale A, James CA, Tichnell C, et al. Incidence and predictors of implantable cardioverter-defibrillator therapy in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy undergoing implantable cardioverter-defibrillator implantation for primary prevention. J Am Coll Cardiol. 2011;58:1485–96.
275. Bhonsale A, James CA, Tichnell C, et al. Risk stratification in arrhythmogenic right ventricular dysplasia/cardiomyopathy-associated desmosomal mutation carriers. Circ Arrhythm Electrophysiol. 2013;6:569–78.
276. Corrado D, Leoni L, Link MS, et al. Implantable cardioverter-defibrillator therapy for prevention of sudden death in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia. Circulation. 2003;108:3084–91.
277. Corrado D, Wichter T, Link MS, et al. Treatment of arrhythmogenic right ventricular cardiomyopathy/dysplasia: an international task force consensus statement. Circulation. 2015;132:441–53.
278. Link MS, Laidlaw D, Polonsky B, et al. Ventricular arrhythmias in the North American multidisciplinary study of ARVC: predictors, characteristics, and treatment. J Am Coll Cardiol. 2014;64:119–25.
279. Corrado D, Calkins H, Link MS, et al. Prophylactic implantable defibrillator in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia and no prior ventricular fibrillation or sustained ventricular tachycardia. Circulation. 2010;122:1144–52.
280. Koplan BA, Soejima K, Baughman K, et al. Refractory ventricular tachycardia secondary to cardiac sarcoid: electrophysiologic characteristics, mapping, and ablation. Heart Rhythm. 2006;3:924–9.
281. Jefic D, Joel B, Good E, et al. Role of radiofrequency catheter ablation of ventricular tachycardia in cardiac sarcoidosis: report from a multicenter registry. Heart Rhythm. 2009;6:189–95.
282. Berte B, Eyskens B, Meyfroidt G, et al. Bidirectional ventricular tachycardia in fulminant myocarditis. Europace. 2008;10:767–8.
283. Winters SL, Cohen M, Greenberg S, et al. Sustained ventricular tachycardia associated with sarcoidosis: assessment of the underlying cardiac anatomy and the prospective utility of programmed ventricular stimulation, drug therapy and an implantable antitachycardia device. J Am Coll Cardiol. 1991;18:937–43.
284. Furushima H, Chinushi M, Sugiura H, et al. Ventricular tachyarrhythmia associated with cardiac sarcoidosis: its mechanisms and outcome. Clin Cardiol. 2004;27:217–22.
285. Hiramitsu S, Morimoto S, Uemura A, et al. National survey on status of steroid therapy for cardiac sarcoidosis in Japan. Sarcoidosis Vasc Diffuse Lung Dis. 2005;22:210–3.
286. Birnie DH, Sauer WH, Bogun F, et al. HRS expert consensus statement on the diagnosis and management of arrhythmias associated with cardiac sarcoidosis. Heart Rhythm. 2014;11:1305–23.
287. Kandolin R, Lehtonen J, Kupari M. Cardiac sarcoidosis and giant cell myocarditis as causes of atrioventricular block in young and middle-aged adults. Circ Arrhythm Electrophysiol. 2011;4:303–9.
288. Chapelon-Abric C, de Zuttere D, Duhaut P, et al. Cardiac sarcoidosis: a retrospective study of 41 cases. Medicine (Baltimore). 2004;83:315–34.
289. Yodogawa K, Seino Y, Ohara T, et al. Effect of corticosteroid therapy on ventricular arrhythmias in patients with cardiac sarcoidosis. Ann Noninvasive Electrocardiol. 2011;16:140–7.
290. Schuller JL, Zipse M, Crawford T, et al. Implantable cardioverter defibrillator therapy in patients with cardiac sarcoidosis. J Cardiovasc Electrophysiol. 2012;23:925–9.
291. Betensky BP, Tschabrunn CM, Zado ES, et al. Long-term follow-up of patients with cardiac sarcoidosis and implantable cardioverter-defibrillators. Heart Rhythm. 2012;9:884–91.
292. Kron J, Sauer W, Schuller J, et al. Efficacy and safety of implantable cardiac defibrillators for treatment of ventricular arrhythmias in patients with cardiac sarcoidosis. Europace. 2013;15:347–54.
293. Namboodiri N, Stiles MK, Young GD, et al. Electrophysiological features of atrial flutter in cardiac sarcoidosis: a report of two cases. Indian Pacing Electrophysiol J. 2012;12:284–9.
294. Mehta D, Mori N, Goldbarg SH, et al. Primary prevention of sudden cardiac death in silent cardiac sarcoidosis: role of programmed ventricular stimulation. Circ Arrhythm Electrophysiol. 2011;4:43–8.
295. Antzelevitch C, Brugada P, Borggrefe M, et al. Brugada syndrome: report of the second consensus conference. Heart Rhythm. 2005;2:429–40.
296. Gehi AK, Duong TD, Metz LD, et al. Risk stratification of individuals with the Brugada electrocardiogram: a meta-analysis. J Cardiovasc Electrophysiol. 2006;17:577–83.
297. Probst V, Veltmann C, Eckardt L, et al. Long-term prognosis of patients diagnosed with Brugada syndrome: results from the FINGER Brugada Syndrome Registry. Circulation. 2010;121:635–43.
298. Sacher F, Arsac F, Wilton SB, et al. Syncope in Brugada syndrome patients: prevalence, characteristics, and outcome. Heart Rhythm. 2012;9:1272–9.
299. Hiraoka M, Takagi M, Yokoyama Y, et al. Prognosis and risk stratification of young adults with Brugada syndrome. J Electrocardiol. 2013;46:279–83.
300. Sacher F, Probst V, Iesaka Y, et al. Outcome after implantation of a cardioverter-defibrillator in patients with Brugada syndrome: a multicenter study. Circulation. 2006;114:2317–24.
301. Priori SG, Gasparini M, Napolitano C, et al. Risk stratification in Brugada syndrome: results of the PRELUDE (PRogrammed ELectrical stimUlation preDictive valuE) registry. J Am Coll Cardiol. 2012;59:37–45.
302. Morita H, Kusano KF, Miura D, et al. Fragmented QRS as a marker of conduction abnormality and a predictor of prognosis of Brugada syndrome. Circulation. 2008;118:1697–704.
303. Sarkozy A, Boussy T, Kourgiannides G, et al. Long-term follow-up of primary prophylactic implantable cardioverter-defibrillator therapy in Brugada syndrome. Eur Heart J. 2007;28:334–44.
304. Rosso R, Glick A, Glikson M, et al. Outcome after implantation of cardioverter defibrillator [corrected] in patients with Brugada syndrome: a multicenter Israeli study (ISRABRU). Isr Med Assoc J. 2008;10:435–9.
305. Gaita F, Giustetto C, Bianchi F, et al. Short QT syndrome: a familial cause of sudden death. Circulation. 2003;108:965–70.
306. Giustetto C, Schimpf R, Mazzanti A, et al. Long-term follow-up of patients with short QT syndrome. J Am Coll Cardiol. 2011;58:587–95.
307. Brugada R, Hong K, Dumaine R, et al. Sudden death associated with short-QT syndrome linked to mutations in HERG. Circulation. 2004;109:30–5.
308. Gollob MH, Redpath CJ, Roberts JD. The short QT syndrome: proposed diagnostic criteria. J Am Coll Cardiol. 2011;57:802–12.
309. Anttonen O, Junttila MJ, Rissanen H, et al. Prevalence and prognostic significance of short QT interval in a middle-aged Finnish population. Circulation. 2007;116:714–20.
310. Funada A, Hayashi K, Ino H, et al. Assessment of QT intervals and prevalence of short QT syndrome in Japan. Clin Cardiol. 2008;31:270–4.
311. Kobza R, Roos M, Niggli B, et al. Prevalence of long and short QT in a young population of 41,767 predominantly male Swiss conscripts. Heart Rhythm. 2009;6:652–7.
312. Gallagher MM, Magliano G, Yap YG, et al. Distribution and prognostic significance of QT intervals in the lowest half centile in 12,012 apparently healthy persons. Am J Cardiol. 2006;98:933–5.
313. Hermosillo AG, Falcón JC, Márquez MF, et al. Positive head-up tilt table test in patients with the long QT syndrome. Europace. 1999;1:213–7.
314. Toft E, Aarøe J, Jensen BT, et al. Long QT syndrome patients may faint due to neurocardiogenic syncope. Europace. 2003;5:367–70.
315. Colman N, Bakker A, Linzer M, et al. Value of history-taking in syncope patients: in whom to suspect long QT syndrome? Europace. 2009;11:937–43.
316. Priori SG, Napolitano C, Schwartz PJ, et al. Association of long QT syndrome loci and cardiac events among patients treated *with* beta-blockers. JAMA. 2004;292:1341–4.
317. Vincent GM, Schwartz PJ, Denjoy I, et al. High efficacy of beta-blockers in long-QT syndrome type 1: contribution of noncompliance and QT-prolonging drugs to the occurrence of beta-blocker treatment "failures". Circulation. 2009;119:215–21.
318. Liu JF, Jons C, Moss AJ, et al. Risk factors for recurrent syncope and subsequent fatal or near-fatal events in children and adolescents with long QT syndrome. J Am Coll Cardiol. 2011;57:941–50.
319. Chockalingam P, Crotti L, Girardengo G, et al. Not all beta-blockers are equal in the management of long QT syndrome types 1 and 2: higher recurrence of events under metoprolol. J Am Coll Cardiol. 2012;60:2092–9.
320. Abu-Zeitone A, Peterson DR, Polonsky B, et al. Efficacy of different beta-blockers in the treatment of long QT syndrome. J Am Coll Cardiol. 2014;64:1352–8.
321. Schwartz PJ, Spazzolini C, Priori SG, et al. Who are the long-QT syndrome patients who receive an implantable cardioverter-defibrillator and what happens to them?: Data from the European Long-QT Syndrome Implantable Cardioverter-Defibrillator (LQTS ICD) Registry. Circulation. 2010;122:1272–82.
322. Horner JM, Kinoshita M, Webster TL, et al. Implantable cardioverter defibrillator therapy for congenital long QT syndrome: a single-center experience. Heart Rhythm. 2010;7:1616–22.

323. Jons C, Moss AJ, Goldenberg I, et al. Risk of fatal arrhythmic events in long QT syndrome patients after syncope. J Am Coll Cardiol. 2010;55:783–8.
324. Zareba W, Moss AJ, Daubert JP, et al. Implantable cardioverter defibrillator in high-risk long QT syndrome patients. J Cardiovasc Electrophysiol. 2003;14:337–41.
325. Ouriel K, Moss AJ. Long QT syndrome: an indication for cervicothoracic sympathectomy. Cardiovasc Surg. 1995;3:475–8.
326. Schwartz PJ, Priori SG, Cerrone M, et al. Left cardiac sympathetic denervation in the management of high-risk patients affected by the long-QT syndrome. Circulation. 2004;109:1826–33.
327. Collura CA, Johnson JN, Moir C, et al. Left cardiac sympathetic denervation for the treatment of long QT syndrome and catecholaminergic polymorphic ventricular tachycardia using video-assisted thoracic surgery. Heart Rhythm. 2009;6:752–9.
328. Leenhardt A, Lucet V, Denjoy I, et al. Catecholaminergic polymorphic ventricular tachycardia in children. A 7-year follow-up of 21 patients. Circulation. 1995;91:1512–9.
329. Sumitomo N, Harada K, Nagashima M, et al. Catecholaminergic polymorphic ventricular tachycardia: electrocardiographic characteristics and optimal therapeutic strategies to prevent sudden death. Heart. 2003;89:66–70.
330. Priori SG, Napolitano C, Tiso N, et al. Mutations in the cardiac ryanodine receptor gene (hRyR2) underlie catecholaminergic polymorphic ventricular tachycardia. Circulation. 2001;103:196–200.
331. Laitinen PJ, Brown KM, Piippo K, et al. Mutations of the cardiac ryanodine receptor (RyR2) gene in familial polymorphic ventricular tachycardia. Circulation. 2001;103:485–90.
332. Lahat H, Pras E, Olender T, et al. A missense mutation in a highly conserved region of CASQ2 is associated with autosomal recessive catecholamine-induced polymorphic ventricular tachycardia in Bedouin families from Israel. Am J Hum Genet. 2001;69:1378–84.
333. Lahat H, Eldar M, Levy-Nissenbaum E, et al. Autosomal recessive catecholamine- or exercise-induced polymorphic ventricular tachycardia: clinical features and assignment of the disease gene to chromosome 1p13-21. Circulation. 2001;103:2822–7.
334. Hayashi M, Denjoy I, Extramiana F, et al. Incidence and risk factors of arrhythmic events in catecholaminergic polymorphic ventricular tachycardia. Circulation. 2009;119:2426–34.
335. Ackerman MJ, Zipes DP, Kovacs RJ, et al. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: Task Force 10: the cardiac channelopathies: a scientific statement from the American Heart Association and American College of Cardiology. J Am Coll Cardiol. 2015;66:2424–8.
336. Priori SG, Napolitano C, Memmi M, et al. Clinical and molecular characterization of patients with catecholaminergic polymorphic ventricular tachycardia. Circulation. 2002;106:69–74.
337. Roston TM, Vinocur JM, Maginot KR, et al. Catecholaminergic polymorphic ventricular tachycardia in children: analysis of therapeutic strategies and outcomes from an international multicenter registry. Circ Arrhythm Electrophysiol. 2015;8:633–42.
338. van der Werf C, Zwinderman AH, Wilde AA.M. Therapeutic approach for patients with catecholaminergic polymorphic ventricular tachycardia: state of the art and future developments. Europace. 2012;14:175–83.
339. Sy RW, Gollob MH, Klein GJ, et al. Arrhythmia characterization and long-term outcomes in catecholaminergic polymorphic ventricular tachycardia. Heart Rhythm. 2011;8:864–71.
340. van der Werf C, Kannankeril PJ, Sacher F, et al. Flecainide therapy reduces exercise-induced ventricular arrhythmias in patients with catecholaminergic polymorphic ventricular tachycardia. J Am Coll Cardiol. 2011;57:2244–54.
341. Padfield GJ, AlAhmari L, Lieve KV, et al. Flecainide monotherapy is an option for selected patients with catecholaminergic polymorphic ventricular tachycardia intolerant of beta-blockade. Heart Rhythm. 2016;13:609–13.
342. Moray A, Kirk EP, Grant P, et al. Prophylactic left thoracic sympathectomy to prevent electrical storms in CPVT patients needing ICD placement. Heart Lung Circ. 2011;20:731–3.
343. Celiker A, Erdoğan I, Karagöz T, et al. Clinical experiences of patients with catecholaminergic polymorphic ventricular tachycardia. Cardiol Young. 2009;19:45–52.
344. Marai I, Khoury A, Suleiman M, et al. Importance of ventricular tachycardia storms not terminated by implantable cardioverter defibrillators shocks in patients with CASQ2 associated catecholaminergic polymorphic ventricular tachycardia. Am J Cardiol. 2012;110:72–6.
345. Roses-Noguer F, Jarman JW.E, Clague JR, et al. Outcomes of defibrillator therapy in catecholaminergic polymorphic ventricular tachycardia. Heart Rhythm. 2014;11:58–66.
346. Swan H, Laitinen P, Kontula K, et al. Calcium channel antagonism reduces exercise-induced ventricular arrhythmias in catecholaminergic polymorphic ventricular tachycardia patients with RyR2 mutations. J Cardiovasc Electrophysiol. 2005;16:162–6.
347. Rosso R, Kalman JM, Rogowski O, et al. Calcium channel blockers and beta-blockers versus beta-blockers alone for preventing exercise-induced arrhythmias in catecholaminergic polymorphic ventricular tachycardia. Heart Rhythm. 2007;4:1149–54.
348. Wilde AA.M, Bhuiyan ZA, Crotti L, et al. Left cardiac sympathetic denervation for catecholaminergic polymorphic ventricular tachycardia. N Engl J Med. 2008;358:2024–9.
349. De Ferrari GM, Dusi V, Spazzolini C, et al. Clinical management of catecholaminergic polymorphic ventricular tachycardia: the role of left cardiac sympathetic denervation. Circulation. 2015;131:2185–93.
350. Waddell-Smith KE, Ertresvaag KN, Li J, et al. Physical and psychological consequences of left cardiac sympathetic denervation for long-QT syndrome and catecholaminergic polymorphic ventricular tachycardia. Circ Arrhythm Electrophysiol 2015
351. Junttila MJ, Sager SJ, Freiser M, et al. Inferolateral early repolarization in athletes. J Interv Card Electrophysiol. 2011;31:33–8.
352. Haïssaguerre M, Derval N, Sacher F, et al. Sudden cardiac arrest associated with early repolarization. N Engl J Med. 2008;358:2016–23.
353. Rosso R, Kogan E, Belhassen B, et al. J-point elevation in survivors of primary ventricular fibrillation and matched control subjects: incidence and clinical significance. J Am Coll Cardiol. 2008;52:1231–8.
354. Derval N, Simpson CS, Birnie DH, et al. Prevalence and characteristics of early repolarization in the CASPER registry: cardiac arrest survivors with preserved ejection fraction registry. J Am Coll Cardiol. 2011;58:722–8.
355. Abe A, Ikeda T, Tsukada T, et al. Circadian variation of late potentials in idiopathic ventricular fibrillation associated with J waves: insights into alternative pathophysiology and risk stratification. Heart Rhythm. 2010;7:675–82.
356. Merchant FM, Noseworthy PA, Weiner RB, et al. Ability of terminal QRS notching to distinguish benign from malignant electrocardiographic forms of early repolarization. Am J Cardiol. 2009;104:1402–6.
357. Sinner MF, Reinhard W, Müller M, et al. Association of early repolarization pattern on ECG with risk of cardiac and all-cause mortality: a population-based prospective cohort study (MONICA/KORA). PLoS Med. 2010;7:e1000314
358. Nunn LM, Bhar-Amato J, Lowe MD, et al. Prevalence of J-point elevation in sudden arrhythmic death syndrome families. J Am Coll Cardiol. 2011;58:286–90.
359. Mahida S, Derval N, Sacher F, et al. Role of electrophysiological studies in predicting risk of ventricular arrhythmia in early repolarization syndrome. J Am Coll Cardiol. 2015;65:151–9.
360. Morady F, DiCarlo LA Jr, Baerman JM, et al. Comparison of coupling intervals that induce clinical and nonclinical forms of ventricular tachycardia during programmed stimulation. Am J Cardiol. 1986;57:1269–73.
361. Mosqueda-Garcia R, Furlan R, Tank J, et al. The elusive pathophysiology of neurally mediated syncope. Circulation. 2000;102:2898–906.
362. Glick G, Yu PN. Hemodynamic changes during spontaneous vasovagal reactions. Am J Med. 1963;34:42–51.
363. Hargreaves AD, Muir AL. Lack of variation in venous tone potentiates vasovagal syncope. Br Heart J. 1992;67:486–90.
364. Manyari DE, Rose S, Tyberg JV, et al. Abnormal reflex venous function in patients with neuromediated syncope. J Am Coll Cardiol. 1996;27:1730–5.
365. Thomson HL, Atherton JJ, Khafagi FA, et al. Failure of reflex venoconstriction during exercise in patients with vasovagal syncope. Circulation. 1996;93:953–9.
366. Rose MS, Koshman ML, Spreng S, et al. The relationship between health-related quality of life and frequency of spells in patients with syncope. J Clin Epidemiol. 2000;53:1209–16.
367. Ganzeboom KS, Colman N, Reitsma JB, et al. Prevalence and triggers of syncope in medical students. Am J Cardiol. 2003;91:1006–8.A8
368. Serletis A, Rose S, Sheldon AG, et al. Vasovagal syncope in medical students and their first-degree relatives. Eur Heart J. 2006;27:1965–70.
369. Romme JJ, Reitsma JB, Black CN, et al. Drugs and pacemakers for vasovagal, carotid sinus and situational syncope. Cochrane Database Syst Rev. 2011:CD004194.

370. Rebecchi M, de Ruvo E, Strano S, et al. Ganglionated plexi ablation in right atrium to treat cardioinhibitory neurocardiogenic syncope. J Interv Card Electrophysiol. 2012;34:231–5.
371. Yao Y, Shi R, Wong T, et al. Endocardial autonomic denervation of the left atrium to treat vasovagal syncope: an early experience in humans. Circ Arrhythm Electrophysiol. 2012;5:279–86.
372. Pachon JC.M, Pachon EI.M, Cunha Pachon MZ, et al. Catheter ablation of severe neurally meditated reflex (neurocardiogenic or vasovagal) syncope: cardioneuroablation long-term results. Europace. 2011;13:1231–42.
373. Brignole M, Croci F, Menozzi C, et al. Isometric arm counter-pressure maneuvers to abort impending vasovagal syncope. J Am Coll Cardiol. 2002;40:2053–9.
374. Krediet CT.P, van Dijk N, Linzer M, et al. Management of vasovagal syncope: controlling or aborting faints by leg crossing and muscle tensing. Circulation. 2002;106:1684–9.
375. van Dijk N, Quartieri F, Blanc JJ, et al. Effectiveness of physical counterpressure maneuvers in preventing vasovagal syncope: the Physical Counterpressure Manoeuvres Trial (PC-Trial). J Am Coll Cardiol. 2006;48:1652–7.
376. Perez-Lugones A, Schweikert R, Pavia S, et al. Usefulness of midodrine in patients with severely symptomatic neurocardiogenic syncope: a randomized control study. J Cardiovasc Electrophysiol. 2001;12:935–8.
377. Samniah N, Sakaguchi S, Lurie KG, et al. Efficacy and safety of midodrine hydrochloride in patients with refractory vasovagal syncope. Am J Cardiol. 2001;88:A780–3
378. Ward CR, Gray JC, Gilroy JJ, et al. Midodrine: a role in the management of neurocardiogenic syncope. Heart. 1998;79:45–9.
379. Romme JCM, van Dijk N, Go-Schön IK, et al. Effectiveness of midodrine treatment in patients with recurrent vasovagal syncope not responding to non-pharmacological treatment (STAND-trial). Europace. 2011;13:1639–47.
380. Kaufmann H, Saadia D, Voustianiouk A, et al. Norepinephrine precursor therapy in neurogenic orthostatic hypotension. Circulation. 2003;108:724–8.
381. Qingyou Z, Junbao D, Chaoshu T. The efficacy of midodrine hydrochloride in the treatment of children with vasovagal syncope. J Pediatr. 2006;149:777–80.
382. Duygu H, Zoghi M, Turk U, et al. The role of tilt training in preventing recurrent syncope in patients with vasovagal syncope: a prospective and randomized study. Pacing Clin Electrophysiol. 2008;31:592–6.
383. Foglia-Manzillo G, Giada F, Gaggioli G, et al. Efficacy of tilt training in the treatment of neurally mediated syncope. A randomized study. Europace. 2004;6:199–204.
384. Kinay O, Yazici M, Nazli C, et al. Tilt training for recurrent neurocardiogenic syncope: effectiveness, patient compliance, and scheduling the frequency of training sessions. Jpn Heart J. 2004;45:833–43.
385. On YK, Park J, Huh J, et al. Is home orthostatic self-training effective in preventing neurally mediated syncope? Pacing Clin Electrophysiol. 2007;30:638–43.
386. Reybrouck T, Heidbüchel H, Van De Werf F, et al. Long-term follow-up results of tilt training therapy in patients with recurrent neurocardiogenic syncope. Pacing Clin Electrophysiol. 2002;25:1441–6.
387. Di Girolamo E, Di Iorio C, Leonzio L, et al. Usefulness of a tilt training program for the prevention of refractory neurocardiogenic syncope in adolescents: A controlled study. Circulation. 1999;100:1798–801.
388. Sheldon R, Raj SR, Rose MS, et al. Fludrocortisone for the prevention of vasovagal syncope: a randomized, placebo-Controlled trial. J Am Coll Cardiol. 2016;68:1–9.
389. Salim MA, Di Sessa TG. Effectiveness of fludrocortisone and salt in preventing syncope recurrence in children: a double-blind, placebo-controlled, randomized trial. J Am Coll Cardiol. 2005;45:484–8.
390. Brignole M, Menozzi C, Gianfranchi L, et al. A controlled trial of acute and long-term medical therapy in tilt-induced neurally mediated syncope. Am J Cardiol. 1992;70:339–42.
391. Flevari P, Livanis EG, Theodorakis GN, et al. Vasovagal syncope: a prospective, randomized, crossover evaluation of the effect of propranolol, nadolol and placebo on syncope recurrence and patients' well-being. J Am Coll Cardiol. 2002;40:499–504.
392. Sheldon R, Connolly S, Rose S, et al. Prevention of Syncope Trial (POST): a randomized, placebo-controlled study of metoprolol in the prevention of vasovagal syncope. Circulation. 2006;113:1164–70.
393. Theodorakis GN, Leftheriotis D, Livanis EG, et al. Fluoxetine vs. propranolol in the treatment of vasovagal syncope: a prospective, randomized, placebo-controlled study. Europace. 2006;8:193–8.
394. Sheldon RS, Morillo CA, Klingenheben T, et al. Age-dependent effect of beta-blockers in preventing vasovagal syncope. Circ Arrhythm Electrophysiol. 2012;5:920–6.
395. Sheldon R, Rose S, Flanagan P, et al. Effect of beta blockers on the time to first syncope recurrence in patients after a positive isoproterenol tilt table test. Am J Cardiol. 1996;78:536–9.
396. El-Sayed H, Hainsworth R. Salt supplement increases plasma volume and orthostatic tolerance in patients with unexplained syncope. Heart. 1996;75:134–40.
397. Lu CC, Li MH, Ho ST, et al. Glucose reduces the effect of water to promote orthostatic tolerance. Am J Hypertens. 2008;21:1177–82.
398. Schroeder C, Bush VE, Norcliffe LJ, et al. Water drinking acutely improves orthostatic tolerance in healthy subjects. Circulation. 2002;106:2806–11.
399. Pitt MS, Hainsworth R. Contrasting effects of carbohydrate and water on blood pressure responses to postural maneuvers in patients with posturally related (vasovagal) syncope. Clin Auton Res. 2004;14:249–54.
400. Gaggioli G, Bottoni N, Mureddu R, et al. Effects of chronic vasodilator therapy to enhance susceptibility to vasovagal syncope during upright tilt testing. Am J Cardiol. 1997;80:1092–4.
401. Di Girolamo E, Di Iorio C, Sabatini P, et al. Effects of paroxetine hydrochloride, a selective serotonin reuptake inhibitor, on refractory vasovagal syncope: a randomized, double-blind, placebo-controlled study. J Am Coll Cardiol. 1999;33:1227–30.
402. Takata TS, Wasmund SL, Smith ML, et al. Serotonin reuptake inhibitor (Paxil) does not prevent the vasovagal reaction associated with carotid sinus massage and/or lower body negative pressure in healthy volunteers. Circulation. 2002;106:1500–4.
403. Grubb BP, Samoil D, Kosinski D, et al. Fluoxetine hydrochloride for the treatment of severe refractory orthostatic hypotension. Am J Med. 1994;97:366–8.
404. Ammirati F, Colivicchi F, Santini M. Permanent cardiac pacing versus medical treatment for the prevention of recurrent vasovagal syncope: a multicenter, randomized, controlled trial. Circulation. 2001;104:52–7.
405. Brignole M, Menozzi C, Moya A, et al. Pacemaker therapy in patients with neurally mediated syncope and documented asystole: Third International Study on Syncope of Uncertain Etiology (ISSUE-3): a randomized trial. Circulation. 2012;125:2566–71.
406. Connolly SJ, Sheldon R, Roberts RS, et al. The North American Vasovagal Pacemaker Study (VPS). A randomized trial of permanent cardiac pacing for the prevention of vasovagal syncope. J Am Coll Cardiol. 1999;33:16–20.
407. Connolly SJ, Sheldon R, Thorpe KE, et al. Pacemaker therapy for prevention of syncope in patients with recurrent severe vasovagal syncope: Second Vasovagal Pacemaker Study (VPS II): a randomized trial. JAMA. 2003;289:2224–9.
408. Raviele A, Giada F, Menozzi C, et al. A randomized, double-blind, placebo-controlled study of permanent cardiac pacing for the treatment of recurrent tilt-induced vasovagal syncope. The vasovagal syncope and pacing trial (SYNPACE). Eur Heart J. 2004;25:1741–8.
409. Sutton R. Pacing in patients with carotid sinus and vasovagal syndromes. Pacing Clin Electrophysiol. 1989;12:1260–3.
410. Sutton R, Brignole M, Menozzi C, et al. Dual-chamber pacing in the treatment of neurally mediated tilt-positive cardioinhibitory syncope: pacemaker versus no therapy: a multicenter randomized study. The Vasovagal Syncope International Study (VASIS) Investigators. Circulation. 2000;102:294–9.
411. Deharo JC, Guieu R, Mechulan A, et al. Syncope without prodromes in patients with normal heart and normal electrocardiogram: a distinct entity. J Am Coll Cardiol. 2013;62:1075–80.
412. Occhetta E, Bortnik M, Audoglio R, et al. Closed loop stimulation in prevention of vasovagal syncope. Inotropy Controlled Pacing in Vasovagal Syncope (INVASY): a multicentre randomized, single blind, controlled study. Europace. 2004;6:538–47.
413. Brignole M, Menozzi C, Lolli G, et al. Long-term outcome of paced and nonpaced patients with severe carotid sinus syndrome. Am J Cardiol. 1992;69:1039–43.
414. Thomas JE. Hyperactive carotid sinus reflex and carotid sinus syncope. Mayo Clin Proc. 1969;44:127–39.
415. Healey J, Connolly SJ, Morillo CA. The management of patients with carotid sinus syndrome: is pacing the answer? Clin Auton Res. 2004;14 suppl 1:80–6.
416. Miller VM, Kenny RA, Slade JY, et al. Medullary autonomic pathology in carotid sinus hypersensitivity. Neuropathol Appl Neurobiol. 2008;34:403–11.

417. Puggioni E, Guiducci V, Brignole M, et al. Results and complications of the carotid sinus massage performed according to the "method of symptoms". Am J Cardiol. 2002;89:599–601.
418. Munro NC, McIntosh S, Lawson J, et al. Incidence of complications after carotid sinus massage in older patients with syncope. J Am Geriatr Soc. 1994;42:1248–51.
419. Brignole M, Menozzi C. The natural history of carotid sinus syncope and the effect of cardiac pacing. Europace. 2011;13:462–4.
420. Brignole M, Deharo JC, De Roy L, et al. Syncope due to idiopathic paroxysmal atrioventricular block: long-term follow-up of a distinct form of atrioventricular block. J Am Coll Cardiol. 2011;58:167–73.
421. Claesson JE, Kristensson BE, Edvardsson N, et al. Less syncope and milder symptoms in patients treated with pacing for induced cardioinhibitory carotid sinus syndrome: a randomized study. Europace. 2007;9:932–6.
422. Parry SW, Steen N, Bexton RS, et al. Pacing in elderly recurrent fallers with carotid sinus hypersensitivity: a randomised, double-blind, placebo controlled crossover trial. Heart. 2009;95:405–9.
423. Lopes R, Gonçalves A, Campos J, et al. The role of pacemaker in hypersensitive carotid sinus syndrome. Europace. 2011;13:572–5.
424. Maggi R, Menozzi C, Brignole M, et al. Cardioinhibitory carotid sinus hypersensitivity predicts an asystolic mechanism of spontaneous neurally mediated syncope. Europace. 2007;9:563–7.
425. Gaggioli G, Brignole M, Menozzi C, et al. A positive response to head-up tilt testing predicts syncopal recurrence in carotid sinus syndrome patients with permanent pacemakers. Am J Cardiol. 1995;76:720–2.
426. Sugrue DD, Gersh BJ, Holmes DR Jr, et al. Symptomatic "isolated" carotid sinus hypersensitivity: natural history and results of treatment with anticholinergic drugs or pacemaker. J Am Coll Cardiol. 1986;7:158–62.
427. Brignole M, Sartore B, Barra M, et al. Is DDD superior to VVI pacing in mixed carotid sinus syndrome? An acute and medium-term study. Pacing Clin Electrophysiol. 1988;11:1902–10.
428. Madigan NP, Flaker GC, Curtis JJ, et al. Carotid sinus hypersensitivity: beneficial effects of dual-chamber pacing. Am J Cardiol. 1984;53:1034–40.
429. McLeod CJ, Trusty JM, Jenkins SM, et al. Method of pacing does not affect the recurrence of syncope in carotid sinus syndrome. Pacing Clin Electrophysiol. 2012;35:827–33.
430. Morley CA, Perrins EJ, Grant P, et al. Carotid sinus syncope treated by pacing. Analysis of persistent symptoms and role of atrioventricular sequential pacing. Br Heart J. 1982;47:411–8.
431. Allan L, Johns E, Doshi M, et al. Abnormalities of sympathetic and parasympathetic autonomic function in subjects with defaecation syncope. Europace. 2004;6:192–8.
432. Bae MH, Kang JK, Kim NY, et al. Clinical characteristics of defecation and micturition syncope compared with common vasovagal syncope. Pacing Clin Electrophysiol. 2012;35:341–7.
433. Bonekat HW, Miles RM, Staats BA. Smoking and cough syncope: follow-up in 45 cases. Int J Addict. 1987;22:413–9.
434. Dicpinigaitis PV, Lim L, Farmakidis C. Cough syncope. Respir Med. 2014;108:244–51.
435. Garg S, Girotra M, Glasser S, et al. Swallow syncope: clinical presentation, diagnostic criteria, and therapeutic options. Saudi J Gastroenterol. 2014;20:207–11.
436. Kapoor WN, Peterson JR, Karpf M. Micturition syncope. A reappraisal. JAMA. 1985;253:796–8.
437. Komatsu K, Sumiyoshi M, Abe H, et al. Clinical characteristics of defecation syncope compared with micturition syncope. Circ J. 2010;74:307–11.
438. Anley C, Noakes T, Collins M, et al. A comparison of two treatment protocols in the management of exercise-associated postural hypotension: a randomised clinical trial. Br J Sports Med. 2011;45:1113–8.
439. Raj SR, Biaggioni I, Black BK, et al. Sodium paradoxically reduces the gastropressor response in patients with orthostatic hypotension. Hypertension. 2006;48:329–34.
440. Humm AM, Mason LM, Mathias CJ. Effects of water drinking on cardiovascular responses to supine exercise and on orthostatic hypotension after exercise in pure autonomic failure. J Neurol Neurosurg Psychiatr. 2008;79:1160–4.
441. Jordan J, Shannon JR, Grogan E, et al. A potent pressor response elicited by drinking water. Lancet. 1999;353:723.
442. Jordan J, Shannon JR, Black BK, et al. The pressor response to water drinking in humans: a sympathetic reflex? Circulation. 2000;101:504–9.
443. Shannon JR, Diedrich A, Biaggioni I, et al. Water drinking as a treatment for orthostatic syndromes. Am J Med. 2002;112:355–60.
444. Young TM, Mathias CJ. The effects of water ingestion on orthostatic hypotension in two groups of chronic autonomic failure: multiple system atrophy and pure autonomic failure. J Neurol Neurosurg Psychiatr. 2004;75:1737–41.
445. Clarke DA, Medow MS, Taneja I, et al. Initial orthostatic hypotension in the young is attenuated by static handgrip. J Pediatr. 2010;156:1019–22, 22.e1.
446. Krediet CTP, van Lieshout JJ, Bogert LWJ, et al. Leg crossing improves orthostatic tolerance in healthy subjects: a placebo-controlled crossover study. Am J Physiol Heart Circ Physiol. 2006;291:H1768–72.
447. ten Harkel AD, van Lieshout JJ, Wieling W. Effects of leg muscle pumping and tensing on orthostatic arterial pressure: a study in normal subjects and patients with autonomic failure. Clin Sci. 1994;87:553–8.
448. Thijs RD, Wieling W, van den Aardweg JG, et al. Respiratory countermaneuvers in autonomic failure. Neurology. 2007;69:582–5.
449. Tutaj M, Marthol H, Berlin D, et al. Effect of physical countermaneuvers on orthostatic hypotension in familial dysautonomia. J Neurol. 2006;253:65–72.
450. van Lieshout JJ, ten Harkel AD, Wieling W. Physical manoeuvres for combating orthostatic dizziness in autonomic failure. Lancet. 1992;339:897–8.
451. Denq JC, Opfer-Gehrking TL, Giuliani M, et al. Efficacy of compression of different capacitance beds in the amelioration of orthostatic hypotension. Clin Auton Res. 1997;7:321–6.
452. Platts SH, Tuxhorn JA, Ribeiro LC, et al. Compression garments as countermeasures to orthostatic intolerance. Aviat Space Environ Med. 2009;80:437–42.
453. Podoleanu C, Maggi R, Brignole M, et al. Lower limb and abdominal compression bandages prevent progressive orthostatic hypotension in elderly persons: a randomized single-blind controlled study. J Am Coll Cardiol. 2006;48:1425–32.
454. Figueroa JJ, Singer W, Sandroni P, et al. Effects of patient-controlled abdominal compression on standing systolic blood pressure in adults with orthostatic hypotension. Arch Phys Med Rehabil. 2015;96:505–10.
455. Yamamoto N, Sasaki E, Goda K, et al. Treatment of post-dialytic orthostatic hypotension with an inflatable abdominal band in hemodialysis patients. Kidney Int. 2006;70:1793–800.
456. Henry R, Rowe J, O'Mahony D. Haemodynamic analysis of efficacy of compression hosiery in elderly fallers with orthostatic hypotension. Lancet. 1999;354:45–6.
457. Protheroe CL, Dikareva A, Menon C, et al. Are compression stockings an effective treatment for orthostatic presyncope? PLoS ONE. 2011;6:e28193
458. Axelrod FB, Krey L, Glickstein JS, et al. Preliminary observations on the use of midodrine in treating orthostatic hypotension in familial dysautonomia. J Auton Nerv Syst. 1995;55:29–35.
459. Fouad-Tarazi FM, Okabe M, Goren H. Alpha sympathomimetic treatment of autonomic insufficiency with orthostatic hypotension. Am J Med. 1995;99:604–10.
460. Jankovic J, Gilden JL, Hiner BC, et al. Neurogenic orthostatic hypotension: a double-blind, placebo-controlled study with midodrine. Am J Med. 1993;95:38–48.
461. Jordan J, Shannon JR, Biaggioni I, et al. Contrasting actions of pressor agents in severe autonomic failure. Am J Med. 1998;105:116–24.
462. Kaufmann H, Brannan T, Krakoff L, et al. Treatment of orthostatic hypotension due to autonomic failure with a peripheral alpha-adrenergic agonist (midodrine). Neurology. 1988;38:951–6.
463. Low PA, Gilden JL, Freeman R, et al. Efficacy of midodrine vs placebo in neurogenic orthostatic hypotension. A randomized, double-blind multicenter study. Midodrine Study Group. JAMA. 1997;277:1046–51.
464. Phillips AA, Krassioukov AV, Ainslie PN, et al. Perturbed and spontaneous regional cerebral blood flow responses to changes in blood pressure after high-level spinal cord injury: the effect of midodrine. J Appl Physiol. 2014;116:645–53.
465. Ramirez CE, Okamoto LE, Arnold AC, et al. Efficacy of atomoxetine versus midodrine for the treatment of orthostatic hypotension in autonomic failure. Hypertension. 2014;64:1235–40.
466. Singer W, Sandroni P, Opfer-Gehrking TL, et al. Pyridostigmine treatment trial in neurogenic orthostatic hypotension. Arch Neurol. 2006;63:513–8.
467. Wright RA, Kaufmann HC, Perera R, et al. A double-blind, dose-response study of midodrine in neurogenic orthostatic hypotension. Neurology. 1998;51:120–4.

468. Biaggioni I, Freeman R, Mathias CJ, et al. Randomized withdrawal study of patients with symptomatic neurogenic orthostatic hypotension responsive to droxidopa. Hypertension. 2015;65:101–7.
469. Freeman R, Landsberg L, Young J. The treatment of neurogenic orthostatic hypotension with 3,4-DL-threo-dihydroxyphenylserine: a randomized, placebo-controlled, crossover trial. Neurology. 1999;53:2151–7.
470. Kaufmann H, Freeman R, Biaggioni I, et al. Droxidopa for neurogenic orthostatic hypotension: a randomized, placebo-controlled, phase 3 trial. Neurology. 2014;83:328–35.
471. Mathias CJ, Senard JM, Braune S, et al. L-threo-dihydroxyphenylserine (L-threo-DOPS; droxidopa) in the management of neurogenic orthostatic hypotension: a multi-national, multi-center, dose-ranging study in multiple system atrophy and pure autonomic failure. Clin Auton Res. 2001;11:235–42.
472. Hauser RA, Hewitt LA, Isaacson S. Droxidopa in patients with neurogenic orthostatic hypotension associated with Parkinson's disease (NOH306A). J Parkinsons Dis. 2014;4:57–65.
473. Campbell IW, Ewing DJ, Clarke BF. 9-Alpha-fluorohydrocortisone in the treatment of postural hypotension in diabetic autonomic neuropathy. Diabetes. 1975;24:381–4.
474. Kochar MS, Itskovitz HD. Treatment of idiopathic orthostatic hypotension (Shy-Drager syndrome) with indomethacin. Lancet. 1978;1:1011–4.
475. Schoffer KL, Henderson RD, O'Maley K, et al. Nonpharmacological treatment, fludrocortisone, and domperidone for orthostatic hypotension in Parkinson's disease. Mov Disord. 2007;22:1543–9.
476. Vernikos J, Convertino VA. Advantages and disadvantages of fludrocortisone or saline load in preventing post-spaceflight orthostatic hypotension. Acta Astronaut. 1994;33:259–66.
477. Rowe PC, Calkins H, DeBusk K, et al. Fludrocortisone acetate to treat neurally mediated hypotension in chronic fatigue syndrome: a randomized controlled trial. JAMA. 2001;285:52–9.
478. Shi SJ, South DA, Meck JV. Fludrocortisone does not prevent orthostatic hypotension in astronauts after spaceflight. Aviat Space Environ Med. 2004;75:235–9.
479. Gupta V, Lipsitz LA. Orthostatic hypotension in the elderly: diagnosis and treatment. Am J Med. 2007;120:841–7.
480. Coursin DB, Wood KE. Corticosteroid supplementation for adrenal insufficiency. JAMA. 2002;287:236–40.
481. Shibao C, Okamoto LE, Gamboa A, et al. Comparative efficacy of yohimbine against pyridostigmine for the treatment of orthostatic hypotension in autonomic failure. Hypertension. 2010;56:847–51.
482. Singer W, Opfer-Gehrking TL, Nickander KK, et al. Acetylcholinesterase inhibition in patients with orthostatic intolerance. J Clin Neurophysiol. 2006;23:476–81.
483. Gales BJ, Gales MA. Pyridostigmine in the treatment of orthostatic intolerance. Ann Pharmacother. 2007;41:314–8.
484. Bordet R, Benhadjali J, Destée A, et al. Octreotide effects on orthostatic hypotension in patients with multiple system atrophy: a controlled study of acute administration. Clin Neuropharmacol. 1995;18:83–9.
485. Hoeldtke RD, Dworkin GE, Gaspar SR, et al. Effect of the somatostatin analogue SMS-201–995 on the adrenergic response to glucose ingestion in patients with postprandial hypotension. Am J Med. 1989;86:673–7.
486. Jarvis SS, Florian JP, Curren MJ, et al. A somatostatin analog improves tilt table tolerance by decreasing splanchnic vascular conductance. J Appl Physiol. 2012;112:1504–11.
487. Raimbach SJ, Cortelli P, Kooner JS, et al. Prevention of glucose-induced hypotension by the somatostatin analogue octreotide (SMS 201–995) in chronic autonomic failure: haemodynamic and hormonal changes. Clin Sci (Lond). 1989;77:623–8.
488. Craig GM. Clinical presentation of orthostatic hypotension in the elderly. Postgrad Med J. 1994;70:638–42.
489. McLachlan CY.L, Yi M, Ling A, et al. Adverse drug events are a major cause of acute medical admission. Intern Med J. 2014;44:633–8.
490. Poon IO, Braun U. High prevalence of orthostatic hypotension and its correlation with potentially causative medications among elderly veterans. J Clin Pharm Ther. 2005;30:173–8.
491. Beckett NS, Connor M, Sadler JD, et al. Orthostatic fall in blood pressure in the very elderly hypertensive: results from the hypertension in the very elderly trial (HYVET) - pilot. J Hum Hypertens. 1999;13:839–40.
492. Fotherby MD, Potter JF. Orthostatic hypotension and anti-hypertensive therapy in the elderly. Postgrad Med J. 1994;70:878–81.
493. Räihä I, Luutonen S, Piha J, et al. Prevalence, predisposing factors, and prognostic importance of postural hypotension. Arch Intern Med. 1995;155:930–5.
494. Perner A, De Backer D. Understanding hypovolaemia. Intensive Care Med. 2014;40:613–5.
495. Journeay WS, Reardon FD, Jean-Gilles S, et al. Lower body positive and negative pressure alter thermal and hemodynamic responses after exercise. Aviat Space Environ Med. 2004;75:841–9.
496. Huang JJ, Desai C, Singh N, et al. Summer syncope syndrome redux. Am J Med. 2015;128:1140–3.
497. Lucas RAI, Ganio MS, Pearson J, et al. Sweat loss during heat stress contributes to subsequent reductions in lower-body negative pressure tolerance. Exp Physiol. 2013;98:473–80.
498. Jeukendrup AE, Currell K, Clarke J, et al. Effect of beverage glucose and sodium content on fluid delivery. Nutr Metab (Lond). 2009;6:9.
499. Maughan RJ, Leiper JB. Sodium intake and post-exercise rehydration in man. Eur J Appl Physiol Occup Physiol. 1995;71:311–9.
500. Merson SJ, Maughan RJ, Shirreffs SM. Rehydration with drinks differing in sodium concentration and recovery from moderate exercise-induced hypohydration in man. Eur J Appl Physiol. 2008;103:585–94.
501. Shirreffs SM, Taylor AJ, Leiper JB, et al. Post-exercise rehydration in man: effects of volume consumed and drink sodium content. Med Sci Sports Exerc. 1996;28:1260–71.
502. Atherly-John YC, Cunningham SJ, Crain EF. A randomized trial of oral vs intravenous rehydration in a pediatric emergency department. Arch Pediatr Adolesc Med. 2002;156:1240–3.
503. Greenleaf JE, Jackson CG, Geelen G, et al. Plasma volume expansion with oral fluids in hypohydrated men at rest and during exercise. Aviat Space Environ Med. 1998;69:837–44.
504. Kenefick RW, O'Moore KM, Mahood NV, et al. Rapid IV versus oral rehydration: responses to subsequent exercise heat stress. Med Sci Sports Exerc. 2006;38:2125–31.
505. Holtzhausen LM, Noakes TD. The prevalence and significance of post-exercise (postural) hypotension in ultramarathon runners. Med Sci Sports Exerc. 1995;27:1595–601.
506. Evans GH, Shirreffs SM, Maughan RJ. Postexercise rehydration in man: the effects of osmolality and carbohydrate content of ingested drinks. Nutrition. 2009;25:905–13.
507. Blake AJ, Morgan K, Bendall MJ, et al. Falls by elderly people at home: prevalence and associated factors. Age Ageing. 1988;17:365–72.
508. Burke V, Beilin LJ, German R, et al. Postural fall in blood pressure in the elderly in relation to drug treatment and other lifestyle factors. Q J Med. 1992;84:583–91.
509. Jansen RW, Kelly-Gagnon MM, Lipsitz LA. Intraindividual reproducibility of postprandial and orthostatic blood pressure changes in older nursing-home patients: relationship with chronic use of cardiovascular medications. J Am Geriatr Soc. 1996;44:383–9.
510. Kamaruzzaman S, Watt H, Carson C, et al. The association between orthostatic hypotension and medication use in the British Women's Heart and Health Study. Age Ageing. 2010;39:51–6.
511. Ooi WL, Barrett S, Hossain M, et al. Patterns of orthostatic blood pressure change and their clinical correlates in a frail, elderly population. JAMA. 1997;277:1299–304.
512. Jodaitis L, Vaillant F, Snacken M, et al. Orthostatic hypotension and associated conditions in geriatric inpatients. Acta Clin Belg. 2015;70:251–8.
513. Panayiotou B, Saeed S, Fotherby M, et al. Antihypertensive therapy and orthostatic hemodynamic responses in acute stroke. Am J Hypertens. 2002;15:37–41.
514. Kanjwal K, Karabin B, Sheikh M, et al. Pyridostigmine in the treatment of postural orthostatic tachycardia: a single-center experience. Pacing Clin Electrophysiol. 2011;34:750–5.
515. Shibao C, Arzubiaga C, Roberts LJ, et al. Hyperadrenergic postural tachycardia syndrome in mast cell activation disorders. Hypertension. 2005;45:385–90.
516. Shibata S, Fu Q, Bivens TB, et al. Short-term exercise training improves the cardiovascular response to exercise in the postural orthostatic tachycardia syndrome. J Physiol. 2012;590:3495–505.
517. Fu Q, Vangundy TB, Shibata S, et al. Exercise training versus propranolol in the treatment of the postural orthostatic tachycardia syndrome. Hypertension. 2011;58:167–75.
518. Gaffney FA, Lane LB, Pettinger W, et al. Effects of long-term clonidine administration on the hemodynamic and neuroendocrine postural responses of patients with dysautonomia. Chest. 1983;83:436–8.
519. Green EA, Raj V, Shibao CA, et al. Effects of norepinephrine reuptake inhibition on postural tachycardia syndrome. J Am Heart Assoc. 2013;2:e000395.

520. Raj SR, Black BK, Biaggioni I, et al. Propranolol decreases tachycardia and improves symptoms in the postural tachycardia syndrome: less is more. Circulation. 2009;120:725–34.
521. Ross AJ, Ocon AJ, Medow MS, et al. A double-blind placebo-controlled cross-over study of the vascular effects of midodrine in neuropathic compared with hyperadrenergic postural tachycardia syndrome. Clin Sci. 2014;126:289–96.
522. Figueroa RA, Arnold AC, Nwazue VC, et al. Acute volume loading and exercise capacity in postural tachycardia syndrome. J Appl Physiol. 2014;117:663–8.
523. Garland EM, Robertson D. Chiari I malformation as a cause of orthostatic intolerance symptoms: a media myth? Am J Med. 2001;111: 546–52.
524. Hubsch C, Baumann C, Hingray C, et al. Clinical classification of psychogenic non-epileptic seizures based on video-EEG analysis and automatic clustering. J Neurol Neurosurg Psychiatr. 2011;82:955–60.
525. Iglesias JF, Graf D, Forclaz A, et al. Stepwise evaluation of unexplained syncope in a large ambulatory population. Pacing Clin Electrophysiol. 2009;32 Suppl 1:S202–6.
526. Elliott JO, Charyton C. Biopsychosocial predictors of psychogenic non-epileptic seizures. Epilepsy Res. 2014;108:1543–53.
527. Mayor R, Howlett S, Grünewald R, et al. Long-term outcome of brief augmented psychodynamic interpersonal therapy for psychogenic non-epileptic seizures: seizure control and health care utilization. Epilepsia. 2010;51:1169–76.
528. Mayor R, Brown RJ, Cock H, et al. Short-term outcome of psychogenic non-epileptic seizures after communication of the diagnosis. Epilepsy Behav. 2012;25:676–81.
529. LaFrance WC Jr, Keitner GI, Papandonatos GD, et al. Pilot pharmacologic randomized controlled trial for psychogenic nonepileptic seizures. Neurology. 2010;75:1166–73.
530. Goldstein LH, Chalder T, Chigwedere C, et al. Cognitive-behavioral therapy for psychogenic nonepileptic seizures: a pilot RCT. Neurology. 2010;74:1986–94.
531. Reuber M, Burness C, Howlett S, et al. Tailored psychotherapy for patients with functional neurological symptoms: a pilot study. J Psychosom Res. 2007;63:625–32.
532. Santos NdO, Benute GRG, Santiago A, et al. Psychogenic non-epileptic seizures and psychoanalytical treatment: results. Rev Assoc Med Bras. 2014;60:577–84.
533. Zeng W, Deng H. Cough syncope: constrictive pericarditis. Intern Med. 2013;52:463–5.
534. Guaricci AI, Basso C, Tarantini G. Recurrent syncope on effort due to concealed constrictive pericarditis. Eur Heart J. 2013;34:1817
535. Dhar R, Duke RJ, Sealey BJ. Cough syncope from constrictive pericarditis: a case report. Can J Cardiol. 2003;19:295–6.
536. Vasquez AF, Seger JJ. An uncommon case of heart failure. South Med J. 2009;102:1183–5.
537. Sviggum HP, Kopp SL, Rettke SR, et al. Perioperative complications in patients with left ventricular non-compaction. Eur J Anaesthesiol. 2011;28:207–12.
538. Koh C, Lee PW, Yung TC, et al. Left ventricular noncompaction in children. Congenit Heart Dis. 2009;4:288–94.
539. Enriquez SG, Entem FR, Cobo M, et al. Uncommon etiology of syncope in a patient with isolated ventricular noncompaction. Pacing Clin Electrophysiol. 2007;30:577–9.
540. Rovetta R, Bonadei I, Vizzardi E, et al. Syncope as presentation of recurrent Tako-Tsubo cardiomyopathy. Minerva Cardioangiol. 2014;62:366–8.
541. Yoshida T, Hibino T, Fujimaki T, et al. Transient mid-ventricular ballooning syndrome complicated by syncope: a variant of tako-tsubo cardiomyopathy. Int J Cardiol. 2009;135:e20–e23.
542. Tisserand G, Gil H, Méaux-Ruault N, et al. [Clinical features of pulmonary embolism in elderly: a comparative study of 64 patients]. Rev Med Interne. 2014;35:353–6.
543. Chakraborty A, Jutley G. Isolated syncope - an uncommon presenting feature of pulmonary embolism. Acute Med. 2011;10:79–80.
544. Linhart A, Kampmann C, Zamorano JL, et al. Cardiac manifestations of Anderson-Fabry disease: results from the international Fabry outcome survey. Eur Heart J. 2007;28:1228–35.
545. Acharya D, Robertson P, Kay GN, et al. Arrhythmias in Fabry cardiomyopathy. Clin Cardiol. 2012;35:738–40.
546. Hwang YT, Tseng CD, Hwang JJ, et al. Cardiac amyloidosis presenting as sick sinus syndrome and intractable heart failure: report of a case. J Formos Med Assoc. 1993;92:283–7.
547. Velazquez-Ceceña JL, Lubell DL, Nagajothi N, et al. Syncope from dynamic left ventricular outflow tract obstruction simulating hypertrophic cardiomyopathy in a patient with primary AL-type amyloid heart disease. Tex Heart Inst J. 2009;36:50–4.
548. Strobel JS, Fuisz AR, Epstein AE, et al. Syncope and inducible ventricular fibrillation in a woman with hemochromatosis. J Interv Card Electrophysiol. 1999;3:225–9.
549. Akashi R, Kizaki Y, Kawano H, et al. Seizures and syncope due to complete atrioventricular block in a patient with acute myocarditis with a normal left ventricular systolic function. Intern Med. 2012;51:3035–40.
550. Mancio J, Bettencourt N, Oliveira M, et al. Acute right ventricular myocarditis presenting with chest pain and syncope. BMJ Case Rep. 2013;2013.
551. Patel RAG, DiMarco JP, Akar JG, et al. Chagas myocarditis and syncope. J Cardiovasc Magn Reson. 2005;7:685–8.
552. Lopez JA, Treistman B, Massumi A. Myocarditis-associated ventricular fibrillation. An unusual cause of syncope in Wolff-Parkinson-White syndrome. Tex Heart Inst J. 1995;22:335–8.
553. Dhar KL, Adlakha A, Phillip PJ. Recurrent seizures and syncope, ventricular arrhythmias with reversible prolonged Q-Tc interval in typhoid myocarditis. J Indian Med Assoc. 1987;85:336–7.
554. Manek M, Kulkarni A, Viera A. Hint of Lyme, an uncommon cause of syncope. BMJ Case Rep. 2014;2014
555. Ciesielski CA, Markowitz LE, Horsley R, et al. Lyme disease surveillance in the United States, 1983–1986. Rev Infect Dis. 1989;11 suppl 6:S1435–41.
556. Rassi A Jr, Rassi A, Marin-Neto JA. Chagas disease. Lancet. 2010;375:1388–402.
557. de Souza ACJ, Salles G, Hasslocher-Moreno AM, et al. Development of a risk score to predict sudden death in patients with Chaga's heart disease. Int J Cardiol. 2015;187:700–4.
558. Leite LR, Fenelon G, Paes AT, et al. The impact of syncope during clinical presentation of sustained ventricular tachycardia on total and cardiac mortality in patients with chronic Chagasic heart disease. Arq Bras Cardiol. 2001;77:439–52.
559. Martinelli Filho M, Sosa E, Nishioka S, et al. Clinical and electrophysiologic features of syncope in chronic chagasic heart disease. J Cardiovasc Electrophysiol. 1994;5:563–70.
560. Josephson ME, Wellens HJJ. Syncope in a patient with myotonic dystrophy. Heart Rhythm. 2015;12:1882–3.
561. Finsterer J, Stöllberger C, Gencik M, et al. Syncope and hyperCKemia as minimal manifestations of short CTG repeat expansions in myotonic dystrophy type 1. Rev Port Cardiol. 2015;34:361–4.
562. Brescia ST, Rossano JW, Pignatelli R, et al. Mortality and sudden death in pediatric left ventricular noncompaction in a tertiary referral center. Circulation. 2013;127:2202–8.
563. Bhatia NL, Tajik AJ, Wilansky S, et al. Isolated noncompaction of the left ventricular myocardium in adults: a systematic overview. J Card Fail. 2011;17:771–8.
564. Hernández-Luis C, García-Morán E, Rubio-Sanz J, et al. [Kearns-Sayre syndrome: recurrent syncope and atrial flutter]. Rev Esp Cardiol. 2007;60:89–90.
565. Letsas KP, Efremidis M, Pappas LK, et al. Pathophysiology and management of syncope in Kearns-Sayre syndrome. Am Heart Hosp J. 2006;4:301–2.
566. Konety SH, Horwitz P, Lindower P, et al. Arrhythmias in tako-tsubo syndrome–benign or malignant? Int J Cardiol. 2007;114:141–4.
567. Alampi G, Nuzzo F, Ronchi E, et al. [Lipomatous hypertrophy and Lev-Lenègre disease]. Cardiologia. 1986;31:67–70.
568. Bracchi G, Vezzoli F, Rossi L. [The pathology of the primitive or idiopathic block (disease of Lenègre and Lev). Critical review and personal casuistic (author's transl)]. G Ital Cardiol. 1973;3:509–18.
569. Barlow JB. Lev's or Lenègre's disease? J Cardiovasc Electrophysiol. 1994;5:897
570. Stéphan E, Aftimos G, Allam C. Familial fascicular block: histologic features of Lev's disease. Am Heart J. 1985;109:1399–401.
571. Rasmussen KS, Paulsen SM. [Total atrioventricular block caused by dystrophic calcification: Lev's disease]. Ugeskr Laeg. 1980;142:2986–7.
572. Dubrey SW, Hawkins PN, Falk RH. Amyloid diseases of the heart: assessment, diagnosis, and referral. Heart. 2011;97:75–84.
573. Kaul P, Adluri K, Javangula K, et al. Successful management of multiple permanent pacemaker complications—infection, 13 year old silent lead perforation and exteriorisation following failed percutaneous extraction, superior vena cava obstruction, tricuspid valve endocarditis, pulmonary embolism and prosthetic tricuspid valve thrombosis. J Cardiothorac Surg. 2009;4:12

574. Garg NK, Kapoor A, Sinha N. Intermittent electromechanical dissociation due to mechanical prosthetic valve dysfunction. J Heart Valve Dis. 2000;9:466–8.
575. Silber H, Khan SS, Matloff JM, et al. The St. Jude valve. Thrombolysis as the first line of therapy for cardiac valve thrombosis. Circulation. 1993;87:30–7.
576. Isner JM, Hawley RJ, Weintraub AM, et al. Cardiac findings in Charcot-Marie-Tooth disease. A prospective study of 68 patients. Arch Intern Med. 1979;139:1161–5.
577. Santos I, Martín de Dios R, Barrios V, et al. [Anomalous origin of the right coronary artery from the left sinus of Valsalva. Apropos of 2 cases]. Rev Esp Cardiol. 1991;44:618–21.
578. Hassan WS, Al-Habeeb WA, El-Shaer FE, et al. Exertional dizziness and syncope caused by anomalous left coronary artery origin from the right sinus of Valsalva. Saudi Med J. 2004;25:1720–2.
579. Lilly SM, Schussler JM, Stoler RC. Anomalous origin of the right coronary artery from the left sinus of Valsalva associated with syncope in a young athlete. Proc (Bayl Univ Med Cent). 2011;24:13–4.
580. Groh WJ, Bhakta D. Arrhythmia management in myotonic dystrophy type 1. JAMA. 2012;308:337–8; author reply 8.
581. Kuhlmann TP, Powers RD. Painless aortic dissection: an unusual cause of syncope. Ann Emerg Med. 1984;13:549–51.
582. Gilon D, Mehta RH, Oh JK, et al. Characteristics and in-hospital outcomes of patients with cardiac tamponade complicating type A acute aortic dissection. Am J Cardiol. 2009;103:1029–31.
583. Hashim PW, Assi R, Grecu L, et al. Symptomatic obstruction of the brachiocephalic and left subclavian arteries obscured by aortic stenosis. Ann Vasc Surg. 2014;28:737.e1–5.
584. Peera MA, LoCurto M, Elfond M. A case of Takayasu arteritis causing subclavian steal and presenting as syncope. J Emerg Med. 2011;40:158–61.
585. Akdemir R, Ozhan H, Tataroglu C. Coronary-subclavian steal syndrome presenting with chest pain and syncope. Acta Cardiol. 2004;59:665–7.
586. Chan-Tack KM. Subclavian steal syndrome: a rare but important cause of syncope. South Med J. 2001;94:445–7.
587. Perryman RA, Bayne E, Miller RH. Bull-worker syncope: congenital subclavian steal syndrome following isometric exercise. Pediatr Cardiol. 1991;12:105–6.
588. Squarzoni G, Bariani L, Fogli B, et al. [Arterial hypertension and syncope in an adult patient with coarctation of the aorta]. Riv Eur Sci Med Farmacol. 1991;13:33–5.
589. Ahern M, Lever JV, Cosh J. Complete heart block in rheumatoid arthritis. Ann Rheum Dis. 1983;42:389–97.
590. Villamayor-Blanco B, Arias M, Sesar-Ignacio A, et al. [Headache and fainting as initial symptoms of syringomyelia associated to Arnold-Chiari and facial angiomatous nevus]. Rev Neurol. 2004;38:1035–7.
591. Massimi L, Della Pepa GM, Caldarelli M, et al. Abrupt clinical onset of Chiari type I/syringomyelia complex: clinical and physiopathological implications. Neurosurg Rev. 2012;35:321–9; discussion 9.
592. Montfort J, Maher R, Grieve SM, et al. Syringomyelia: a rare extracardiac contributor to syncope detected incidentally by CMR. Int J Cardiol. 2011;150:e62–e64.
593. Masson C, Colombani JM. [Chiari type 1 malformation and magnetic resonance imaging]. Presse Med. 2005;34:1662–7.
594. Ziegler DK, Mallonee W. Chiari-1 malformation, migraine, and sudden death. Headache. 1999;39:38–41.
595. Arias M, Castillo J, Castro A, et al. [Syncope as the initial manifestation of syringomyelia associated with an Arnold-Chiari abnormality: diagnostic value of computerized tomography]. Med Clin (Barc). 1986;86:550–1.
596. Hampton F, Williams B, Loizou LA. Syncope as a presenting feature of hindbrain herniation with syringomyelia. J Neurol Neurosurg Psychiatr. 1982;45:919–22.
597. Williams B. Simultaneous cerebral and spinal fluid pressure recordings. 2. Cerebrospinal dissociation with lesions at the foramen magnum. Acta Neurochir (Wien). 1981;59:123–42.
598. Mangubat EZ, Wilson T, Mitchell BA, et al. Chiari I malformation associated with atlanto-occipital assimilation presenting as orthopnea and cough syncope. J Clin Neurosci. 2014;21:320–3.
599. Child JS, Perloff JK, Bach PM, et al. Cardiac involvement in Friedreich's ataxia: a clinical study of 75 patients. J Am Coll Cardiol. 1986;7:1370–8.
600. Ju JH, Kang MH, Kim HG, et al. Successful treatment of syncope with chemotherapy irresponsive to cardiac pacemaker in head and neck cancer. Yonsei Med J. 2009;50:725–8.
601. Okmen E, Erdinler I, Oguz E, et al. An unusual cause of reflex cardiovascular syncope: vagal paraganglioma. Ann Noninvasive Electrocardiol. 2003;8:173–6.
602. Suchard JR. Recurrent near-syncope with flushing. Acad Emerg Med. 1997;4:718–24.
603. Roshan J, George OK, Vineet S, et al. Torsade de pointes in a case of pheochromocytoma–an unusual presentation of an uncommon disease. Indian Heart J. 2004;56:248–9.
604. Castells M, Austen KF. Mastocytosis: mediator-related signs and symptoms. Int Arch Allergy Immunol. 2002;127:147–52.
605. Akin C. Anaphylaxis and mast cell disease: what is the risk? Curr Allergy Asthma Rep. 2010;10:34–8.
606. Bains SN, Hsieh FH. Current approaches to the diagnosis and treatment of systemic mastocytosis. Ann Allergy Asthma Immunol. 2010;104:1–10.
607. Shaffer HC, Parsons DJ, Peden DB, et al. Recurrent syncope and anaphylaxis as presentation of systemic mastocytosis in a pediatric patient: case report and literature review. J Am Acad Dermatol. 2006;54:S210–3.
608. Escribano L, Akin C, Castells M, et al. Current options in the treatment of mast cell mediator-related symptoms in mastocytosis. Inflamm Allergy Drug Targets. 2006;5:61–77.
609. Koide T, Nakajima T, Makifuchi T, et al. Systemic mastocytosis and recurrent anaphylactic shock. Lancet. 2002;359:2084
610. Kremastinos DT, Farmakis D, Aessopos A, et al. Beta-thalassemia cardiomyopathy: history, present considerations, and future perspectives. Circ Heart Fail. 2010;3:451–8.
611. Surges R, Scott CA, Walker MC. Peri-ictal atrioventricular conduction block in a patient with a lesion in the left insula: case report and review of the literature. Epilepsy Behav. 2009;16:347–9.
612. Schuele SU, Bermeo AC, Alexopoulos AV, et al. Video-electrographic and clinical features in patients with ictal asystole. Neurology. 2007;69:434–41.
613. Novy J, Carruzzo A, Pascale P, et al. Ictal bradycardia and asystole: an uncommon cause of syncope. Int J Cardiol. 2009;133:e90–3.
614. Monté CP.J.A, de Krom MCTFM, Weber WEJ, et al. The ictal bradycardia syndrome. Acta Neurol Belg. 2007;107:22–5.
615. Bruce CJ. Cardiac tumours: diagnosis and management. Heart. 2011;97:151–60.
616. Reynen K. Cardiac myxomas. N Engl J Med. 1995;333:1610–7.
617. Driscoll DJ, Jacobsen SJ, Porter CJ, et al. Syncope in children and adolescents. J Am Coll Cardiol. 1997;29:1039–45.
618. Massin MM, Bourguignont A, Coremans C, et al. Syncope in pediatric patients presenting to an emergency department. J Pediatr. 2004;145:223–8.
619. McLeod KA. Syncope in childhood. Arch Dis Child. 2003;88:350–3.
620. Chen L, Wang C, Wang H, et al. Underlying diseases in syncope of children in China. Med Sci Monit. 2011;17:PH49–PH53.
621. Brignole M, Alboni P, Benditt D, et al. Guidelines on management (diagnosis and treatment) of syncope. Eur Heart J. 2001;22:1256–306.
622. Lewis DA, Dhala A. Syncope in the pediatric patient. The cardiologist's perspective. Pediatr Clin North Am. 1999;46:205–19.
623. Kanjwal K, Calkins H. Syncope in children and adolescents. Cardiol Clin. 2015;33:397–409.
624. Lerman-Sagie T, Rechavia E, Strasberg B, et al. Head-up tilt for the evaluation of syncope of unknown origin in children. J Pediatr. 1991;118:676–9.
625. MacCormick JM, Crawford JR, Chung SK, et al. Symptoms and signs associated with syncope in young people with primary cardiac arrhythmias. Heart Lung Circ. 2011;20:593–8.
626. Ritter S, Tani LY, Etheridge SP, et al. What is the yield of screening echocardiography in pediatric syncope? Pediatrics. 2000;105:E58.
627. Tretter JT, Kavey RE.W. Distinguishing cardiac syncope from vasovagal syncope in a referral population. J Pediatr. 2013;163:1618–23.e1.
628. Vlahos AP, Kolettis TM. Family history of children and adolescents with neurocardiogenic syncope. Pediatr Cardiol. 2008;29:227.
629. Zhang Q, Du J, Wang C, et al. The diagnostic protocol in children and adolescents with syncope: a multi-centre prospective study. Acta Paediatr. 2009;98:879–84.
630. Zhang Q, Zhu L, Wang C, et al. Value of history taking in children and adolescents with cardiac syncope. Cardiol Young. 2013;23:54–60.
631. Lerman-Sagie T, Lerman P, Mukamel M, et al. A prospective evaluation of pediatric patients with syncope. Clin Pediatr (Phila). 1994;33:67–70.
632. Wren C. Cardiac causes for syncope or sudden death in childhood. Arch Dis Child. 1999;81:289–91.

633. Miyake CY, Motonaga KS, Fischer-Colbrie ME, et al. Risk of cardiac disease and observations on lack of potential predictors by clinical history among children presenting for cardiac evaluation of mid-exertional syncope. Cardiol Young20151–7.
634. Ackerman MJ, Tester DJ, Porter CJ. Swimming, a gene-specific arrhythmogenic trigger for inherited long QT syndrome. Mayo Clin Proc. 1999;74:1088–94.
635. Schimpf R, Veltmann C, Wolpert C, et al. Channelopathies: Brugada syndrome, long QT syndrome, short QT syndrome, and CPVT. Herz. 2009;34:281–8.
636. Rossano J, Bloemers B, Sreeram N, et al. Efficacy of implantable loop recorders in establishing symptom-rhythm correlation in young patients with syncope and palpitations. Pediatrics. 2003;112:e228–e233.
637. Al Dhahri KN, Potts JE, Chiu CC, et al. Are implantable loop recorders useful in detecting arrhythmias in children with unexplained syncope? Pacing Clin Electrophysiol. 2009;32:1422–7.
638. Frangini PA, Cecchin F, Jordao L, et al. How revealing are insertable loop recorders in pediatrics? Pacing Clin Electrophysiol. 2008;31: 338–43.
639. Babikar A, Hynes B, Ward N, et al. A retrospective study of the clinical experience of the implantable loop recorder in a paediatric setting. Int J Clin Pract. 2008;62:1520–5.
640. Ergul Y, Tanidir IC, Ozyilmaz I, et al. Evaluation rhythm problems in unexplained syncope etiology with implantable loop recorder. Pediatr Int. 2015;57:359–66.
641. Younoszai AK, Franklin WH, Chan DP, et al. Oral fluid therapy. A promising treatment for vasodepressor syncope. Arch Pediatr Adolesc Med. 1998;152:165–8.
642. Chu W, Wang C, Wu L, et al. Oral rehydration salts: an effective choice for the treatment of children with vasovagal syncope. Pediatr Cardiol. 2015;36:867–72.
643. Fouad FM, Sitthisook S, Vanerio G, et al. Sensitivity and specificity of the tilt table test in young patients with unexplained syncope. Pacing Clin Electrophysiol. 1993;16:394–400.
644. Grubb BP, Temesy-Armos P, Moore J, et al. The use of head-upright tilt table testing in the evaluation and management of syncope in children and adolescents. Pacing Clin Electrophysiol. 1992;15:742–8.
645. Numan M, Alnajjar R, Lankford J, et al. Cardiac asystole during head up tilt (HUTT) in children and adolescents: is this benign physiology? Pediatr Cardiol. 2015;36:140–5.
646. Qingyou Z, Junbao D, Jianjun C, et al. Association of clinical characteristics of unexplained syncope with the outcome of head-up tilt tests in children. Pediatr Cardiol. 2004;25:360–4.
647. Thilenius OG, Quinones JA, Husayni TS, et al. Tilt test for diagnosis of unexplained syncope in pediatric patients. Pediatrics. 1991;87:334–8.
648. Udani V, Bavdekar M, Karia S. Head up tilt test in the diagnosis of neurocardiogenic syncope in childhood and adolescence. Neurol India. 2004;52:185–7.
649. Yilmaz S, Gökben S, Levent E, et al. Syncope or seizure? The diagnostic value of synchronous tilt testing and video-EEG monitoring in children with transient loss of consciousness. Epilepsy Behav. 2012;24:93–6.
650. Alehan D, Celiker A, Ozme S. Head-up tilt test: a highly sensitive, specific test for children with unexplained syncope. Pediatr Cardiol. 1996;17:86–90.
651. Pongiglione G, Fish FA, Strasburger JF, et al. Heart rate and blood pressure response to upright tilt in young patients with unexplained syncope. J Am Coll Cardiol. 1990;16:165–70.
652. Ross BA, Hughes S, Anderson E, et al. Abnormal responses to orthostatic testing in children and adolescents with recurrent unexplained syncope. Am Heart J. 1991;122:748–54.
653. Strieper MJ, Campbell RM. Efficacy of alpha-adrenergic agonist therapy for prevention of pediatric neurocardiogenic syncope. J Am Coll Cardiol. 1993;22:594–7.
654. Balaji S, Oslizlok PC, Allen MC, et al. Neurocardiogenic syncope in children with a normal heart. J Am Coll Cardiol. 1994;23:779–85.
655. Scott WA, Pongiglione G, Bromberg BI, et al. Randomized comparison of atenolol and fludrocortisone acetate in the treatment of pediatric neurally mediated syncope. Am J Cardiol. 1995;76:400–2.
656. McLeod KA, Wilson N, Hewitt J, et al. Cardiac pacing for severe childhood neurally mediated syncope with reflex anoxic seizures. Heart. 1999;82:721–5.
657. Kelly AM, Porter CJ, McGoon MD, et al. Breath-holding spells associated with significant bradycardia: successful treatment with permanent pacemaker implantation. Pediatrics. 2001;108:698–702.
658. Zhang Q, Jin H, Wang L, et al. Randomized comparison of metoprolol versus conventional treatment in preventing recurrence of vasovagal syncope in children and adolescents. Med Sci Monit. 2008;14:CR199–CR203.
659. Müller G, Deal BJ, Strasburger JF, et al. Usefulness of metoprolol for unexplained syncope and positive response to tilt testing in young persons. Am J Cardiol. 1993;71:592–5.
660. Bouchardy J, Therrien J, Pilote L, et al. Atrial arrhythmias in adults with congenital heart disease. Circulation. 2009;120:1679–86.
661. Kumar S, Tedrow UB, Triedman JK. Arrhythmias in adult congenital heart disease: diagnosis and management. Cardiol Clin. 2015;33:571–88.viii.
662. Murphy JG, Gersh BJ, Mair DD, et al. Long-term outcome in patients undergoing surgical repair of tetralogy of Fallot. N Engl J Med. 1993;329:593–9.
663. Mylotte D, Pilote L, Ionescu-Ittu R, et al. Specialized adult congenital heart disease care: the impact of policy on mortality. Circulation. 2014;129:1804–12.
664. Khairy P, Landzberg MJ, Gatzoulis MA, et al. Value of programmed ventricular stimulation after tetralogy of Fallot repair: a multicenter study. Circulation. 2004;109:1994–2000.
665. Khairy P, Harris L, Landzberg MJ, et al. Sudden death and defibrillators in transposition of the great arteries with intra-atrial baffles: a multicenter study. Circ Arrhythm Electrophysiol. 2008;1:250–7.
666. Anpalahan M, Gibson S. The prevalence of neurally mediated syncope in older patients presenting with unexplained falls. Eur J Intern Med. 2012;23:e48–e52.
667. Richardson DA, Bexton RS, Shaw FE, et al. Prevalence of cardioinhibitory carotid sinus hypersensitivity in patients 50 years or over presenting to the accident and emergency department with "unexplained" or "recurrent" falls. Pacing Clin Electrophysiol. 1997;20:820–3.
668. Paling D, Vilches-Moraga A, Akram Q, et al. Carotid sinus syndrome is common in very elderly patients undergoing tilt table testing and carotid sinus massage because of syncope or unexplained falls. Aging Clin Exp Res. 2011;23:304–8.
669. Rafanelli M, Ruffolo E, Chisciotti VM, et al. Clinical aspects and diagnostic relevance of neuroautonomic evaluation in patients with unexplained falls. Aging Clin Exp Res. 2014;26:33–7.
670. Shaw FE, Kenny RA. The overlap between syncope and falls in the elderly. Postgrad Med J. 1997;73:635–9.
671. Matthews IG, Tresham IA.E, Parry SW. Syncope in the older person. Cardiol Clin. 2015;33:411–21.
672. Newton J, Kenny R. Syncope and falls in older people: defining the size of the problem. Expert Rev Pharmacoecon Outcomes Res. 2001;1:187–97.
673. Duncan GW, Tan MP, Newton JL, et al. Vasovagal syncope in the older person: differences in presentation between older and younger patients. Age Ageing. 2010;39:465–70.
674. O'Dwyer C, Bennett K, Langan Y, et al. Amnesia for loss of consciousness is common in vasovagal syncope. Europace. 2011;13:1040–5.
675. Parry SW, Steen IN, Baptist M, et al. Amnesia for loss of consciousness in carotid sinus syndrome: implications for presentation with falls. J Am Coll Cardiol. 2005;45:1840–3.
676. Lakatta EG, Levy D. Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: Part I: aging arteries: a "set up" for vascular disease. Circulation. 2003;107:139–46.
677. Grubb BP, Karabin B. Syncope: evaluation and management in the geriatric patient. Clin Geriatr Med. 2012;28:717–28.
678. Esposito C, Dal Canton A. Functional changes in the aging kidney. J Nephrol. 2010;23 Suppl 15:S41–5.
679. Racco F, Sconocchini C, Alesi C, et al. Long-term follow-up after syncope. A group of 183 patients observed for 5 years. Minerva Cardioangiol. 2000;48:69–78.
680. Kapoor WN, Hanusa BH. Is syncope a risk factor for poor outcomes? Comparison of patients with and without syncope. Am J Med. 1996;100:646–55.
681. Ruwald MH, Hansen ML, Lamberts M, et al. Comparison of incidence, predictors, and the impact of co-morbidity and polypharmacy on the risk of recurrent syncope in patients <85 versus ≥85 years of age. Am J Cardiol. 2013;112:1610–15.
682. Ungar A, Galizia G, Morrione A, et al. Two-year morbidity and mortality in elderly patients with syncope. Age Ageing. 2011;40:696–702.
683. Forman DE, Rich MW, Alexander KP, et al. Cardiac care for older adults. Time for a new paradigm. J Am Coll Cardiol. 2011;57:1801–10.
684. O'Mahony D, Foote C. Prospective evaluation of unexplained syncope, dizziness, and falls among community-dwelling elderly adults. J Gerontol A Biol Sci Med Sci. 1998;53:M435–M440.

685. Tan MP, Kenny RA. Cardiovascular assessment of falls in older people. Clin Interv Aging. 2006;1:57–66.
686. Ryan DJ, Nick S, Colette SM, et al. Carotid sinus syndrome, should we pace? A multicentre, randomised control trial (Safepace 2). Heart. 2010;96:347–51.
687. Davies AJ, Kenny RA. Falls presenting to the accident and emergency department: types of presentation and risk factor profile. Age Ageing. 1996;25:362–6.
688. Cohen RA, Poppas A, Forman DE, et al. Vascular and cognitive functions associated with cardiovascular disease in the elderly. J Clin Exp Neuropsychol. 2009;31:96–110.
689. Vernooij MW, Ikram MA, Vrooman HA, et al. White matter microstructural integrity and cognitive function in a general elderly population. Arch Gen Psychiatry. 2009;66:545–53.
690. Vogels RLC, Oosterman JM, van Harten B, et al. Profile of cognitive impairment in chronic heart failure. J Am Geriatr Soc. 2007;55:1764–70.
691. Numé AK, Gislason G, Christiansen CB, et al. Syncope and motor vehicle crash risk: a Danish nationwide study. JAMA Intern Med. 2016;176:503–10.
692. Simpson C, Dorian P, Gupta A, et al. Assessment of the cardiac patient for fitness to drive: drive subgroup executive summary. Can J Cardiol. 2004;20:1314–20.
693. Larsen GC, Stupey MR, Walance CG, et al. Recurrent cardiac events in survivors of ventricular fibrillation or tachycardia. Implications for driving restrictions. JAMA. 1994;271:1335–9.
694. Tan VH, Ritchie D, Maxey C, et al. Prospective assessment of the risk of vasovagal syncope during driving. JACC Clin Electrophysiol. 2016;2:203–8.
695. Blumenthal R, Braunstein J, Connolly H, et al. Cardiovascular Advisory Panel Guidelines for the medical examination of commerical motor vehicle drivers. Available at: https://www.fmcsa.dot.gov/sites/fmcsa.dot.gov/files/docs/cardio.pdf. Accessed January 10, 2017.
696. Akiyama T, Powell JL, Mitchell LB, et al. Resumption of driving after life-threatening ventricular tachyarrhythmia. N Engl J Med. 2001;345:391–7.
697. Maas R, Ventura R, Kretzschmar C, et al. Syncope, driving recommendations, and clinical reality: survey of patients. BMJ. 2003;326:21
698. Epstein AE, Miles WM, Benditt DG, et al. Personal and public safety issues related to arrhythmias that may affect consciousness: implications for regulation and physician recommendations. A medical/scientific statement from the American Heart Association and the North American Society of Pacing and Electrophysiology. Circulation. 1996;94:1147–66.
699. Bänsch D, Brunn J, Castrucci M, et al. Syncope in patients with an implantable cardioverter-defibrillator: incidence, prediction and implications for driving restrictions. J Am Coll Cardiol. 1998;31:608–15.
700. Antonelli D, Peres D, Freedberg NA, et al. Incidence of postdischarge symptomatic paroxysmal atrial fibrillation in patients who underwent coronary artery bypass graft: long-term follow-up. Pacing Clin Electrophysiol. 2004;27:365–7.
701. Thijssen J, Borleffs CJ, van Rees JB, et al. Driving restrictions after implantable cardioverter defibrillator implantation: an evidence-based approach. Eur Heart J. 2011;32:2678–87.
702. Vijgen J, Botto G, Camm J, et al. Consensus statement of the European Heart Rhythm Association: updated recommendations for driving by patients with implantable cardioverter defibrillators. Europace. 2009;11:1097–107.
703. Colivicchi F, Ammirati F, Santini M. Epidemiology and prognostic implications of syncope in young competing athletes. Eur Heart J. 2004;25:1749–53.
704. Maron BJ, Udelson JE, Bonow RO, et al. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: Task Force 3: hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy and other cardiomyopathies, and myocarditis: a scientific statement from the American Heart Association and American College of Cardiology. Circulation. 2015;132:e273–80.
705. Link MS, Mark Estes NA. Sudden cardiac death in athletes. Prog Cardiovasc Dis. 2008;51:44–57.
706. Pelliccia A, Zipes DP, Maron BJ. Bethesda Conference #36 and the European Society of Cardiology Consensus Recommendations revisited a comparison of U.S. and European criteria for eligibility and disqualification of competitive athletes with cardiovascular abnormalities. J Am Coll Cardiol. 2008;52:1990–6.
707. Zipes DP, Link MS, Ackerman MJ, et al. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: Task Force 9: arrhythmias and conduction defects: a scientific statement from the American Heart Association and American College of Cardiology. Circulation. 2015;132:e315–e325.
708. Albert RK, Schuller JL, Network CCR. Macrolide antibiotics and the risk of cardiac arrhythmias. Am J Respir Crit Care Med. 2014;189:1173–80.
709. Hastings JL, Levine BD. Syncope in the athletic patient. Prog Cardiovasc Dis. 2012;54:438–44.
710. O'Connor FG, Levine BD, Childress MA, et al. Practical management: a systematic approach to the evaluation of exercise-related syncope in athletes. Clin J Sport Med. 2009;19:429–34.
711. Murrell C, Cotter JD, George K, et al. Influence of age on syncope following prolonged exercise: differential responses but similar orthostatic intolerance. J Physiol (Lond). 2009;587:5959–69.
712. Vettor G, Zorzi A, Basso C, et al. Syncope as a warning symptom of sudden cardiac death in athletes. Cardiol Clin. 2015;33:423–32.
713. Asplund CA, O'Connor FG, Noakes TD. Exercise-associated collapse: an evidence-based review and primer for clinicians. Br J Sports Med. 2011;45:1157–62.
714. O'Connor FG, Levine B. Syncope in athletes of cardiac origin: 2B. From personal history and physical examination sections. Curr Sports Med Rep. 2015;14:254–6.
715. Elliott PM, Anastasakis A, Borger MA, et al. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: the Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC). Eur Heart J. 2014;35:2733–79.
716. Zaidi A, Sheikh N, Jongman JK, et al. Clinical differentiation between physiological remodeling and arrhythmogenic right ventricular cardiomyopathy in athletes with marked electrocardiographic repolarization anomalies. J Am Coll Cardiol. 2015;65:2702–11.
717. The European Society of Cardiology guidelines for the diagnosis and management of syncope. Eur Heart J. 2009;30:2539–40.
718. Paisey JR, Yue AM, Treacher K, et al. Implantable loop recorders detect tachyarrhythmias in symptomatic patients with negative electrophysiological studies. Int J Cardiol. 2005;98:35–8.
719. Christou GA, Kouidi EJ, Anifanti MA, et al. A novel strategy for evaluating tilt test in athletes with syncope. Eur J Prev Cardiol. 2016;23:1003–10.
720. Walsh JAr, Topol EJ, Steinhubl SR. Novel wireless devices for cardiac monitoring. Circulation. 2014;130:573–81.
721. Maron BJ, Doerer JJ, Haas TS, et al. Sudden deaths in young competitive athletes: analysis of 1866 deaths in the United States, 1980–2006. Circulation. 2009;119:1085–92.
722. Maron BJ, Spirito P, Shen WK, et al. Implantable cardioverter-defibrillators and prevention of sudden cardiac death in hypertrophic cardiomyopathy. JAMA. 2007;298:405–12.
723. Corrado D, Basso C, Pavei A, et al. Trends in sudden cardiovascular death in young competitive athletes after implementation of a preparticipation screening program. JAMA. 2006;296:1593–601.
724. James CA, Bhonsale A, Tichnell C, et al. Exercise increases age-related penetrance and arrhythmic risk in arrhythmogenic right ventricular dysplasia/cardiomyopathy-associated desmosomal mutation carriers. J Am Coll Cardiol. 2013;62:1290–7.
725. Anderson JB, Czosek RJ, Knilans TK, et al. The effect of paediatric syncope on health-related quality of life. Cardiol Young. 2012;22:583–8.
726. Barón-Esquivias G, Gómez S, Aguilera A, et al. Short-term evolution of vasovagal syncope: influence on the quality of life. Int J Cardiol. 2005;102:315–9.
727. Giada F, Silvestri I, Rossillo A, et al. Psychiatric profile, quality of life and risk of syncopal recurrence in patients with tilt-induced vasovagal syncope. Europace. 2005;7:465–71.
728. Linzer M, Pontinen M, Gold DT, et al. Impairment of physical and psychosocial function in recurrent syncope. J Clin Epidemiol. 1991;44:1037–43.
729. Romme JJCM, Reitsma JB, Go-Schön IK, et al. Prospective evaluation of non-pharmacological treatment in vasovagal syncope. Europace. 2010;12:567–73.
730. Rose MS, Koshman ML, Ritchie D, et al. The development and preliminary validation of a scale measuring the impact of syncope on quality of life. Europace. 2009;11:1369–74.

731. Santhouse J, Carrier C, Arya S, et al. A comparison of self-reported quality of life between patients with epilepsy and neurocardiogenic syncope. Epilepsia. 2007;48:1019–22.
732. van Dijk N, Sprangers MA, Colman N, et al. Clinical factors associated with quality of life in patients with transient loss of consciousness. J Cardiovasc Electrophysiol. 2006;17:998–1003.
733. van DN, Sprangers MA, Boer KR, et al. Quality of life within one year following presentation after transient loss of consciousness. Am J Cardiol. 2007;100:672–6.
734. Faddis MN, Rich MW. Pacing interventions for falls and syncope in the elderly. Clin Geriatr Med. 2002;18:279–94.
735. Finkler SA. The distinction between cost and charges. Ann Intern Med. 1982;96:102–9.
736. Sun BC, Emond JA, Camargo CA Jr, Direct medical costs of syncope-related hospitalizations in the United States. Am J Cardiol. 2005;95:668–71.
737. Farwell DJ, Sulke AN. Does the use of a syncope diagnostic protocol improve the investigation and management of syncope? Heart. 2004;90:52–8.
738. Barón-Esquivias G, Moreno SG, Martínez A, et al. Cost of diagnosis and treatment of syncope in patients admitted to a cardiology unit. Europace. 2006;8:122–7.

Appendix 1. Author Relationships With Industry and Other Entities (Relevant)—2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope (March 2015)

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
Win-Kuang Shen, Chair	Mayo Clinic Arizona—Professor of Medicine; Mayo Clinic College of Medicine—Chair, Department of Cardiovascular Diseases	None	None	None	None	None	None	None
Robert S. Sheldon, Vice Chair	University of Calgary, Department of Medicine—Professor	None	None	None	None	None	None	None
David G. Benditt	University of Minnesota Medical School, Cardiovascular Division—Professor of Medicine	• Medtronic† • St. Jude Medical†	None	None	None	None	None	3.2, 3.2.3, 3.2.5, 4.1.1–4.1.3, 4.2.1–4.2.5, 4.3.1–4.3.5, 5.1–5.3, 10.1, 10.2, 10.3, 10.5, 12
Mitchell I. Cohen	University of Arizona School of Medicine-Phoenix—Clinical Professor of Child Health; Phoenix Children's Heart Center—Co-Director; Phoenix Children's Hospital, Pediatric Cardiology—Chief	None	None	None	None	None	None	None
Daniel E. Forman	University of Pittsburgh—Professor of Medicine; University of Pittsburgh Medical Center—Chair, Geriatric Cardiology Section; VA Pittsburg Healthcare Systems—Director, Cardiac Rehabilitation	None	None	None	None	None	None	None
Roy Freeman‡	Harvard Medical School—Professor of Neurology; Beth Israel Deaconess Medical Center, Center for Autonomic and Peripheral Nerve Disorders—Director	• Lundbeck†	None	None	None	None	None	4.3.1–4.3.5, 5.1, 6.1, 10.1, 10.3, 10.5, 12
Zachary D. Goldberger	University of Washington School of Medicine, Harborview Medical Center Division of Cardiology—Assistant Professor of Medicine	None	None	None	None	None	None	None
Blair P. Grubb	University of Toledo Medical Center, Medicine and Pediatrics—Professor	• Biotronik • Medtronic	None	None	None	None	None	3.2, 3.2.3, 3.2.5, 4.1.1–4.1.3, 4.2.1–4.2.5, 4.3.1–4.3.5, 5.1–5.3, 10.1, 10.2, 10.3, 10.5, 12
Mohamed H. Hamdan	University of Wisconsin School of Medicine, Cardiovascular Medicine—Professor and Chief of Cardiovascular Medicine	None	None	• F2 Solutions	None	None	None	2.3.3, 2.3.4, 12

(*Continued*)

Appendix 1. Continued

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
Andrew D. Krahn	The University of British Columbia, Division of Cardiology—Professor of Medicine and Head of Division	• Medtronic	None	None	None	• Boston Scientific† • Medtronic†	None	3.2, 3.2.3, 3.2.5, 4.1.1–4.1.3, 4.2.1–4.2.5, 4.3.1–4.3.5, 5.1–5.3, 10.1, 10.2, 10.3, 10.5, 12
Mark S. Link	University of Texas Southwestern Medical Center, Department of Medicine, Division of Cardiology—Director, Cardiac Electrophysiology; Professor of Medicine	None	None	None	None	None	None	None
Brian Olshansky	University of Iowa Carver College of Medicine, Cardiovascular Medicine—Emeritus Professor of Internal Medicine; Mercy Hospital North Iowa—Electrophysiologist	• Lundbeck†	None	None	None	None	None	None
Satish R. Raj	University of Calgary, Cardiac Sciences—Associate Professor	• GE Healthcare • Lundbeck†	None	None	• Medtronic	None	None	2.3.2, 2.3.4, 3.2–3.2.5, 3.3.2, 4.1.1–4.1.3, 4.2.1–4.2.5, 4.3.1–4.3.5, 5.1–5.3, 6.1, 7, 10.1–10.3, 10.5, 12
Roopinder Kaur Sandhu	University of Alberta, Medical Division of Cardiology—Assistant Professor of Medicine	None	None	None	None	None	None	None
Dan Sorajja	Mayo Clinic Arizona, Cardiovascular Diseases—Assistant Professor of Medicine	None	None	None	None	None	None	None
Benjamin C. Sun	Oregon Health & Science University—Associate Professor	None	None	None	None	None	None	None
Clyde W. Yancy	Northwestern University Feinberg School of Medicine, Division of Cardiology—Professor of Medicine and Chief; Diversity & Inclusion—Vice Dean	None	None	None	None	None	None	None

This table represents the relationships of committee members with industry and other entities that were determined to be relevant to this document. These relationships were reviewed and updated in conjunction with all meetings and/or conference calls of the writing committee during the document development process. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or ownership of ≥$5000 of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted.

According to the ACC/AHA, a person has a relevant relationship IF: a) the relationship or interest relates to the same or similar subject matter, intellectual property or asset, topic, or issue addressed in the document; or b) the company/entity (with whom the relationship exists) makes a drug, drug class, or device addressed in the *document*, or makes a competing drug or device addressed in the document; or c) the person or a member of the person's household, has a reasonable potential for financial, professional or other personal gain or loss as a result of the issues/content addressed in the document.

*Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry and other entities may apply.

†Significant relationship.

‡Dr. Roy Freeman, the official representative of the American Academy of Neurology, resigned from the writing committee in November 2016, before the final balloting process; recusals noted are from the initial round of balloting. We thank him for his contributions.

ACC indicates American College of Cardiology; AHA, American Heart Association; HRS, Heart Rhythm Society; and VA, Veterans Affairs.

Appendix 2. Reviewer Relationships With Industry and Other Entities (Comprehensive)—2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope (June 2016)

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Italo Biaggioni	Official Reviewer—AHA	Vanderbilt University School of Medicine—Professor of Medicine	• Lundbeck* • Shire Pharmaceuticals* • Theravance*	None	None	• Astellas Pharma (DSMB) • AstraZeneca* • Forest Pharmaceuticals* • Janssen Pharmaceuticals (DSMB) • Lundbeck* • Theravance*	None	None
Joaquin E. Cigarroa	Official Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	Oregon Health & Science University—Clinical Professor of Medicine	None	None	None	None	• NIH† • AHA† • SCAI† • ASA† • Catheterization and Cardiovascular Intervention†	None
Kenneth A. Ellenbogen	Official Reviewer—AHA	VCU Medical Center—Director, Clinical EP Laboratory	• AHA • Atricure* • Biosense Webster* • Biotronik* • Boston Science* • HRS* • Janssen Pharmaceuticals • Medtronic* • Pfizer* • Sentra Heart • St. Jude Medical*	None	None	• Atricure* • Boston Science • Biosense Webster • Daiichi-Sankyo* • Medtronic (DSMB) • Medtronic • NIH • Sanofi-aventis	• AHA • American Heart Journal • Biosense Webster* • Boston Science* • HRS • JCE • Medtronic* • PACE • Sanofi-aventis	• Defendant, Catheter ablation complication, 2015 • Plantiff, Lead extraction complication, 2015
Rakesh Gopinathannair	Official Reviewer—HRS	University of Louisville School of Medicine and Jewish Hospital Division of Cardiovascular Medicine—Associate Professor of Medicine, Director of Cardiac EP	• Boston Scientific • Health Trust PG • St. Jude Medical*	• AHA • Bristol-Myers Squibb • Pfizer* • Zoll Medical	None	None	None	None
Robert Helm	Official Reviewer—HRS	Boston University School of Medicine—Assistant Professor of Medicine, Assistant Professor of Radiology	None	None	None	None	• Boston Scientific • St. Jude Medical	None
Dhanunjaya Lakkireddy	Official Reviewer—ACC Board of Governors	University of Kansas Medical Center—Professor of Medicine; Center for Excellence in AF and Complex Arrhythmias—Director	• Biosense Webster • St. Jude Medical	• Boehringer Ingelheim • Bristol-Myers Squibb • Janssen Pharmaceuticals • Pfizer	None	None	None	None
Thad Waites	Official Reviewer—ACC Board of Trustees	Forrest General Hospital—Director of Catheterization Laboratory	None	None	None	None	None	None

(*Continued*)

Appendix 2. Continued

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Christopher Gibbons	Organizational Reviewer—AAN	Beth Israel Deaconess Medical Center Neuropathy Clinic—Director	• Lundbeck	None	None	• Astellas Pharma (DSMB) • Janssen Pharmaceuticals (DSMB)	None	None
Kaushal H. Shah	Organizational Reviewer—ACEP/SAEM	The Mount Sinai Hospital—Associate Professor of Emergency Medicine	None	None	None	None	None	None
Mike Silka	Organizational Reviewer—PACES	Children's Hospital Los Angeles—Professor of Pediatrics, Cardiology	None	None	None	None	None	• Defendant, SCD in CPVT patient, 2016
Sana M. Al-Khatib	Content Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	Duke Clinical Research Institute—Professor of Medicine	None	None	None	• FDA* • NHLBI* • PCORI* • VA Health System (DSMB)	• Elsevier* • AHA	None
Kim K. Birtcher	Content Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	University of Houston College of Pharmacy—Clinical Professor	• Jones & Bartlett Learning	None	None	None	None	None
Michele Brignole	Content Reviewer	Arrhythmologic Centre, Ospedali del Tigullio—Head of Cardiology	None	None	• F2 Solutions†	None	None	None
Hugh Calkins	Content Reviewer—ACC EP Section Leadership Council	Johns Hopkins Hospital—Professor of Medicine, Director of EP	• Abbott • Atricure • Boehringer Ingelheim* • Medtronic*	None	None	• Boehringer Ingelheim† • St. Jude Medical*	• Abbott Laboratories	• Defendant, SCD, 2015
Coletta Barrett	Content Reviewer—Lay Reviewer	Our Lady of the Lake Regional Medical Center—Vice President	None	None	None	None	None	None
Lin Yee Chen	Content Reviewer	University of Minnesota Medical School—Associate Professor of Medicine	None	None	None	None	• NIH*	None
Andrew Epstein	Content Reviewer	University of Pennsylvania Hospital and the Veteran's Administration Medical Center—Professor of Medicine	None	None	None	• Biosense Webster* • Biotronik* • Boston Scientific* (DSMB) • Boston Scientific* • C.R. Bard* • Medtronic (DSMB) • Medtronic* • St. Jude Medical* (DSMB) • St. Jude Medical	None	None

(*Continued*)

Circulation. 2017;136:e60–e122. DOI: 10.1161/CIR.0000000000000499

Appendix 2. Continued

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Susan Etheridge	Content Reviewer—ACC EP Section Leadership Council	University of Utah—Training Program Director	None	None	None	• SADS Foundation • PACES†	• Up-to-Date†	None
Marci Farquhar-Snow	Content Reviewer	Mayo Clinic School of Health Sciences—Program Director, Cardiology Nurse Practitioner, Fellowship	None	None	None	None	None	None
Samuel S. Gidding	Content Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	Nemours/Alfred I. duPont Hospital for Children—Chief, Division of Pediatric Cardiology	• FH Foundation† International • FH Foundation†	None	None	• FH Foundation† • NIH*	None	None
Bulent Gorenek	Content Reviewer—ACC EP Section Leadership Council	Eskisehir Osmangazi University Cardiology Department—Chair	None	None	None	None	None	None
Paul LeLorier	Content Reviewer—ACC Heart Failure and Transplant Section Leadership Council	LSU Health Sciences Center—Associate Professor of Medicine and Neurology; EP Service—Director	None	None	None	• Medtronic*	• Medtronic*	None
Patrick McBride	Content Reviewer	University of Wisconsin School of Medicine & Public Health—Professor of Medicine and Family Medicine; Dean for Faculty Affairs—Associate; Prevention Cardiology—Associate Director	None	None	None	None	None	None
Carlos Morillo	Content Reviewer	Cumming School of Medicine—Professor Department of Cardiac Sciences; University of Calgary—Section Chief Division of Cardiology, Libin Cardiovascular Institute	• Bayer HealthCare • Boehringer Ingelheim • Boston Scientific	None	None	• Biosense Webster • Canadian Institutes of Health Research† • Medtronic† • Merck • Pfizer • St. Jude Medical	• Biotronik • Pfizer	None
Rick Nishimura	Content Reviewer	Mayo Clinic Division of Cardiovascular Disease—Professor of Medicine	None	None	None	None	None	None

(*Continued*)

Appendix 2. Continued

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Richard Page	Content Reviewer	University of Wisconsin School of Medicine & Public Health—Chair, Department of Medicine	None	None	None	None	• FDA	None
Antonio Raviele	Content Reviewer	Alliance to Fight Atrial Fibrillation—President; Venice Arrhythmias—President	None	None	None	None	None	None
Marwan Refaat	Content Reviewer—ACC EP Section Leadership Council	American University of Beirut—Faculty of Medicine and Medical Center	None	None	None	None	None	None
Melissa Robinson	Content Reviewer	University of Washington—Assistant Professor of Medicine; Director, Ventricular Arrhythmia Program	• Medtronic*	None	None	None	None	None
Paola Sandroni	Content Reviewer	Mayo Clinic—Professor of Neurology, Practice Chair of Neurology	None	None	None	None	None	None
Colette Seifer	Content Reviewer	University of Manitoba—Associate Professor, Section of Cardiology	None	None	None	None	None	None
Monica Solbiati	Content Reviewer	Fondazione IRCCS CA' Granda, Ospedale Maggiore Policlinico, Milano—Senior Physician	None	None	None	None	None	None
Richard Sutton	Content Reviewer	National Heart and Lung Institute, Imperial College London—Emeritus Professor	• Medtronic*	• St. Jude Medical*	• Boston Scientific* • Edwards Lifesciences* • Shire Pharmaceuticals • AstraZeneca	• Medtronic*	None	• Defendant, Fatal car accident caused by VVS patient, 3 trials in 2016*
Gaurav Upadhyay	Content Reviewer—ACC EP Section Leadership Council	University of Chicago—Assistant Professor of Medicine	• Biosense Webster • Biotronik • Boston Scientific • Medtronic • St. Jude Medical • Zoll Medical	None	None	• Biosense Webster • Biotronik* • Medtronic*	None	None

(*Continued*)

Circulation. 2017;136:e60–e122. DOI: 10.1161/CIR.0000000000000499

Appendix 2. Continued

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Paul Varosy	Content Reviewer	University of Colorado Hospital, Clinical Cardiac EP Training program—Associate Program Director; VA Eastern Colorado Healthcare System—Director of Cardiovascular EP	None	None	None	• AHA† • VA Office of Health Services Research and Development (PI)*	None	None

This table represents the relationships of reviewers with industry and other entities that were disclosed at the time of peer review, including those not deemed to be relevant to this document, at the time this document was under review. The table does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of ≥5% of the voting stock or share of the business entity, or ownership of ≥$5000 of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. Relationships that exist with no financial benefit are also included for the purpose of transparency. Relationships in this table are modest unless otherwise noted. Names are listed in alphabetical order within each category of review. Please refer to http://www.acc.org/guidelines/about-guidelines-and-clinical-documents/relationships-with-industry-policy for definitions of disclosure categories or additional information about the ACC/AHA Disclosure Policy for Writing Committees.

*Significant relationship.

†No financial benefit.

AAN indicates American Academy of Neurology; ACC; American College of Cardiology; ACEP, American College of Emergency Physicians; AHA, American Heart Association; ASA, American Stroke Association; DSMB, data safety monitoring board; CPVT, catecholaminergic polymorphic ventricular tachycardia; EP, electrophysiology; FDA, US Food and Drug Administration; FH, familial hypercholesterolemia; HRS, Heart Rhythm Society; ICD, implantable cardioverter-defibrillator; JCE, Journal of Cardiovascular Electrophysiology; LSU, Louisiana State University; NHLBI, National Heart, Lung, and Blood Institute; PACE, Partners in Advanced Cardiac Evaluation; PACES, Pediatric and Congenital Electrophysiology Society; PCORI, Patient-Centered Outcomes Research Institute; PI, principal investigator; SADS, Sudden Arrhythmia Death Syndromes Foundation; SAEM, Society for Academic Emergency Medicine; SCAI, Society for Cardiovascular Angiography and Interventions; SCD, sudden cardiac death; VA, Veterans Affairs; VCU, Virginia Commonwealth University; and VVS, vasovagal syncope.

Appendix 3. Abbreviations

ACHD = adult congenital heart disease
ARVC = arrhythmogenic right ventricular cardiomyopathy
AV = atrioventricular
CHD = congenital heart disease
CPVT = catecholaminergic polymorphic ventricular tachycardia
CT = computed tomography
ECG = electrocardiogram/electrocardiographic
ED = emergency department
EEG = electroencephalogram/electroencephalography
EPS = electrophysiological study
GDMT = guideline-directed management and therapy
HCM = hypertrophic cardiomyopathy
HF = heart failure
ICD = implantable cardioverter-defibrillator
ICM = implantable cardiac monitor
LCSD = left cardiac sympathetic denervation
LQTS = long-QT syndrome
LV = left ventricular
MRI = magnetic resonance imaging
OH = orthostatic hypotension
QoL= quality of life
RCT = randomized controlled trial
POTS = postural tachycardia syndrome
SCD = sudden cardiac death
SVT = supraventricular tachycardia
VA = ventricular arrhythmia
VF = ventricular fibrillation
VT = ventricular tachycardia
VVS = vasovagal syncope

Circulation. 2017;136:e60–e122. DOI: 10.1161/CIR.0000000000000499