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[‡¶]

ACC/AHA Task Force Members

Glenn N. Levine, MD, FACC, FAHA, *Chair*
Patrick T. O'Gara, MD, MACC, FAHA, *Chair-Elect*
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Joaquin E. Cigarroa, MD, FACC
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Lee A. Fleisher, MD, FACC, FAHA
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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

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

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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 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 intervention 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

Table 1 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.

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 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

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]

AATS indicates American Association for Thoracic Surgery; 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 Surgeons.
*Revisions to the current documents are being prepared, with publication expected in 2017.

guideline recommendations in 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 1,925 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]

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 (i.e., 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 $\geq$1 of these symptoms associated with reduced ability to maintain upright posture.
Orthostatic tachycardia	A sustained increase in heart rate of $\geq$30 bpm within 10 min of moving from a recumbent to a quiet (nonexertional) standing position (or $\geq$40 bpm in individuals 12–19 y of age).[24,30,31]
Orthostatic hypotension (OH)	A drop in systolic BP of $\geq$20 mm Hg or diastolic BP of $\geq$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 $\geq$20 mm Hg or diastolic BP of $\geq$10 mm Hg within 3 min of assuming upright posture.[31]
• **Delayed OH**	A sustained reduction of systolic BP of $\geq$20 mm Hg (or 30 mm Hg in patients with supine hypertension) or diastolic BP of $\geq$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 (e.g., 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 $\geq$3 s and/or a decrease of systolic pressure $\geq$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 (e.g., lightheadedness, palpitations, tremulousness, generalized weakness, blurred vision, exercise intolerance, and fatigue); and 2) an increase in heart rate of $\geq$30 bpm during a positional change from supine to standing (or $\geq$40 bpm in those 12–19 y of age); and 3) the absence of OH ($>$20 mm Hg reduction in systolic BP). Symptoms associated with POTS include those that occur with standing (e.g., lightheadedness, palpitations); those not associated with particular postures (e.g., bloating, nausea, diarrhea, abdominal pain); and those that are systemic (e.g., 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]

BP indicates blood pressure; ECG, electrocardiogram; OH, orthostatic hypotension; POTS, postural tachycardia syndrome; and VVS, vasovagal syncope.
*These definitions are derived from previously published definitions from scientific investigations, guidelines, expert consensus statements, and Webster dictionary after obtaining consensus from the WC.

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

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.

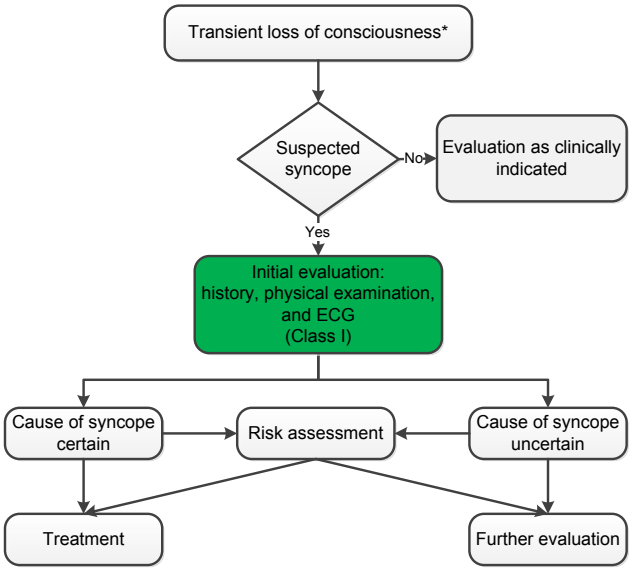

Figure 1 Syncope Initial Evaluation.
*See relevant terms and definitions in Table 3. Colors correspond to Class of Recommendation in Table 1. This figure shows the general principles for initial evaluation of all patients after an episode of syncope.
ECG indicates electrocardiogram.

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.

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.

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 (e.g., 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]

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]	

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.
*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.

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

Table 6 (*Continued*)

Study/Reference	Year	Sample N	Events N (%)	Outcome Definition	ED Events*	Predictors	NPV (%)†
STePS[68]	2008	676	41 (6%)	10-d serious events¶	Yes	Abnormal ECG‡; trauma; no prodrome; male sex	—
Syncope Risk Score[75]	2009	2,584	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

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.

*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.

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 (e.g., 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 (e.g., severe anemia from a gastrointestinal bleed).

(*Continued*)

(*Continued*)

COR	LOE	Recommendations
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.

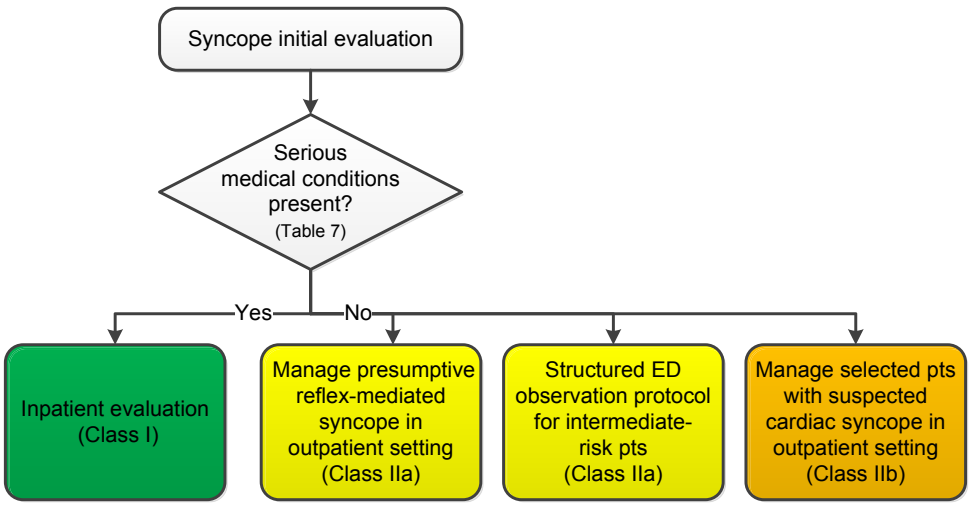

Figure 2 Patient Disposition After Initial Evaluation for Syncope.
Colors correspond to Class of Recommendation in Table 1.
ED indicates emergency department; and pts, patients.

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

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

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.

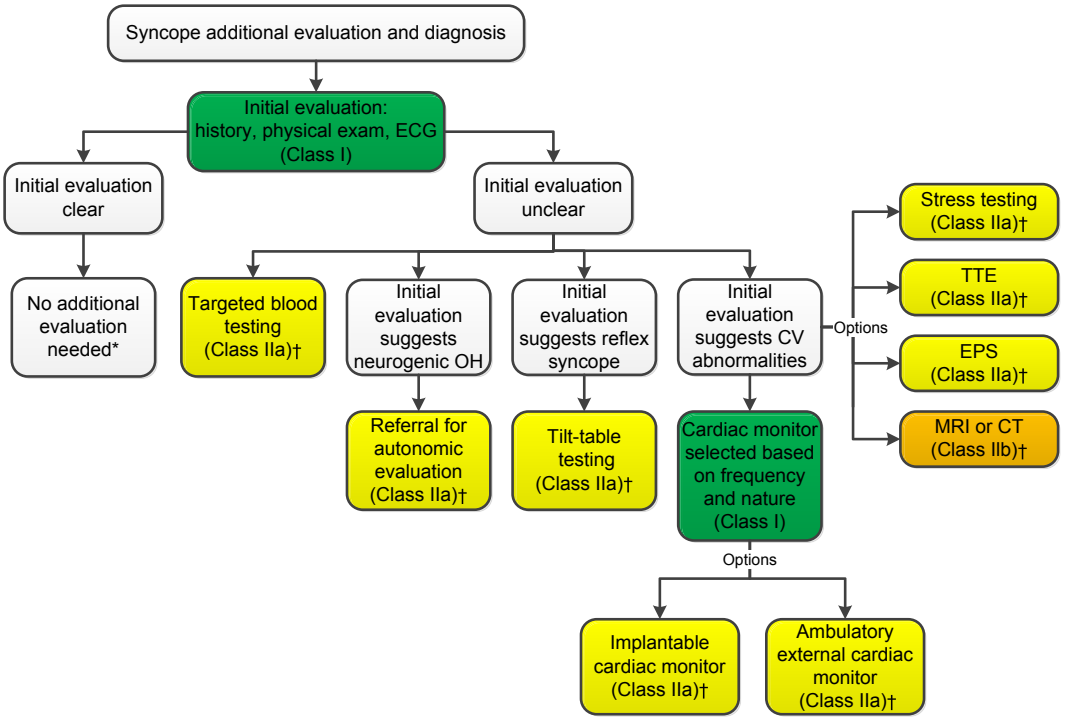

Figure 3 Additional Evaluation and Diagnosis for Syncope.
Colors correspond to Class of Recommendation in Table 1. *Applies to patients after a normal initial evaluation without significant injury or cardiovascular morbidities; patients followed up by primary care physician as needed. †In selected patients (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.

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 (e.g., 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]

(*Continued*)

(*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 (e.g., 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 $\leq$40%) in 24 patients[80]; and 50% of patients with LV systolic dysfunction had manifest arrhythmias, compared with 9% with minor, incidental abnormalities ($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 (e.g., 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]

(*Continued*)

COR	LOE	Recommendations
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 2,106 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 (e.g., 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]

(*Continued*)

(*Continued*)

COR	LOE	Recommendations
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 recorder may 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, there was 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.

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 (e.g., 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 (e.g., 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

Table 8 (*Continued*)

Types of Monitor	Device Description	Patient Selection
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 (e.g., 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

ECG indicates electrocardiogram.
*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.

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 2,240 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 2,106 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]

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 $\leq$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 (e.g., 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.
III: 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]

(*Continued*)

COR	LOE	Recommendations
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 (e.g., 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]

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 2,728 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.

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COR	LOE	Recommendations
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 2,084 patients and established a diagnosis in 0.7%.[36,77,254–258] EEGs should not be routinely used in the assessment of syncope.

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 (e.g., 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.

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COR	LOE	Recommendations
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 $\geq$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 $\geq$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.

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COR	LOE	Recommendations
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 $\geq$2 mm in $\geq$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 1,000 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]
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 (e.g., 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 (e.g., 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 (i.e., fluid, salt intake, counseling, and avoidance) was superior to conventional therapy in preventing syncope recurrence.[375]
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]

(*Continued*)

(*Continued*)

COR	LOE	Recommendations
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]

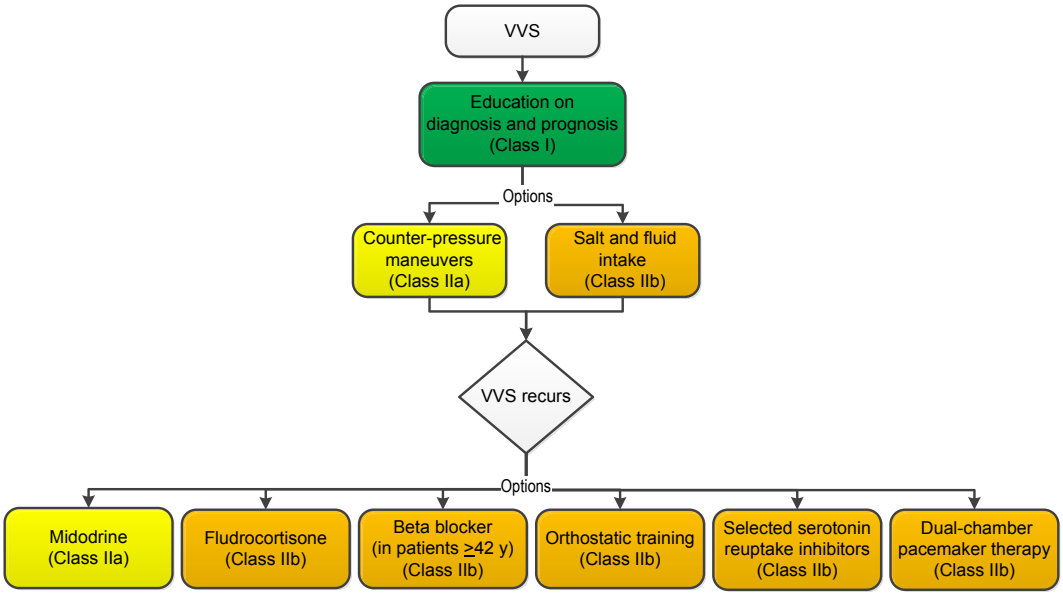

Figure 4 Vasovagal Syncope.
Colors correspond to Class of Recommendation in Table 1.
VVS indicates vasovagal syncope.

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 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 and 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 and 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 and 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 and 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 and 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 and 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 and 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 (e.g., 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 and 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 and 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]

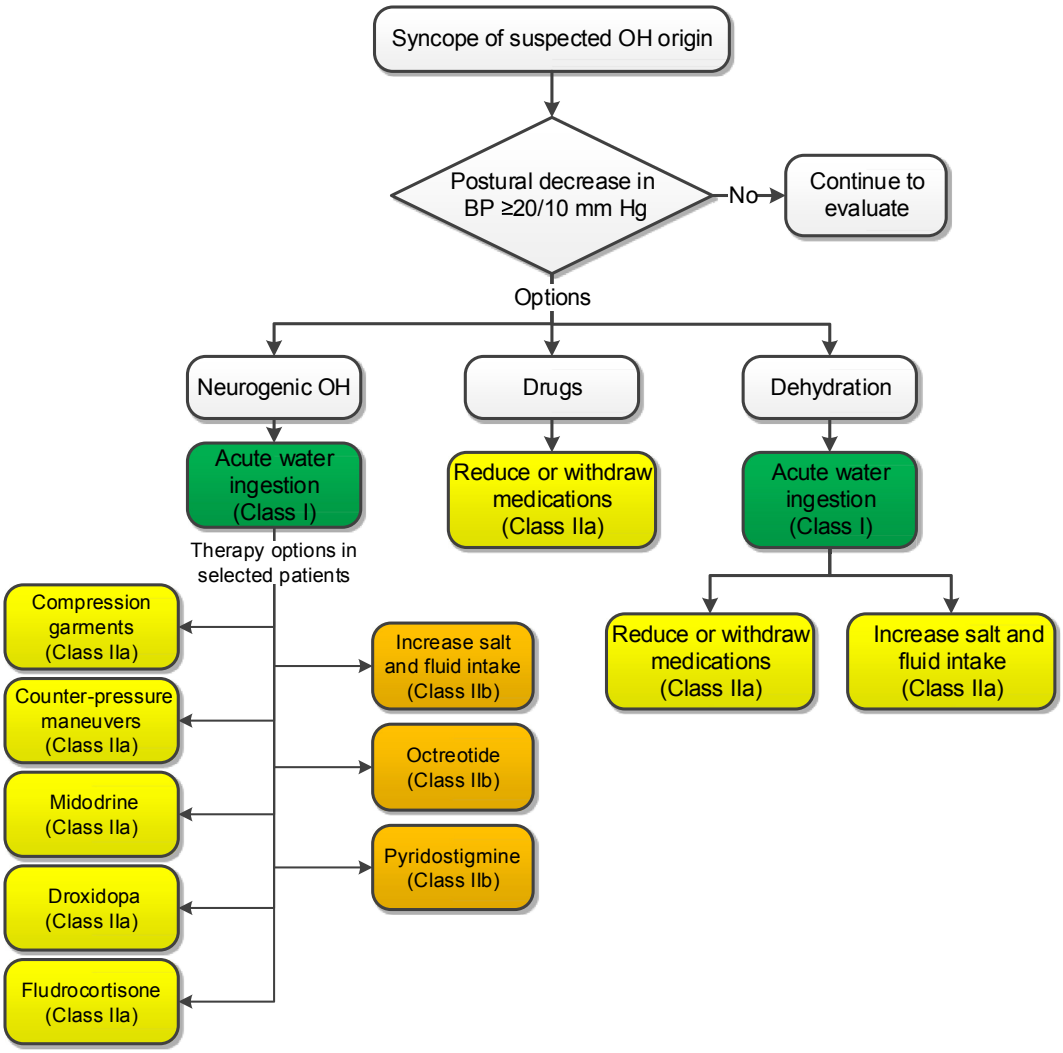

Figure 5 Orthostatic Hypotension.
Colors correspond to Class of Recommendation in Table 1. BP indicates blood pressure; and OH, orthostatic hypotension.

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 (e.g., because of glucose content).[498–501,503,506]

(*Continued*)

(*Continued*)

COR	LOE	Recommendations
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 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.

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.

(*Continued*)

Table 9 (*Continued*)

Condition	Clinical Characteristics	Notes
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.
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.

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]

(*Continued*)

(*Continued*)

COR	LOE	Recommendations
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

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

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 (e.g., Mustard, Senning, Fontan, Ebstein anomaly, and tetralogy of Fallot).[665]

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 (e.g., 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 1,500.[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 (i.e., 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 U.S. 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 (e.g., 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 U.S. 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 U.S. 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.

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

Table 10 (*Continued*)

Condition	Symptom-Free Waiting Time*
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

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

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 (e.g., >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]

(*Continued*)

(*Continued*)

COR	LOE	Recommendations
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 U.S. Healthcare Utilization Project, total annual hospital costs exceeded $4.1 billion in 2014 dollars, with a mean cost of $9,400 per admission.[736] Total costs and costs per admission for presumptive undiagnosed syncope were $1.6 billion and $7,200, 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]

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 U.S. 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 ($1,100) 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.

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.

Presidents and Staff

Gayle R. Whitman, PhD, RN, FAHA, FAAN, Senior Vice President, Office of Science Operations

Jody Hundley, Production Manager, Scientific Publications, Office of Science Operations

Appendix

Supplementary data

Writing Committee Comprehensive Relationship With Industry table and Data Supplement associated with this article can be found at http://dx.doi.org/10.1016/j.hrthm.2017.03.004.

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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
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

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

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 ≥$5,000 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.

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 Pharma-ceuticals* • Theravance*	None	None	• Astellas Pharma (DSMB) • AstraZeneca* • Forest Pharma-ceuticals* • 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 Pharma-ceuticals • 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
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	Childrens 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

(*Continued*)

Appendix 2 (*Continued*)

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
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
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
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

(*Continued*)

Appendix 2 (*Continued*)

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Richard Sutton	Content Reviewer	National Heart and Lung Institute, Imperial College London—Emeritus Professor	• Medtronic*	• St. Jude Medical*	• Boston Scientific* • Edwards Life-sciences* • Shire Pharma-ceuticals • 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
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 ≥$5,000 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.

AAN = 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 = U.S. 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.

*Significant relationship.

†No financial benefit.

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