2017 ACC/AHA/HRS guideline for the evaluation and management of patients with syncope: Executive summary

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

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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 reevaluation. Similarly, the presentation and delivery of guidelines are reevaluated 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]

The reader is encouraged to consult the full-text guideline[9] for additional guidance and details with regard to syncope because this executive summary contains limited information.

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) *(Generally, LOE A or B use only)*	**Benefit = Risk**
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.[10]

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 endorsed by the American College of Emergency Physicians, 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 (in the full-text guideline) 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 when applicable or when appropriate.

2. General Principles

For the purpose of this guideline, definitions of syncope and relevant terms are provided in Table 2. See Table 3 for historical characteristics associated with, although not diagnostic, cardiac and noncardiac syncope; Table 4 for short- and long-term risk factors; Table 5 for the type of events, event rates, and study durations from investigations that estimate risk scores; Table 6 for examples of serious conditions associated with syncope which may require inpatient evaluation and "treatment"; Figure 1 for the algorithm on initial evaluation for syncope; and Figure 2 for patient disposition after initial evaluation for syncope. See Online Data Supplements 1 through 4 for data supporting Section 2.

2.1. Definitions: Terms and Classification

Table 2 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.[11,12] 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).[11,12]
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[11] 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.[12] 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).[11-13]
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.[13]
• **Initial (immediate) OH**	A transient BP decrease within 15 s after standing, with presyncope or syncope.[13,14]
• **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.[13]
• **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.[13]
• **Neurogenic OH**	A subtype of OH that is due to dysfunction of the autonomic nervous system and not solely due to environmental triggers (such as dehydration or drugs).[15,16] 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.[17,18]
Noncardiac syncope	Syncope due to noncardiac causes, which includes reflex syncope, OH, volume depletion, dehydration, and blood loss.[17]
Reflex (neurally mediated) syncope	Syncope due to a reflex that causes vasodilation, bradycardia, or both.[11-13]
• **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.[12] 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.[11] 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.

(*Continued*)

Table 2 (*Continued*)

Term	Definition/Comments and References
• **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 ≥30 bpm during a positional change from supine to standing (or ≥40 bpm in those 12–19 y of age); and 3) the absence of OH (>20 mm Hg reduction in systolic BP). Symptoms associated with POTS include those that occur with standing (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).[19] The standing heart rate is often >120 bpm.[13,20-24]
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.[11]

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.

2.2. Epidemiology and Demographics

Studies of syncope report prevalence rates as high as 41%, with recurrent syncope occurring in 13.5%.[25] 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;

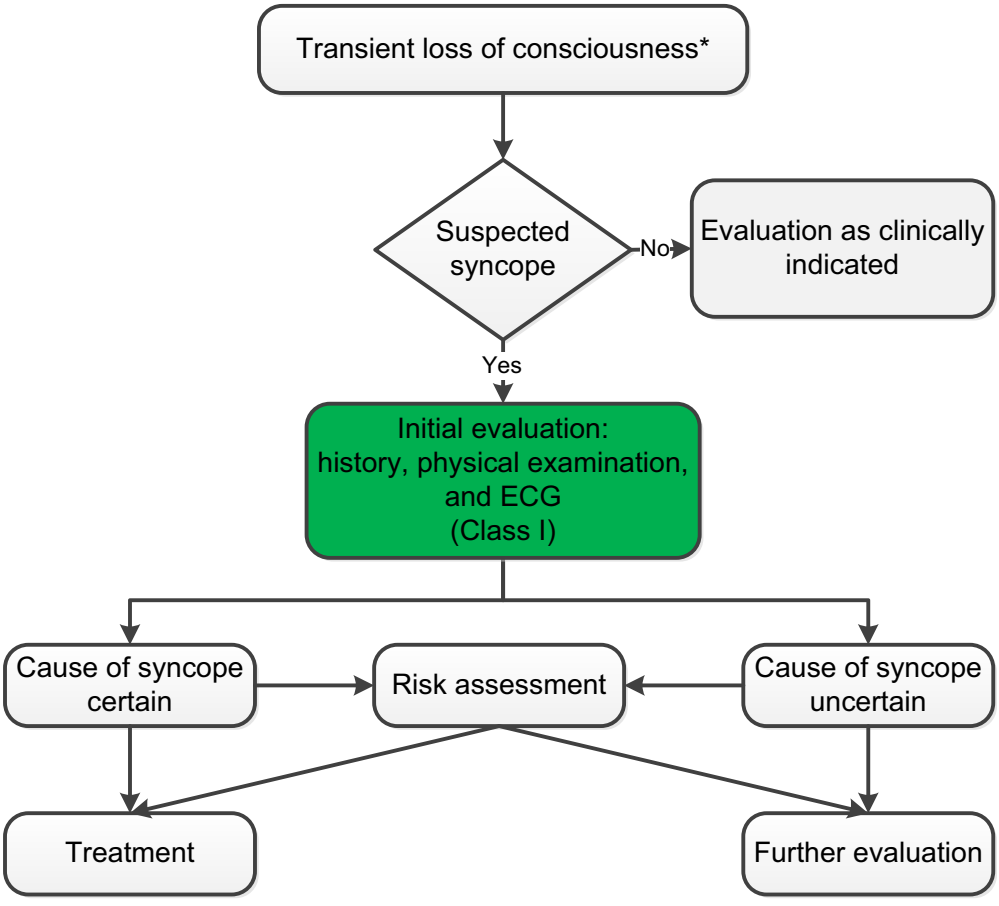

Figure 1 Syncope Initial Evaluation.
*See relevant terms and definitions in Table 2.
Colors correspond to Class of Recommendation in Table 1. This figure shows the general principles for initial evaluation of all patients after an episode of syncope.
ECG indicates electrocardiogram.

the estimated prevalence of syncope was 19%. Females reported a higher prevalence of syncope (22% versus 15%, p<0.001).[26] 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.[27] Predictors of recurrent syncope in older adults are aortic stenosis, impaired renal function, atrioventricular or left bundle-branch block, male sex, chronic obstructive pulmonary disorder, heart failure, atrial fibrillation, advancing age, and orthostatic medications,[27] with a sharp increase in incidence after 70 years of age.[17] Reflex syncope was most common (21%), followed by cardiac syncope (9%) and OH (9%), with the cause of syncope unknown in 37%.[17] In patients with New York Heart Association class III–IV heart failure, syncope is present in 12% to 14% of patients.[28,29]

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, or 0.77% of all ED patients. Among patients >80 years of age, 58% were admitted to hospital.[30] 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.[31–37]

2.3. Initial Evaluation of Patients With Syncope: Recommendations

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.**[38-46]

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.**[56]

Table 3 Historical Characteristics Associated With Increased Probability of Cardiac and Noncardiac Causes of Syncope[40,47-55]

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.

2.3.3. Risk Assessment: Recommendations

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 4).**[48,57-59]
IIb	B-NR	**Use of risk stratification scores may be reasonable in the management of patients with syncope.**[47,48,52,53,55,59-62]

Table 4 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[54,62-64]	Male sex[48,65]
Older age (>60 y)[66]	Older age[47,54,55,65]
No prodrome[48]	Absence of nausea/vomiting preceding syncopal event[67]
Palpitations preceding loss of consciousness[58]	VA[48,65]
Exertional syncope[58]	Cancer[48]
Structural heart disease[50,58,62,66,68]	Structural heart disease[48,68]
HF[54,58,64,66]	HF[65]
Cerebrovascular disease[50]	Cerebrovascular disease[48]
Family history of SCD[50]	Diabetes mellitus[69]
Trauma[48,62]	High CHADS-2 score[70]
Physical Examination or Laboratory Investigation	
Evidence of bleeding[58]	Abnormal ECG[65,67,71]
Persistent abnormal vital signs[50]	Lower GFR
Abnormal ECG[48,52,54,55,72]	
Positive troponin[55]	

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 Data Supplements 3 and 4 and summarized in Table 5 for selected studies. This table includes individual risk predictors from history, physical examination, and laboratory studies associated with adverse outcomes from selected studies.

Table 5 Examples of Syncope Risk Scores

Study/Reference	Year	Sample N	Events N (%)	Outcome Definition	ED Events*	Predictors	NPV (%)†
Martin[65]	1997	252	104 (41%)	1-y death/arrhythmia	Yes	Abnormal ECG‡; >45 y of age; VA; HF	93
Sarasin[54]	2003	175	30 (17%)	Inpatient arrhythmia	Yes	Abnormal ECG‡; >65 y of age; HF	98
OESIL[47]	2003	270	31 (11%)	1-y death	N/A	Abnormal ECG‡; >65 y of age; no prodrome; cardiac history	100
SFSR[52]	2004	684	79 (12%)	7-d serious events§	Yes	Abnormal ECG‡; dyspnea; hematocrit; systolic BP <90 mm Hg; HF	99
Boston Syncope Rule[50]	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[49]	2008	260	44 (17%)	Cardiac etiology	N/A	Abnormal ECG‡/cardiac history; palpitations; exertional; supine; precipitant (a low-risk factor); autonomic prodrome (low-risk factors)	99
STePS[48]	2008	676	41 (6%)	10-d serious events¶	Yes	Abnormal ECG‡; trauma; no prodrome; male sex	—
Syncope Risk Score[55]	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[53]	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.

2.3.4. Disposition After Initial Evaluation: Recommendations

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.**[72-74]
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.**[17]
IIa	B-R	**In intermediate-risk patients with an unclear cause of syncope, use of a structured emergency department observation protocol can be effective in reducing hospital admission.**[75-78]
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.**[73,79-81]

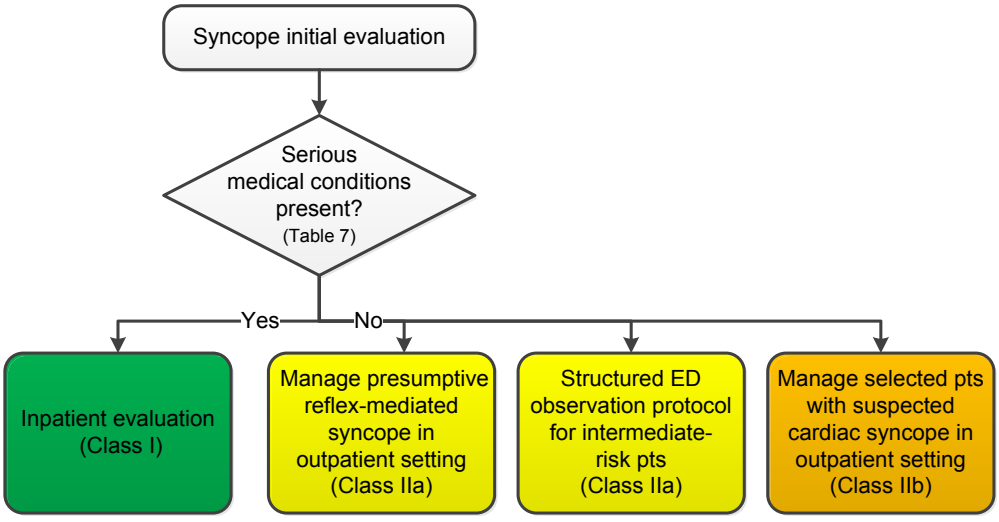

Figure 2 Patient Disposition After Initial Evaluation for Syncope.
Colors correspond to Class of Recommendation in Table 1.
ED indicates emergency department; and pts, patients.

Table 6 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

See Figure 3 for additional evaluation and diagnosis for syncope and Table 7 for a summary of types of ambulatory cardiac rhythm monitoring devices. See Online Data Supplements 7 through 16 for data supporting Section 3.

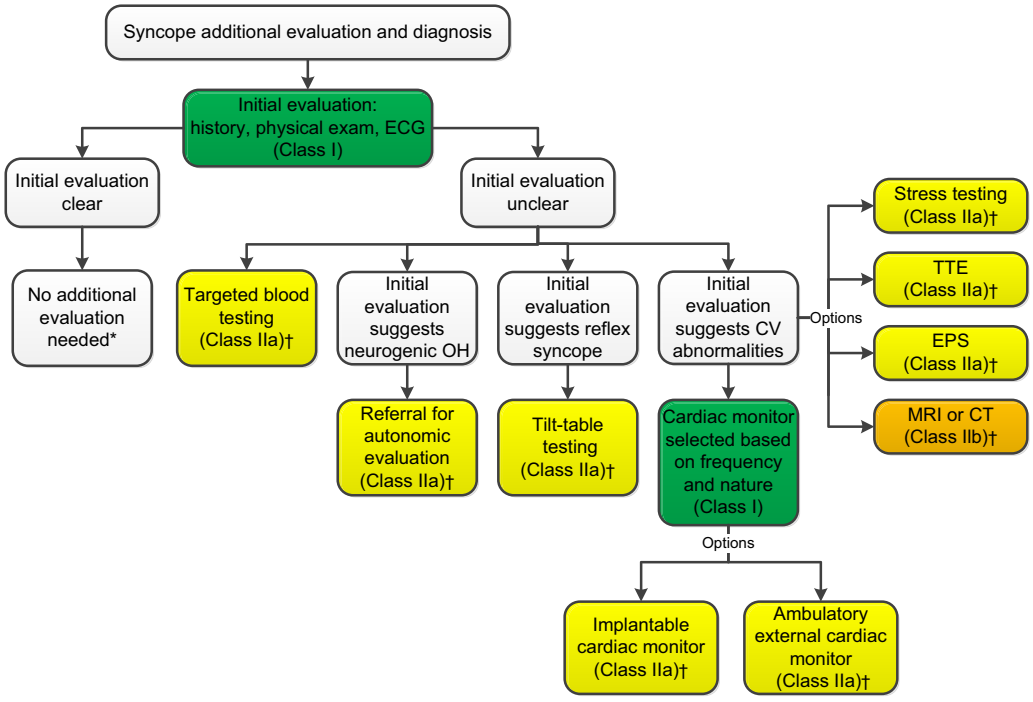

Figure 3 Additional Evaluation and Diagnosis for Syncope.
Colors correspond to Class of Recommendation in Table 1. *Applies to patients after a normal initial evaluation without significant injury or cardiovascular morbidities; patients followed up by primary care physician as needed. †In selected patients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

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.[82]
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.[83-86]
III: No Benefit	B-NR	Routine and comprehensive laboratory testing is not useful in the evaluation of patients with syncope.[87,88]

3.2. Cardiovascular Testing: Recommendations

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.[82,89,90]
IIb	B-NR	Computed tomography or magnetic resonance imaging may be useful in selected patients presenting with syncope of suspected cardiac etiology.[91]
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.[89,92]

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.[93,94]**

3.2.3. Cardiac Monitoring: Recommendations

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.**
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[95-99]** **2. Transtelephonic monitor[96,100,101]** **3. External loop recorder[96,100-102]** **4. Patch recorder[103-105]** **5. Mobile cardiac outpatient telemetry.[106,107]**
IIa	**B-R**	**To evaluate selected ambulatory patients with syncope of suspected arrhythmic etiology, an implantable cardiac monitor can be useful.[95,96,99,107-121]**

Table 7 Cardiac Rhythm Monitors

Types of Monitor	Device Description	Patient Selection
Holter monitor[97-99]	• 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)[96,100,101]	• 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)†[96,100,101]	• 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
External patch recorders[103-105]	• 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

(*Continued*)

Table 7 (*Continued*)

Types of Monitor	Device Description	Patient Selection
Mobile cardiac outpatient telemetry[106,107]	• 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[108,113,122-124]	• 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.**[92,125,126]

3.2.5. *Electrophysiological Study: Recommendations*

Recommendations for Electrophysiological Study (EPS)		
COR	LOE	Recommendations
IIa	B-NR	**EPS can be useful for evaluation of selected patients with syncope of suspected arrhythmic etiology.**[97,127-134]
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.**[134-136]

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 vasovagal syncope (VVS).**[137-142]
IIa	B-NR	**Tilt-table testing can be useful for patients with syncope and suspected delayed OH when initial evaluation is not diagnostic.**[143,144]
IIa	B-NR	**Tilt-table testing is reasonable to distinguish convulsive syncope from epilepsy in selected patients.**[145-148]
IIa	B-NR	**Tilt-table testing is reasonable to establish a diagnosis of pseudosyncope.**[149-151]
III: No Benefit	B-R	**Tilt-table testing is not recommended to predict a response to medical treatments for VVS.**[152,153]

3.3. Neurological Testing: Recommendations

3.3.1. Autonomic Evaluation: Recommendation

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.[144,154-157]

3.3.2. Neurological and Imaging Diagnostics: Recommendations

Recommendations for Neurological Diagnostics		
COR	LOE	Recommendations
IIa	C-LD	Simultaneous monitoring of an electroencephalogram and hemodynamic parameters during tilt-table testing can be useful to distinguish among syncope, pseudosyncope, and epilepsy.[151,158-160]
III: No Benefit	B-NR	Magnetic resonance imaging and computed tomography 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.[161,162]
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.[92,161-164]
III: No Benefit	B-NR	Routine recording of an electroencephalogram is not recommended in the evaluation of patients with syncope in the absence of specific neurological features suggestive of a seizure.[18,92,163-167]

4. Management of Cardiovascular Conditions

See Online Data Supplements 17 through 24 for data supporting Section 4.

4.1. Arrhythmic Conditions: Recommendations

4.1.1. Bradycardia: Recommendation

Recommendation for Bradycardia		
COR	LOE	Recommendation
I	C-EO	In patients with syncope associated with bradycardia, GDMT is recommended.[169]

4.1.2. Supraventricular Tachycardia: Recommendations

Recommendations for Supraventricular Tachycardia		
COR	LOE	Recommendations
I	C-EO	In patients with syncope and supraventricular tachycardia, GDMT is recommended.[170]
I	C-EO	In patients with atrial fibrillation, GDMT is recommended.[171]

4.1.3. Ventricular Arrhythmia: Recommendation

Recommendation for Ventricular Arrhythmia (VA)		
COR	LOE	Recommendation
I	C-EO	In patients with syncope and VA, GDMT is recommended.[169,172-174]

4.2. Structural Conditions: Recommendations

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.[169,172]

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.[175]

4.2.3. Hypertrophic Cardiomyopathy: Recommendation

Recommendation for Hypertrophic Cardiomyopathy (HCM)		
COR	LOE	Recommendation
I	C-EO	In patients with syncope associated with HCM, GDMT is recommended.[176]

4.2.4. Arrhythmogenic Right Ventricular Cardiomyopathy: Recommendations

Recommendations for Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)

COR	LOE	Recommendations
I	B-NR	Implantable cardioverter-defibrillator (ICD) implantation is recommended in patients with ARVC who present with syncope and have a documented sustained VA.[177-181]
IIa	B-NR	ICD implantation is reasonable in patients with ARVC who present with syncope of suspected arrhythmic etiology.[177-182]

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.[169,183-189]
I	C-EO	In patients with cardiac sarcoidosis presenting with syncope and conduction abnormalities, GDMT is recommended.[169,189-192]
IIa	B-NR	ICD implantation is reasonable in patients with cardiac sarcoidosis and syncope of suspected arrhythmic origin, particularly with left ventricular dysfunction or pacing indication.[193-196]
IIa	B-NR	EPS is reasonable in patients with cardiac sarcoidosis and syncope of suspected arrhythmic etiology.[197]

4.3. Inheritable Arrhythmic Conditions: Recommendations

4.3.1. Brugada Syndrome: Recommendations

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.[198-202]
IIb	B-NR	Invasive EPS study may be considered in patients with Brugada ECG pattern and syncope of suspected arrhythmic etiology.[199,203,204]
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.[205,206]

4.3.2. Short-QT Syndrome: Recommendation

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.

4.3.3. Long-QT Syndrome: Recommendations

Recommendations for Long-QT Syndrome (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.[207-209]
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.[208,210-214]
IIa	C-LD	Left cardiac sympathetic denervation 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.[215-217]

4.3.4. Catecholaminergic Polymorphic Ventricular Tachycardia: Recommendations

Recommendations for Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)

COR	LOE	Recommendations
I	C-LD	Exercise restriction is recommended in patients with CPVT presenting with syncope of suspected arrhythmic etiology.[218-220]
I	C-LD	Beta blockers lacking intrinsic sympathomimetic activity are recommended in patients with CPVT and stress-induced syncope.[218,221-225]
IIa	C-LD	Flecainide is reasonable in patients with CPVT who continue to have syncope of suspected VA despite beta-blocker therapy.[212,226]
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 left cardiac sympathetic denervation.[174,227,228]
IIb	C-LD	In patients with CPVT who continue to experience syncope or VA, verapamil with or without beta-blocker therapy may be considered.[229,230]
IIb	C-LD	Left cardiac sympathetic denervation may be reasonable in patients with CPVT, syncope, and symptomatic VA despite optimal medical therapy.[231-233]

4.3.5. Early Repolarization Pattern: Recommendations

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.
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.[234]

5. Reflex Conditions: Recommendations

See Figure 4 for the algorithm for treatment of VVS. See Online Data Supplements 25 through 32 for data supporting Section 5.

5.1. Vasovagal Syncope: Recommendations

Recommendations for Vasovagal Syncope		
COR	LOE	Recommendations
I	C-EO	Patient education on the diagnosis and prognosis of VVS is recommended.
IIa	B-R	Physical counter-pressure maneuvers can be useful in patients with VVS who have a sufficiently long prodromal period.[235-237]
IIa	B-R	Midodrine is reasonable in patients with recurrent VVS with no history of hypertension, heart failure, or urinary retention.[238-242]
IIb	B-R	The usefulness of orthostatic training is uncertain in patients with frequent VVS.[243-247]
IIb	B-R	Fludrocortisone might be reasonable for patients with recurrent VVS and inadequate response to salt and fluid intake, unless contraindicated.[248,249]
IIb	B-NR	Beta blockers might be reasonable in patients 42 years of age or older with recurrent VVS.[250-253]
IIb	C-LD	Encouraging increased salt and fluid intake may be reasonable in selected patients with VVS, unless contraindicated.[254-257]
IIb	C-LD	In selected patients with VVS, it may be reasonable to reduce or withdraw medications that cause hypotension when appropriate.[258]
IIb	C-LD	In patients with recurrent VVS, a selective serotonin reuptake inhibitor might be considered.[253,259,260]

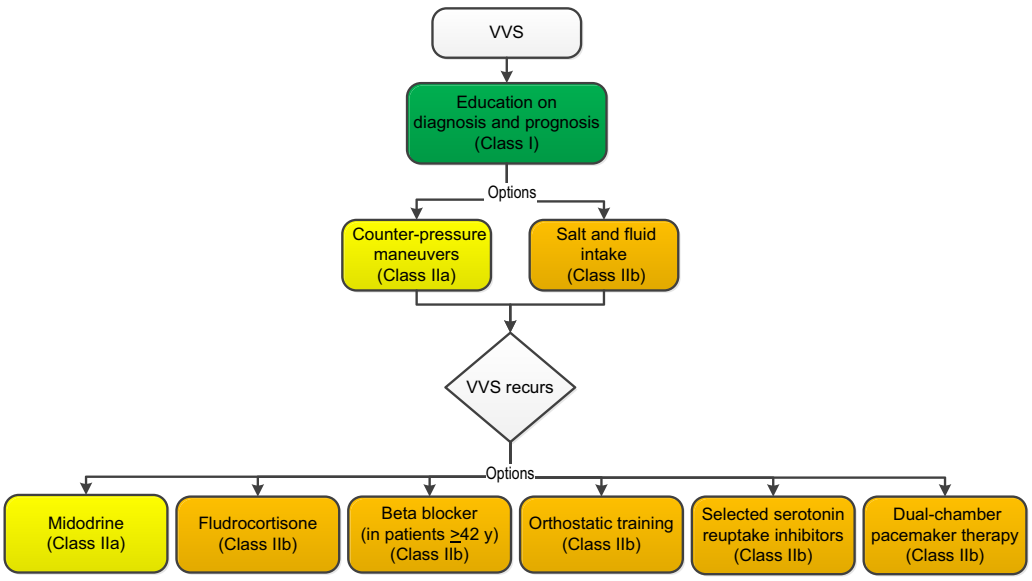

Figure 4 Vasovagal Syncope.
Colors correspond to Class of Recommendation in Table 1.
VVS indicates vasovagal syncope.

5.2. Pacemakers in Vasovagal Syncope: Recommendation

See the ERC systematic review report "Pacing as a Treatment for Reflex-Mediated (Vasovagal, Situational, or Carotid Sinus Hypersensitivity) Syncope" for the complete systematic evidence review.[10] Recommendations that are based on a body of evidence that includes the systematic review conducted by the ERC are denoted by the superscript SR (e.g., LOE B-R [SR]).

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.[261-266]

SR indicates systematic review.

5.3. Carotid Sinus Syndrome: Recommendations

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.[280–286] Appropriate investigations should be undertaken to determine an underlying etiology, including causes that may be reversible.[280,282–285] Evidence for treatment is limited mainly to case reports, small case series, and small observational studies.[280,282–285] 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.[285]

6. Orthostatic Hypotension: Recommendations

See Figure 5 for the algorithm for treating orthostatic hypotension (OH). See Online Data Supplements 33 through 37 for data supporting Section 6.

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.[267-275]
IIb	B-R	It may be reasonable to implant a dual-chamber pacemaker in patients with carotid sinus syndrome who require permanent pacing.[276-279]

6.1. Neurogenic Orthostatic Hypotension: Recommendations

Recommendations for Neurogenic Orthostatic Hypotension (OH)

COR	LOE	Recommendations
I	B-R	Acute water ingestion is recommended in patients with syncope caused by neurogenic OH for occasional, temporary relief.[287,288]
IIa	C-LD	Physical counter-pressure maneuvers can be beneficial in patients with neurogenic OH with syncope.[236,289-294]
IIa	C-LD	Compression garments can be beneficial in patients with syncope and OH.[295-299]
IIa	B-R	Midodrine can be beneficial in patients with syncope due to neurogenic OH.[300-309]
IIa	B-R	Droxidopa can be beneficial in patients with syncope due to neurogenic OH.[242,310-313]
IIa	C-LD	Fludrocortisone can be beneficial in patients with syncope due to neurogenic OH.[314-317]
IIb	C-LD	Encouraging increased salt and fluid intake may be reasonable in selected patients with neurogenic OH.[254,256,324-326]
IIb	C-LD	Pyridostigmine may be beneficial in patients with syncope due to neurogenic OH who are refractory to other treatments.[308,318,319]
IIb	C-LD	Octreotide may be beneficial in patients with syncope and refractory recurrent postprandial or neurogenic OH.[320-323]

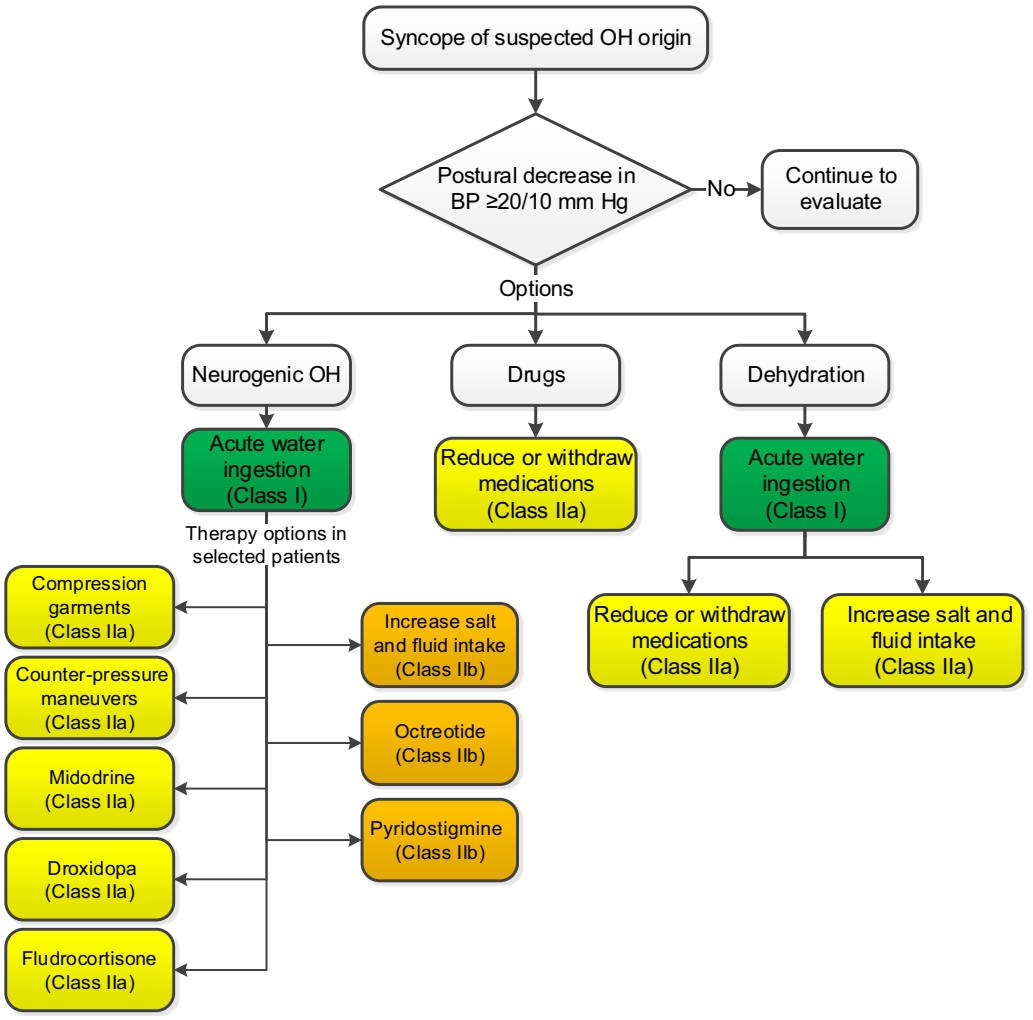

Figure 5 Orthostatic Hypotension
Colors correspond to Class of Recommendation in Table 1.
BP indicates blood pressure; and OH, orthostatic hypotension.

6.2. Dehydration and Drugs: Recommendations

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.[287,327-331]
IIa	B-NR	Reducing or withdrawing medications that may cause hypotension can be beneficial in selected patients with syncope.[332-339]
IIa	C-LD	In selected patients with syncope due to dehydration, it is reasonable to encourage increased salt and fluid intake.[254,328,330,331,340,341]

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.[8] 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.[8] The pathophysiology is quite varied. One condition of note is Postural Tachycardia Syndrome (POTS), in which upright posture results in an apparently inappropriate tachycardia, usually with heart rates >120 bpm.[9]

Although syncope occurs in patients with POTS, it is relatively infrequent, and there is little evidence that the syncope is due to POTS.[9,10] Treatments that improve symptoms of POTS might decrease the occurrence of syncope, although this is unknown.[9–19] For further guidance on the management of POTS, we refer readers to the Heart Rhythm Society consensus statement.[9]

8. Pseudosyncope: Recommendations

See Online Data Supplements 38 and 39 for data supporting Section 8.

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.[11,342-344]
IIb	C-LD	Cognitive behavioral therapy may be beneficial in patients with pseudosyncope.[345-347]

9. Uncommon Conditions Associated With Syncope

Table 9 in the full-text guideline[9] provides a list of less common conditions associated with syncope.

10. Age, Lifestyle, and Special Populations: Recommendations

See Online Data Supplements 40 to 42 for data supporting Section 10.

10.1. Pediatric Syncope: Recommendations

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.[348-357]
I	C-LD	Noninvasive diagnostic testing should be performed in pediatric patients presenting with syncope and suspected congenital heart disease, cardiomyopathy, or primary rhythm disorder.[209,349,351,352,354,357,358]
I	C-EO	Education on symptom awareness of prodromes and reassurance are indicated in pediatric patients with VVS.
IIa	C-LD	Tilt-table testing can be useful for pediatric patients with suspected VVS when the diagnosis is unclear.[350,356,359-366]
IIa	B-R	In pediatric patients with VVS not responding to lifestyle measures, it is reasonable to prescribe midodrine.[348,367,368]
IIb	B-R	Encouraging increased salt and fluid intake may be reasonable in selected pediatric patients with VVS.[369]
IIb	C-LD	The effectiveness of fludrocortisone is uncertain in pediatric patients with OH associated with syncope.[249,370,371]
IIb	B-NR	Cardiac pacing may be considered in pediatric patients with severe neurally mediated syncope secondary to pallid breath-holding spells.[372,373]
III: No Benefit	B-R	Beta blockers are not beneficial in pediatric patients with VVS.[371,374]

10.2. Adult Congenital Heart Disease: Recommendations

Recommendations for ACHD

COR	LOE	Recommendations
IIa	C-EO	For evaluation of patients with ACHD and syncope, referral to a specialist with expertise in ACHD can be beneficial.
IIa	B-NR	EPS is reasonable in patients with moderate or severe ACHD and unexplained syncope.[375,376]

10.3. Geriatric Patients: Recommendations

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.
IIa	B-NR	It is reasonable to consider syncope as a cause of nonaccidental falls in older adults.[377-381]

10.4. Driving and Syncope: Recommendation

The suggestions in Table 8 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.[20]

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.**

Table 8 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[382]	No restriction
VVS, 1–6 syncope per year[383]	1 month
VVS, >6 syncope per year[382,383]	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[382]	Not fit to drive
Carotid sinus syncope, treated with permanent pacemaker[382]	1 week
Syncope due to nonreflex bradycardia, untreated[382]	Not fit to drive
Syncope due to nonreflex bradycardia, treated with permanent pacemaker[169,382]	1 week
Syncope due to SVT, untreated[382]	Not fit to drive
Syncope due to SVT, pharmacologically suppressed[382]	1 month
Syncope due to SVT, treated with ablation[382]	1 week
Syncope with LVEF <35% and a presumed arrhythmic etiology without an ICD[384,385]	Not fit to drive
Syncope with LVEF <35% and presumed arrhythmic etiology with an ICD[386,387]	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[386,387]	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[382]	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

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.**
IIa	**C-LD**	**Assessment by a specialist with disease-specific expertise is reasonable for athletes with syncope and high-risk markers.[388,389]**
IIa	**C-LD**	**Extended monitoring can be beneficial for athletes with unexplained exertional syncope after an initial cardiovascular evaluation.[390,391]**
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.[392-396]**

11. Quality of Life and Healthcare Cost of Syncope

11.1. Impact of Syncope on Quality of Life

QoL is reduced with recurrent syncope,[397–405] as demonstrated in studies that compared patients with and without syncope.[399,405] QoL associated with recurrent syncope was equivalent to severe rheumatoid arthritis and chronic low-back pain in an adult population.[400] 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.[397]

11.2. Healthcare Costs Associated With Syncope

High healthcare costs are associated with the evaluation and management of syncope. These high costs have been estimated both in the United States and abroad.

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

- 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 quality of life, 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

- 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

- 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

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.2017.03.005.

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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

(*Continued*)

Appendix 1 (*Continued*)

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness	Voting Recusals by Section*
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 (section numbers correspond to the full-text guideline).

†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 Pharmaceuticals* • Theravance*	None	None	• Astellas Pharma (DSMB) • AstraZeneca* • Forest Pharmaceuticals* • Janssen Pharmaceuticals (DSMB) • Lundbeck* • Theravance*	None	None
Joaquin E. Cigarroa	Official Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	Oregon Health & Science University—Clinical Professor of Medicine	None	None	None	None	• NIH† • AHA† • SCAI† • ASA† • Catheterization and Cardiovascular Intervention†	None
Kenneth A. Ellenbogen	Official Reviewer—ACC/AHA	VCU Medical Center—Director, Clinical EP Laboratory	• AHA • Atricure* • Biosense Webster* • Biotronik* • Boston Science* • HRS* • Janssen Pharmaceuticals • Medtronic* • Pfizer* • Sentra Heart • St. Jude Medical*	None	None	• Atricure* • Boston Science • Biosense Webster • Daiichi-Sankyo* • Medtronic (DSMB) • Medtronic • NIH • Sanofi-aventis	• AHA • *American Heart Journal* • Biosense Webster* • Boston Science* • HRS • JCE • Medtronic* • PACE • Sanofi-aventis	• Defendant, Catheter ablation complication, 2015 • Plantiff, Lead extraction complication, 2015
Rakesh Gopinathannair	Official Reviewer—HRS	University of Louisville School of Medicine and Jewish Hospital Division of Cardiovascular Medicine—Associate Professor of Medicine, Director of Cardiac EP	• Boston Scientific • Health Trust PG • St. Jude Medical*	• AHA • Bristol-Myers Squibb • Pfizer* • Zoll Medical	None	None	None	None

(*Continued*)

Appendix 2 (*Continued*)

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
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	Children's Hospital Los Angeles—Professor of Pediatrics, Cardiology	None	None	None	None	None	• Defendant, SCD in CPVT patient, 2016
Sana M. Al-Khatib	Content Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	Duke Clinical Research Institute—Professor of Medicine	None	None	None	• FDA* • NHLBI* • PCORI* • VA Health System (DSMB)	• Elsevier* • AHA	None
Kim K. Birtcher	Content Reviewer—ACC/AHA Task Force on Clinical Practice Guidelines	University of Houston College of Pharmacy—Clinical Professor	• Jones & Bartlett Learning	None	None	None	None	None

Michele Brignole	Content Reviewer	Arrhythmologic Centre, Ospedali del Tigullio—Head of Cardiology	None	None	• F2 Solutions†	None	None	None
Hugh Calkins	Content Reviewer—ACC EP Section Leadership Council	Johns Hopkins Hospital—Professor of Medicine, Director of EP	• Abbott • Atricure • Boehringer Ingelheim* • Medtronic*	None	None	• Boehringer Ingelheim† • St. Jude Medical*	• Abbott Laboratories	• Defendant, SCD, 2015
Coletta Barrett	Content Reviewer—Lay Reviewer	Our Lady of the Lake Regional Medical Center—Vice President	None	None	None	None	None	None
Lin Yee Chen	Content Reviewer	University of Minnesota Medical School—Associate Professor of Medicine	None	None	None	None	• NIH*	None
Andrew Epstein	Content Reviewer	University of Pennsylvania Hospital and the Veteran's Administration Medical Center—Professor of Medicine	None	None	None	• Biosense Webster* • Biotronik* • Boston Scientific* (DSMB) • Boston Scientific* • C.R. Bard* • Medtronic (DSMB) • Medtronic* • St. Jude Medical* (DSMB) • St. Jude Medical	None	None
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

(*Continued*)

Appendix 2 (*Continued*)

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

Richard Sutton	Content Reviewer	National Heart and Lung Institute, Imperial College London—Emeritus Professor	• Medtronic*	• St. Jude Medical*	• Boston Scientific* • Edwards Lifesciences* • Shire Pharmaceuticals • AstraZeneca	• Medtronic*	None	• Defendant, Fatal car accident caused by VVS patient, 3 trials in 2016*
Gaurav Upadhyay	Content Reviewer—ACC EP Section Leadership Council	University of Chicago—Assistant Professor of Medicine	• Biosense Webster • Biotronik • Boston Scientific • Medtronic • St. Jude Medical • Zoll Medical	None	None	• Biosense Webster • Biotronik* • Medtronic*	None	None
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
CPVT = catecholaminergic polymorphic ventricular tachycardia
ECG = electrocardiogram/electrocardiographic
EPS = electrophysiological study
GDMT = guideline-directed management and therapy
HCM = hypertrophic cardiomyopathy
ICD = implantable cardioverter-defibrillator
LQTS = long-QT syndrome
OH = orthostatic hypotension
RCT = randomized controlled trial
POTS = postural tachycardia syndrome
SCD = sudden cardiac death
VA = ventricular arrhythmia
VVS = vasovagal syncope