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ESC Guidelines

Guidelines on Management (Diagnosis and Treatment) of Syncope — Update 2004☆ Executive Summary

The Task Force on Syncope, European Society of Cardiology☆☆

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Preamble

Guidelines and Expert Consensus documents aim to present all the relevant evidence on a particular issue in order to help physicians to weigh the benefits and risks of a particular diagnostic or therapeutic procedure. They should be helpful in everyday clinical decision-making.

A great number of Guidelines and Expert Consensus Documents have been issued in recent years by the European Society of Cardiology (ESC) and by different organisations and other related societies. This profusion can put at stake the authority and validity of guidelines, which can only be guaranteed if they have been developed by an unquestionable decision-making process. This is one of the reasons why the ESC and others have issued recommendations for formulating and issuing Guidelines and Expert Consensus Documents.

In spite of the fact that standards for issuing good quality Guidelines and Expert Consensus Documents are well defined, recent surveys of Guidelines and Expert Consensus Documents published in peer-reviewed journals between 1985 and 1998 have shown that methodological standards were not complied with in the vast majority of cases. It is therefore of great importance that guidelines and recommendations are presented in formats that are easily interpreted. Subsequently, their implementation programmes must also be well conducted. Attempts have been made to determine whether guidelines improve the quality of clinical practice and the utilization of health resources.

The *ESC Committee for Practice Guidelines* (*CPG*) supervises and coordinates the preparation of new *Guidelines* and *Expert Consensus Documents* produced by Task Forces, expert groups or consensus panels. The chosen experts in these writing panels are asked to provide disclosure statements of all relationships they may have which might be perceived as real or potential conflicts of interest. These disclosure forms are kept on file at the European Heart House, headquarters of the ESC. The Committee is also responsible for the endorsement of these Guidelines and Expert Consensus Documents or statements.

The Task Force has classified and ranked the usefulness or efficacy of the recommended procedure and/or treatments and the Level of Evidence as indicated in the tables below:

Classes of recommendations

Class I	Evidence and/or general agreement that a given diagnostic procedure/treatment is beneficial, useful and effective;
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the treatment;
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy;
Class IIb	Usefulness/efficacy is less well established by evidence/opinion;
Class III*	Evidence or general agreement that the treatment is not useful/effective and in some cases may be harmful.

*Use of Class III is discouraged by the ESC.

Levels of evidence

Level of evidence A	Data derived from multiple randomised clinical trials or meta-analyses
Level of evidence B	Data derived from a single randomised clinical trial or large non-randomised studies
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries

Introduction

The European Society of Cardiology guidelines for the management (diagnosis and treatment) of syncope were published in August 2001.[1] Since then, more clinical trials and observational studies have been published, some of which alter the recommendations made in that document. The panel reconvened in September 2003, made revisions where appropriate and developed the consensus recommendations. This executive summary reports the most important changes.

Furthermore, since the strategies for the assessment of syncope vary widely among physicians and among hospitals in Europe, we recognised the need to coordinate the evaluation of syncope. The panel sought to define ESC standards for the management of syncope and proposed a model of organisation for the evaluation of the syncope patient. A new section was thus added to the document on this topic.

The full revised text, including all references, of this document is available on the website of the European Society of Cardiology (www.escardio.org) in the section 'Knowledge Centre', Guidelines and Scientific Statements and it was published in Europace 2004;**6**: 467—537.

Part 1. The initial evaluation

The diagnostic strategy based on the initial evaluation

The 'Initial evaluation' of a patient presenting with syncope consists of: careful history, physical examination including orthostatic blood pressure measurements and standard electrocardiogram (ECG).[2—9]

Differentiating true syncope from 'non-syncopal' conditions associated with real or apparent transient loss of consciousness is generally the first diagnostic challenge and influences the subsequent diagnostic strategy (Fig. 1).

Table 1 provides a clinical classification of the principal known causes of transient loss of consciousness

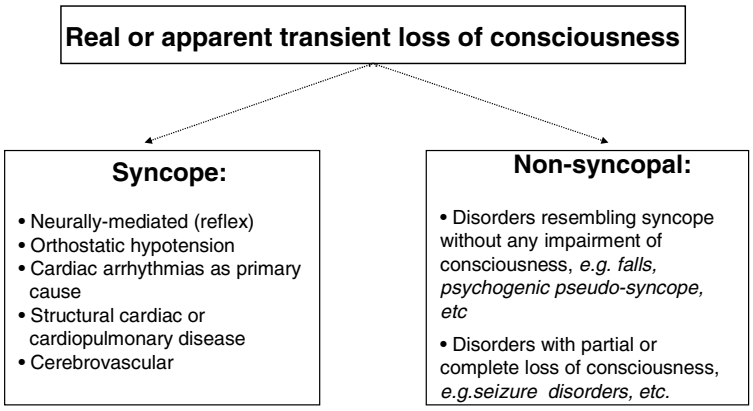

Fig. 1 Classification of transient loss of consciousness.

Table 1 Causes of syncope

Neurally-mediated (reflex)
- Vasovagal syncope (common faint)
  - classical
  - non-classical
- Carotid sinus syncope
- Situational syncope
  - acute haemorrhage
  - cough, sneeze
  - gastrointestinal stimulation (swallow, defaecation, visceral pain)
  - micturition (post-micturition)
  - post-exercise
  - post-prandial
  - others (e.g., brass instrument playing, weightlifting)
- Glossopharyngeal neuralgia

Orthostatic hypotension
- Autonomic failure
  - primary autonomic failure syndromes (e.g., pure autonomic failure, multiple system atrophy, Parkinson's disease with autonomic failure)
  - secondary autonomic failure syndromes (e.g., diabetic neuropathy, amyloid neuropathy)
  - post-exercise
  - post-prandial
- Drug (and alcohol)-induced orthostatic syncope
- Volume depletion
  - Haemorrhage, diarrhoea, Addison's disease

Cardiac Arrhythmias as primary cause
- Sinus node dysfunction (including bradycardia/tachycardia syndrome)
- Atrioventricular conduction system disease
- Paroxysmal supraventricular and ventricular tachycardias
- Inherited syndromes (e.g., long QT syndrome, Brugada syndrome)
- Implanted device (pacemaker, ICD) malfunction
- Drug-induced proarrhythmias

Structural cardiac or cardiopulmonary disease
- Obstructive cardiac valvular disease
- Acute myocardial infarction / ischaemia
- Obstructive cardiomyopathy
- Atrial myxoma
- Acute aortic dissection
- Pericardial disease/tamponade
- Pulmonary embolus / pulmonary hypertension

Cerebrovascular
- Vascular steal syndromes

(TLOC). The subdivision of syncope is based on pathophysiology as follows:

- 'Neurally-mediated (reflex) syncope' refers to a reflex response that, when triggered, gives rise to vasodilatation and bradycardia; however, the contribution of each of these two factors to systemic hypotension and cerebral hypoperfusion may differ considerably. The triggering events might vary considerably over time in any individual patient. The 'classical vasovagal syncope' is mediated by emotional or orthostatic stress and can be diagnosed by history taking. 'Carotid sinus syncope' is defined as syncope which, by history, seems to occur in close relationship with accidental mechanical manipulation of the carotid sinuses, and which can be reproduced by carotid sinus massage. 'Situational syncope' refers to those forms of neurally-mediated syncope associated with specific scenarios (e.g., micturition, coughing, defecating, etc.). Often, however, neurally-mediated syncopes have a 'non-classical' presentation. These forms are diagnosed by minor clinical criteria, exclusion of other causes for syncope (absence of structural heart disease) and the positive response to tilt testing or carotid sinus massage. Examples of non-classical vasovagal syncope include episodes without clear triggering events or premonitory symptoms.
- 'Orthostatic hypotension' refers to syncope in which the upright position (most often the movement from sitting or lying to an upright position) causes arterial hypotension. This occurs when the autonomic nervous system is incapacitated and fails to respond to the challenges imposed by upright position. A second major cause is 'volume depletion' in which the autonomic nervous system is itself not deranged, but is unable to maintain blood pressure due to decreased circulating volume. Note that vasovagal syncope can also be provoked by standing (e.g., soldiers fainting on parade), but these events are grouped under 'neurally-mediated (reflex) syncope'.
- 'Cardiac arrhythmias' can cause a decrease in cardiac output, which usually occurs irrespective of circulatory demands.
- 'Structural heart disease' can cause syncope when circulatory demands outweigh the impaired ability of the heart to increase its output.

Table 2 Causes of non-syncopal attacks (commonly misdiagnosed as syncope)

Disorders without any impairment of consciousness
- Falls
- Cataplexy
- Drop attacks
- Psychogenic pseudo-syncope
- Transient ischaemic attacks (TIA) of carotid origin

Disorders with partial or complete loss of consciousness
- Metabolic disorders, including hypoglycaemia, hypoxia, hyperventilation with hypocapnia
- Epilepsy
- Intoxications
- Vertebro-basilar transient ischaemic attack

Recommendations. Neurological and psychiatric investigations

Guidelines 2001	Update 2004
Neurological and psychiatric investigations are not routinely performed. Neurologic referral is indicated in patients in whom loss of consciousness cannot be attributed to syncope. Psychiatric evaluation is recommended when symptoms suggest a somatization disorder or if the patient has a known psychiatric disorder. In the case of unequivocal syncope, neurological referral is warranted when syncope may be due to autonomic failure or to a cerebrovascular cause	**Class I:** Neurological and psychiatric investigations are not routinely performed • Neurological referral is indicated in patients in whom loss of consciousness cannot be attributed to syncope • In case of unequivocal syncope neurological referral is warranted when syncope may be due to autonomic failure or to a cerebrovascular steal syndrome • Psychiatric evaluation is recommended when symptoms suggest psychogenic pseudo-syncope or if true syncope is due to psychiatric medication, which may need to be altered **Class III:** In all other patients with syncope, neurological and psychiatric investigations are not recommended

- 'Steal' syndromes can cause syncope when a blood vessel has to supply both part of the brain and an arm.

Non-syncopal conditions

Several disorders may resemble syncope in two different ways. In some, consciousness is truly lost, but the mechanism is something other than cerebral hypoperfusion. Examples are epilepsy, several metabolic disorders (including hypoxia and, hypoglycaemia) and intoxications. In several other disorders, consciousness is only apparently lost; this is the case in 'psychogenic pseudo-syncope', cataplexy and drop attacks. Table 2 lists the most common conditions misdiagnosed as the cause of syncope. A differentiation such as this is important because the clinician is usually confronted with patients with sudden loss of consciousness, which may be due to causes not associated with decreased cerebral blood flow such as seizure and/or conversion reaction.

The initial evaluation may lead to certain or suspected diagnosis or no diagnosis (here termed as unexplained syncope) (Fig. 2).

Certain diagnosis

Initial evaluation may lead to a certain diagnosis based on symptoms, signs or ECG findings. Under such circumstances, no further evaluation of the disease or disorder may be needed and treatment, if any, can be planned. This is the case in the following recommendations:

Recommendations. Diagnostic criteria based on the initial evaluation

Guidelines 2001	Update 2004
Diagnosis **Class I:** The results of the initial measures are diagnostic of the cause of syncope in the following situations:	**Diagnosis** **Class I:** The results of the initial evaluation are diagnostic of the cause of syncope in the following situations:
• Vasovagal syncope is diagnosed if precipitating events such as fear, severe pain, emotional distress, instrumentation or prolonged standing are associated with typical prodromal symptoms	• Classical vasovagal syncope is diagnosed if precipitating events such as fear, severe pain, emotional distress, instrumentation or prolonged standing are associated with typical prodromal symptoms.
• Situational syncope is diagnosed if syncope occurs during or Immediately after urination, defaecation, cough or swallowing.	• No change
• Orthostatic syncope is diagnosed when there is documentation of orthostatic hypotension associated with syncope or presyncope. Orthostatic blood pressure measurements are recommended after 5 min of lying supine, followed by each minute, or more often, after standing for 3 min. Measurements may be continued longer, if blood pressure is still falling at 3 min. If the patient does not tolerate standing for this period, the lowest systolic blood pressure during the upright posture should be recorded. A decrease in systolic blood pressure $\geqslant$20 mm Hg or a decrease of systolic blood pressure to <90 mm Hg is defined as orthostatic hypotension regardless of whether or not symptoms occur	• No change
• Cardiac ischaemia related syncope is diagnosed when symptoms are present with ECG evidence of acute ischaemia with or without myocardial infarction, independently of its mechanism	• No change
• Arrhythmia related syncope is diagnosed by ECG when there is: – Sinus bradycardia <40 beats/min or repetitive sinoatrial blocks or sinus pauses >3 s in the absence of negatively chronotropic medications – Mobitz II 2nd or 3rd degree atrioventricular block – Alternating left and right bundle branch block – Rapid paroxysmal supraventricular tachycardia or ventricular tachycardia – Pacemaker malfunction with cardiac pauses	• No change

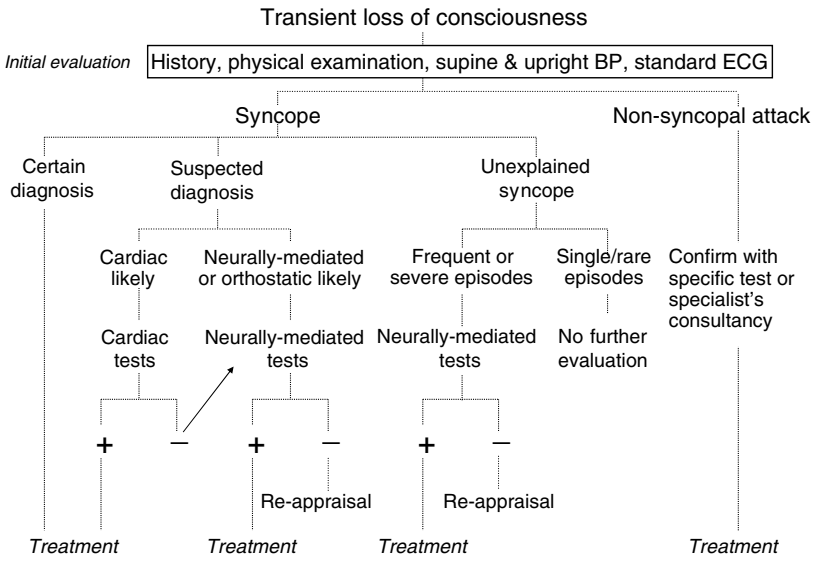

Fig. 2 The flow diagram proposed by the Task Force on Syncope of an approach to the evaluation of loss of consciousness based on the Initial Evaluation.

Instructions for the use of the flow diagram. Differentiating true syncope from other 'non-syncopal' conditions associated with real or apparent transient loss of consciousness is generally the first diagnostic step and influences the subsequent diagnostic strategy. For the classification of syncope refer to Table 1 and for the classification of non-syncopal attack refer to Table 2. The conditions in which the results of the initial evaluation are diagnostic of the cause of syncope and no further evaluation is required are listed as recommendations in the section ''The initial evaluation''. The features which suggest a cardiac or a neurally-mediated cause of syncope are listed in Tables 3 and 4. Among cardiac investigations, echocardiography, prolonged electrocardiographic monitoring, stress test, electrophysiological study and implantable loop recorder are most useful. Among neurally-mediated investigations, tilt test, carotid sinus massage and implantable loop recorder are most useful. When a cardiac diagnosis cannot be confirmed, neurally-mediated tests are usually performed. Once the evaluation, as outlined, is completed and no cause of syncope is determined, re-appraisal of the work-up may be needed. BP: blood pressure; ECG: electrocardiogram.

Table 3 Clinical features suggestive of specific causes of syncope

Neurally-mediated syncope:
- Absence of cardiac disease
- Long history of syncope
- After unpleasant sight, sound, smell or pain
- Prolonged standing or crowded, hot places
- Nausea, vomiting associated with syncope
- During or in the absorptive state after a meal
- With head rotation, pressure on carotid sinus(as in tumours, shaving, tight collars)
- After exertion

Syncope due to orthostatic hypotension:
- After standing up
- Temporal relationship with start of medication leading to hypotension or changes of dosage
- Prolonged standing especially in crowded, hot places
- Presence of autonomic neuropathy or Parkinsonism
- After exertion

Cardiac syncope:
- Presence of severe structural heart disease
- During exertion, or supine
- Preceded by palpitation or accompanied by chest pain
- Family history of sudden death

Cerebrovascular syncope:
- With arm exercise
- Differences in blood pressure or pulse in the two arms

Suspected diagnosis

More commonly, the initial evaluation leads to a suspected diagnosis, when one or more of the features listed in Tables 3 and 4 are present. A suspected diagnosis needs to be confirmed by directed testing. If a diagnosis is confirmed by specific testing, treatment may be initiated. On the other hand, if the diagnosis is not confirmed, then patients are considered to have unexplained syncope and are evaluated as follows.

Unexplained syncope

The initial evaluation may lead to no diagnosis (here termed as unexplained syncope). The strategy of evaluation varies according to the severity and frequency of the episodes. In patients with unexplained syncope the likely diagnosis is neurally-mediated. The tests for neurally mediated syncope consist of tilt testing and carotid massage. The majority of patients with single or rare episodes in this category probably have neurally mediated syncope and tests for confirmation are usually not necessary. If it is not clear that it was syncope, the term 'transient loss of consciousness (TLOC) is preferable and reappraisal is warranted.

Re-appraisal

Once the evaluation, as outlined, is completed and no cause of syncope is determined, re-appraisal of the work-up is needed since subtle findings or new historical information may change the entire differential diagnosis.

Table 4 ECG abnormalities suggesting an arrhythmic syncope

- Bifascicular block (defined as either left bundle branch block or right bundle branch block combined with left anterior or left posterior fascicular block)
- Other intraventricular conduction abnormalities (QRS duration $\geqslant$0.12 s)
- Mobitz I second degree atrioventricular block
- Asymptomatic sinus bradycardia (<50 bpm), sinoatrial block or sinus pause $\geqslant$3 s in the absence of negatively chronotropic medications
- Pre-excited QRS complexes
- Prolonged QT interval
- Right bundle branch block pattern with ST-elevation in leads V1–V3 (Brugada syndrome)
- Negative T waves in right precordial leads, epsilon waves and ventricular late potentials suggestive of arrhythmogenic right ventricular dysplasia
- Q waves suggesting myocardial infarction

Recommendations. Diagnostic work-up based on the initial evaluation

Guidelines 2001	Update 2004
When the mechanism of syncope is not evident, the presence of suspected or certain heart disease is associated with a higher risk of arrhythmias and a higher mortality at one year. In these patients, cardiac evaluation (consisting of echocardiography, stress testing and tests for arrhythmia detection such as prolonged electrocardiographic and loop monitoring or electrophysiological study) is recommended. If cardiac evaluation does not show evidence of arrhythmia as a cause of syncope, evaluation for neurally mediated syndromes is recommended in those with recurrent or severe syncope	When the mechanism of syncope is not evident, the presence of suspected or certain heart disease is associated with a higher risk of arrhythmias and a higher mortality at one year. In the patients with the clinical features suggesting a cardiac syncope listed in Tables 3 and 4, cardiac evaluation is recommended. Cardiac evaluation consists of echocardiography, stress testing, prolonged ECG monitoring (Holter, external or implantable loop recorder as appropriate) and electrophysiological study. If cardiac evaluation does not show evidence of arrhythmia as a cause of syncope, evaluation for neurally mediated syncope is recommended in those with recurrent or severe syncope
In patients without suspected or certain heart disease, evaluation for neurally mediated syncope is recommended for those with recurrent or severe syncope. The tests for neurally mediated syncope consist of tilt testing and carotid massage. The majority of patients with single or rare episodes in this category probably have neurally mediated syncope. An additional consideration is psychiatric illness. Psychiatric assessment is recommended in patients with frequent recurrent syncope who have multiple other somatic complaints and initial evaluation raises concerns for stress, anxiety and possible other psychiatric disorders	In patients without suspected or certain heart disease, evaluation for neurally mediated syncope is recommended for those with recurrent or severe syncope. The tests for neurally mediated syncope consist of tilt testing and carotid massage and, if negative, prolonged ECG monitoring and implantable loop recorder. The majority of patients with single or rare episodes in this category probably have neurally mediated syncope and tests for confirmation are usually not necessary

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Recommendations. Diagnostic work-up based on the initial evaluation

Guidelines 2001	Update 2004
Indications **Class I:** • Basic laboratory tests are only indicated if syncope may be due to loss of circulating volume, or if a syncope-like disorder with a metabolic cause is suspected • In patients with suspected heart disease, echocardiography, prolonged electrocardiographic monitoring and, if non-diagnostic, electrophysiological studies are recommended as first evaluation steps • In patients with palpitations associated with syncope, electrocardiographic monitoring and echocardiography are recommended as first evaluation steps • In patients with chest pain suggestive of ischaemia before or after loss of consciousness, stress testing, echocardiography, and electrocardiographic monitoring are recommended as first evaluation steps • In young patients without suspicion of heart or neurological disease and recurrent syncope, tilt testing and, in older patients, carotid sinus massage are recommended as first evaluation steps • In patients with syncope occurring during neck turning, carotid sinus massage is recommended at the outset • In patients with syncope during or after effort, echocardiography and stress testing are recommended as first evaluation steps • In patients with signs of autonomic failure or neurological disease a specific diagnosis should be made	**Specific indications** • Basic laboratory tests are only indicated if syncope may be due to loss of circulating volume, or if a syncope-like disorder with a metabolic cause is suspected • In patients with suspected heart disease, echocardiography, prolonged electrocardiographic monitoring and, if non-diagnostic, electrophysiological studies are recommended as first evaluation steps • In patients with palpitations associated with syncope, electrocardiographic monitoring and echocardiography are recommended as first evaluation steps • In patients with chest pain suggestive of ischaemia before or after loss of consciousness, stress testing, echocardiography, and electrocardiographic monitoring are recommended as first evaluation steps • In young patients without suspicion of heart or neurological disease and recurrent syncope, tilt testing and, in older patients, carotid sinus massages are recommended as first evaluation steps • In patients with syncope occurring during neck turning, carotid sinus massage is recommended at the outset • In patients with syncope during or after effort, echocardiography and stress testing are recommended as first evaluation steps • In patients with signs of autonomic failure or neurological disease a specific diagnosis should be made • In patients with frequent recurrent syncope who have multiple other somatic complaints and initial evaluation raises concerns for stress, anxiety and possible psychiatric disorders, psychiatric assessment is recommended • When the mechanism of syncope remains unclear after full evaluation, an implantable loop recorder is indicated in patients who have the clinical or ECG features suggesting an arrhythmic syncope listed in Tables 3 and 4 or a history of recurrent syncopes with injury

Re-appraisal may consist of obtaining details of history and re-examining patients as well as review of the entire work-up. If unexplored clues to possible cardiac or neurological disease are apparent, further cardiac and neurological assessment is recommended. In these circumstances, consultation with appropriate speciality services may be needed. An additional consideration is psychiatric illness. Psychiatric assessment is recommended in patients with frequent recurrent syncope who have multiple other somatic complaints and initial evaluation raises concerns for stress, anxiety and possible other psychiatric disorders.

Part 2. Diagnostic tests

Electrocardiographic monitoring (non-invasive and invasive)

As a general rule ECG monitoring is indicated only when there is a high pre-test probability of identifying an arrhythmia responsible for syncope. These conditions are those listed in Tables 3 and 4.

In-hospital monitoring (in bed or telemetric) is warranted only when the patient is at high risk of life-threatening arrhythmias. A few days of ECG monitoring may be of value, especially if the monitoring is applied immediately after a syncopal attack.

In a recent study,[10] external loop recorder was not useful for diagnosis of syncope in patients with 3 ± 4 episodes ($\geqslant$2) of syncope during the previous 6 months, no overt heart disease and a negative tilt testing.

In the initial clinical experience Implantable Loop Recorder was used for diagnosis in patients with unexplained syncope after a comprehensive conventional work-up. Pooled data from 4 studies[11–14] for a total of 247 patients showed that a correlation between syncope and ECG was found in 84 patients (34%); of these 52% had a bradycardia or asystole at the time of the recorded event, 11% had tachycardia and 37% had no rhythm variation. One study[15] randomized 60 patients with unexplained syncope to ''conventional'' testing with

external loop recorder, tilt and electrophysiological testing or to prolonged monitoring with the Implantable Loop Recorder. The results showed that a strategy of implantation of the Loop recorder in an initial phase of the work-up is more likely to provide a diagnosis than conventional testing (52% vs. 20%) (level B). There are several areas of interest that merit further clarification:

- patients in whom epilepsy was suspected but the treatment has proven ineffective;[16]
- patients with recurrent unexplained syncope without structural heart disease when the understanding of the exact mechanism of spontaneous syncope may alter the therapeutic approach;[11]
- patients who have a diagnosis of neurally-mediated syncope when the understanding of the exact mechanism of spontaneous syncope may alter the therapeutic approach;[11]
- patients with bundle branch block in whom a paroxysmal AV block is suspected despite a complete negative electrophysiological evaluation;[17]
- patients with definite structural heart disease and/or non-sustained ventricular tachyarrhythmias in whom a ventricular tachyarrhythmia is suspected despite a completely negative electrophysiological study;[17]
- patients with unexplained falls.[18]

Recommendations. Electrocardiographic monitoring

Guidelines 2001	Update 2004
Indications **Class I:** • Holter monitoring is indicated in patients with structural heart disease and frequent symptoms or even infrequent when there is a high pre-test probability of identifying an arrhythmia responsible of syncope • When the mechanism of syncope remains unclear after full evaluation, External or Implantable Loop Recorders are recommended when there is a high pre-test probability of identifying an arrhythmia responsible for syncope	**Indications** **Class I:** • In-hospital monitoring (in bed or telemetric) is warranted when the patient has an important structural heart disease and is at high risk of life-threatening arrhythmias (see chapter 'Need for hospitalisation') • Holter monitoring is indicated in patients who have the clinical or ECG features suggesting an arrhythmic syncope such as those listed in Tables 3 and 4 and very frequent syncopes or pre-syncopes • When the mechanism of syncope remains unclear after full evaluation, Implantable Loop Recorder is indicated in patients who have the clinical or ECG features suggesting an arrhythmic syncope such as those listed in Tables 3 and 4 or a history of recurrent syncope with injury **Class II:** • Holter monitoring may be useful in patients who have the clinical or ECG features suggesting an arrhythmic syncope such as those listed in Tables 3 and 4 in order to guide subsequent examinations (i.e. electrophysiological study) • External Loop Recorder may be indicated in patients who have the clinical or ECG features suggesting an arrhythmic syncope such as those listed in Tables 3 and 4 and inter-symptom interval $\leqslant$4 weeks • Implantable Loop Recorder may be indicated: – In an initial phase of the work-up instead of completion of conventional investigations in patients with preserved cardiac function who have the clinical or ECG features suggesting an arrhythmic syncope as those listed in Tables 3 and 4 – To assess the contribution of bradycardia before embarking on cardiac pacing in patients with suspected or certain neurally-mediated syncope presenting with frequent or traumatic syncopal episodes **Class III:** ECG monitoring is unlikely to be useful in patients who do not have the clinical or ECG features suggesting an arrhythmic syncope as those listed in Tables 3 and 4 and, therefore, it should not be performed

(*Continued on next page*)

Recommendations. Electrocardiographic monitoring

Guidelines 2001	Update 2004
Diagnosis **Class I:** • ECG monitoring is diagnostic when a correlation between syncope and an electrocardiographic abnormality (brady- or tachyarrhythmia) is detected • ECG monitoring excludes an arrhythmic cause when there is a correlation between syncope and sinus rhythm • In the absence of such correlations additional testing is recommended with possible exception of: – ventricular pauses longer than 3 s when awake – periods of Mobitz II or 3rd degree atrioventricular block when awake – rapid paroxysmal ventricular tachycardia	**Diagnosis** **Class I:** • ECG monitoring is diagnostic when a correlation between syncope and an electrocardiographic abnormality (brady- or tachyarrhythmia) is detected • ECG monitoring excludes an arrhythmic cause when there is a correlation between syncope and no rhythm variation • In the absence of such correlations additional testing is recommended with possible exception of: – ventricular pauses longer than 3 s when awake – periods of Mobitz II or 3rd degree atrioventricular block when awake – rapid paroxysmal ventricular tachycardia **Class II:** • Presyncope may not be an accurate surrogate for syncope in establishing a diagnosis and, therefore, therapy should not be guided by presyncopal findings

Electrophysiological testing

Suspected ventricular tachycardia

The outcome largely depends on the clinical features of the patients. It seems that only the inducibility of sustained ventricular tachycardia and/or very depressed systolic function can predict a life-threatening arrhythmic syncope and, conversely, their absence suggests a more favourable outcome.

The specificity of the induction of polymorphic ventricular tachycardia and ventricular fibrillation probably depends on the clinical setting. On one hand, in coronary artery disease and syncope, the follow-up of patients with and without inducible ventricular fibrillation did not demonstrate any difference in survival between the two groups.[19] On the other hand, the induction of polymorphic ventricular arrhythmias seems to have a predictive value in patients with the Brugada syndrome,[20,21] in survivors of cardiac arrest with significant coronary artery disease undergoing

Recommendations. Electrophysiological testing

Guidelines 2001	Update 2004
Indications **Class I:** • An invasive electrophysiological procedure is indicated when the initial evaluation suggests an arrhythmic cause of syncope (in patients with abnormal electrocardiography and/or structural heart disease or syncope associated with palpitations or family history of sudden death). **Class II:** • Diagnostic reasons: to evaluate the exact nature of an arrhythmia which has already been identified as the cause of the syncope • Prognostic reasons: in patients with cardiac disorders, in which arrhythmia induction has a bearing on the selection of therapy; and in patients with high-risk occupations, in whom every effort to exclude a cardiac cause of syncope is warranted **Class III:** • In patients with normal electrocardiograms and no heart disease and no palpitations an electrophysiological study is not usually undertaken	**Indications** **Class I:** • An invasive electrophysiological procedure is indicated when the initial evaluation suggests an arrhythmic cause of syncope such as those listed in Tables 3 and 4 **Class II:** • To evaluate the exact nature of an arrhythmia which has already been identified as the cause of the syncope • In patients with high-risk occupations, in whom every effort to exclude a cardiac cause of syncope is warranted **Class III:** • No change

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Recommendations. Electrophysiological testing

Guidelines 2001	Update 2004
Diagnosis **Class I:** • Normal electrophysiological findings cannot completely exclude an arrhythmic cause of syncope; when an arrhythmia is likely, further evaluations (for example loop recording) are recommended. • Depending on the clinical context, abnormal electrophysiological findings may not be diagnostic of the cause of syncope. • An electrophysiological study is diagnostic, and usually no additional tests are required, in the following cases: — sinus bradycardia and a very prolonged CSNRT (as discussed in the text) — bifascicular block and: — a baseline HV interval of ⩾100 ms, or — 2nd or 3rd degree His-Purkinje block is demonstrated during incremental atrial pacing, or — (if the baseline electrophysiological study is inconclusive) high-degree His-Purkinje block is provoked by intravenous administration of ajmaline, procainamide, or disopyramide — previous myocardial infarction and induction of sustained monomorphic ventricular tachycardia — arrhythmogenic right ventricular dysplasia and induction of ventricular tachyarrhythmias — induction of rapid supraventricular arrhythmia which reproduces hypotensive or spontaneous symptoms **Class II:** Divergence of opinion exists on the diagnostic value of electrophysiological study in case of: — HV interval of >70 ms but <100 ms — induction of polymorphic ventricular tachycardia or ventricular fibrillation in patients with ischaemic or dilated cardiomyopathy — Brugada syndrome	**Diagnosis** **Class I:** • No change • No change • An electrophysiological study is diagnostic, and usually no additional tests are required, in the following cases: — sinus bradycardia and a very prolonged CSNRT (as discussed in the text) — bifascicular block and: — a baseline HV interval of ⩾100 ms, or — 2nd or 3rd degree His-Purkinje block is demonstrated during incremental atrial pacing, or — (if the baseline electrophysiological study is inconclusive) high-degree His-Purkinje block is provoked by intravenous administration of ajmaline, procainamide, or disopyramide — induction of sustained monomorphic ventricular tachycardia — induction of rapid supraventricular arrhythmia which reproduces hypotensive or spontaneous symptoms **Class II:** The diagnostic value of an electophysiological study is less well established in case of: • HV interval of >70 ms but <100 ms • Induction of polymorphic ventricular tachycardia or ventricular fibrillation in patients with Brugada syndrome, arrhythmogenic right ventricular dysplasia and patients resuscitated from cardiac arrest **Class III:** The induction of polymorphic ventricular tachycardia or ventricular fibrillation in patients with ischaemic or dilated cardiomyopathy has a low predictive value

coronary by-pass surgery and in idiopathic ventricular fibrillation.[22–24]

Programmed ventricular stimulation has a low predictive value in patients with nonischaemic dilated cardiomyopathy. In a study[25] of selected patients affected by idiopathic dilated cardiomyopathy who received an ICD, there was a high incidence of appropriate shocks both in the inducible and in non-inducible sustained monomorphic ventricular tachycardia groups. In another study[26] the induction of polymorphic ventricular tachycardia or fibrillation during electrophysiological study was of no value for predicting syncopal events or ventricular tachyarrhythmias.

ATP test

Endogenous adenosine release may be involved in the triggering mechanism of syncope induced during tilt testing.[27] In a prospective follow-up study,[28] using an Implantable Loop Recorder for arrhythmia detection, the mechanism of syncope was heterogeneous and ATP-induced AV block predicted AV block as the mechanism of the spontaneous syncope only in a few patients; the overall outcome was benign and there were no complications.

Recommendations. ATP test

Guidelines 2001	Update 2004
The test requires the rapid injection of a 20 mg bolus of ATP during electrocardiographic monitoring. Asystole lasting more than 6 s, or AV block lasting more than 10 s, is considered abnormal	No change
ATP testing produces an abnormal response in some patients with syncope of unknown origin, but not in controls. The diagnostic and predictive value of the test remains to be confirmed by prospective studies. In the absence of sufficient hard data, the test may be indicated at the end of the diagnostic work-up (Class II)	ATP testing produces an abnormal response in some patients with syncope of unknown origin, but not in controls. ATP testing identifies a group of patients with otherwise unexplained syncope with definite clinical features and benign prognosis but possibly heterogeneous mechanism of syncope. Thus specific treatment should be postponed until a definite mechanism of syncope can be obtained (Class II)

Part 3. Treatment

Neurally-mediated (reflex) syncope

Non-pharmacological ''physical'' treatments are emerging as a new front line treatment of vasovagal syncope. In highly motivated patients with recurrent vasovagal symptoms, the prescription of progressively prolonged periods of enforced upright posture (so-called 'tilt-training') may reduce syncope recurrence. However, this treatment is hampered by the low compliance of patients to continue the training programme for a long period[29–32] (Level B). Two recent clinical trials[33,34] have shown that isometric counter-pressure manoeuvres of the legs (leg crossing) or of the arms (hand grip and arm

Recommendations. Treatment of neurally-mediated (reflex) syncope

Guidelines 2001	Update 2004
It is valuable to assess the relative contribution of cardioinhibition and vasodepression before embarking on specific treatment as there are different therapeutic strategies for the two aspects. Even if evidence of utility of such an assessment exists only for the carotid sinus massage, it is recommended to extend this assessment also by means of tilt testing or implantable loop recorder	In general, initial treatment, e.g. education and reassurance, is sufficient. Additional treatment may be necessary in high risk or high frequency settings when: • syncope is very frequent, e.g. alters the quality of life • syncope is recurrent and unpredictable (absence of premonitory symptoms) and exposes patients at ''high risk'' of trauma • syncope occurs during the prosecution of a 'high risk' activity (e.g., driving, machine operator, flying, competitive athletics, etc.)
Patients who have syncope in a 'high risk' setting (e.g., commercial vehicle driver, machine operator, pilot, commercial painter, competitive athlete) merit specific consideration for treatment. There is no information available regarding the efficacy of treatment in this type of patient, and whether it differs from other patients with neurally-mediated faints	
Treatment is not necessary in patients who have sustained a single syncope and are not having syncope in a high risk setting	Treatment is not necessary in patients who have sustained a single syncope and are not having syncope in a high risk setting It is valuable to assess the relative contribution of cardioinhibition and vasodepression before embarking on specific treatment as there are different therapeutic strategies for the two aspects. Even if evidence of utility of such an assessment exists only for the carotid sinus massage, it is recommended to extend this assessment also by means of tilt testing or implantable loop recorder.

(*Continued on next page*)

Recommendations. Treatment of neurally-mediated (reflex) syncope

Guidelines 2001	Update 2004
Class I: • Explanation of the risk, and reassurance about the prognosis in vasovagal syncope • Avoidance of trigger events as much as possible and reducing magnitude of potential triggers when feasible (e.g. emotional upset) and causal situation in situational syncope • Modification or discontinuation of hypotensive drug treatment for concomitant conditions • Cardiac pacing in patients with cardioinhibitory or mixed carotid sinus syndrome	**Class I:** • No change
Class II: • Volume expansion by salt supplements, an exercise programme or sleeping >10° head-up in posture-related syncope • Cardiac pacing in patients with cardioinhibitory vasovagal syncope with a frequency >5 attacks per year or severe physical injury or accident and age >40 • Tilt training in patients with vasovagal syncope	**Class II:** • Volume expansion by salt supplements, an exercise program or head-up tilt sleeping (>10°) in posture-related syncope • Tilt training in patients with vasovagal syncope • Isometric leg and arm counter-pressure manoeuvres in patients with vasovagal syncope • Cardiac pacing in patients with cardioinhibitory vasovagal syncope with a frequency >5 attacks per year or severe physical injury or accident and age >40
Class III: • The evidence fails to support the efficacy of beta-adrenergic blocking drugs. Beta-adrenergic blocking drugs may aggravate bradycardia in some cardioinhibitory cases	**Class III:** • No change

tensing) are able to induce a significant blood pressure increase during the phase of impending vasovagal syncope, which allow the patient to avoid or delay losing consciousness in most cases (level B).

Pacing for vasovagal syncope has been the subject of five major multicentre randomised controlled trials:[35–39] three gave positive and two negative results. Putting together the results of the 5 trials, 318 patients were evaluated; syncope recurred in 21% (33/156) of the paced patients and in 44% (72/162) of not paced patients ($p < 0.001$). However, all the studies have weaknesses and further follow-up studies addressing many of these limitations (particularly the pre-implant selection criteria of the patients who might benefit from pacemaker therapy) need to be completed before pacing can considered an established therapy.

Part 4. Special issues

Syncope in paediatric patients

Careful personal and family history and standard ECG is most important in distinguishing the benign neurally-mediated syncopes (also called reflex anoxic seizure or breath holding spells in infants and children). There are numerous warning signs from the history that should indicate a potentially life-threatening cause.[40] These are:

- syncope in response to loud noise, fright, or extreme emotional stress
- syncope during exercise including swimming (near drowning)
- syncope while supine
- family history of sudden death in young person <30 years old

Recommendations. Syncope in paediatric patients

Guidelines 2001	Update 2004
No recommendations	**Class I:** • Syncope in childhood is common. The vast majority of episodes are benign and are due to neurally-mediated syncope. Only a minority have some potentially life-threatening cause • The diagnosis and differentiation of benign from more serious causes is made primarily by the history and standard ECG

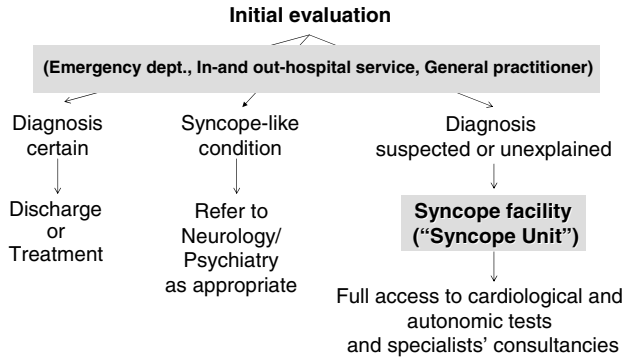

Fig. 3 A proposed model of organisation for the evaluation of the syncope patient in a community.

Probably the most important investigation is ECG, primarily to exclude inherited syndromes.

Syncope management facilities

Syncope is a common symptom in the community and in emergency medicine. In one study,[41] syncope and collapse were the sixth commonest reason for admission of adults aged over 65 years to acute medical hospital beds. The average length of stay for these admissions was 5–17 days – emphasising the diversity of syncope management strategies and availability of existing investigations. Hospital admission alone accounted for 74% of the cost of investigating syncope.[41] In a study, based on administrative data from Medicare, there were estimated to be 193,164 syncope hospital discharges in 1993 in the USA.[42] The cost per discharge was calculated to $4,132 and increased to $5,281 for those patients who were readmitted for recurrent syncope. In the UK[41] the overall cost per patient was £611, with 74% attributed to the costs of hospital stay alone. Cost per diagnosis of patients admitted to hospital was £1080.

Currently, the strategies for assessment of syncope vary widely among physicians and among hospitals and clinics. More often than not, the evaluation and treatment of syncope is haphazard and not stratified. The result is a wide variation in the diagnostic tests applied, the proportion and types of attributable diagnoses and the proportion of syncope patients in whom the diagnosis remains unexplained.[41,43–45] For example, in a prospective registry[43] enrolling patients referred to the emergency department from 28 general hospitals in Italy, carotid sinus massage was performed in 0–58% and head up tilt tests in from 0% to 50% of the syncope patients. Consequently the final diagnosis for neurally-mediated syncope ranged from 10% to 79%. These disparate patterns of assessment can explain why pacing rates for carotid sinus syndrome vary, even within countries, from 1% to 25% of implants, depending on whether carotid sinus hypersensitivity is systematically assessed in the investigation profile. If the evaluation of syncope remains unchanged, diagnostic and treatment effectiveness is unlikely to improve substantially. Furthermore, the implementation of the published syncope management guidelines will be diverse and incomplete. Thus, to maximise implementation of the guidelines it is recommended that models of care for assessment and management of syncope are in place and that information about the models within each organisation is adequately communicated to all parties involved with syncope patients.

It is the view of the European Society of Cardiology Syncope Task Force that a cohesive, structured care pathway – either delivered within a single syncope facility or as a more multi-faceted service – is the optimal for quality service delivery (Fig. 3).

Professional skill mix for the syncope evaluation facility

It is probably not appropriate to be dogmatic regarding the training needs of personnel responsible for a dedicated syncope facility. These skills will depend on the pre-determined requirements of local professional bodies, the level of screening evaluation provided prior to referral, and the nature of the patient population typically encountered in a given setting. In general, experience and training in key components of cardiology, neurology, emergency and geriatric medicine are pertinent to the assessment and diagnosis of syncope. In addition, access to other specialties such as psychiatry, physiotherapy, occupational therapy, Ear Nose and Throat specialties and clinical psychology is important.

Core medical and support personnel should be involved full time or most of the time in the management of the Unit and should interact with all other stakeholders in the hospital and in the community.

Staff responsible for the clinical management of the facility should be conversant with the recent syncope guidelines. A structured approach to the management of syncope also expedites clinical audit, patient information systems, service developments, and continuous professional training.

Equipment

Core equipment for the syncope evaluation facility include: surface ECG recording, phasic blood pressure monitoring, tilt table testing equipment, external and internal (implantable) ECG loop recorder systems, 24 h ambulatory blood pressure monitoring, 24 h ambulatory ECG monitoring, and autonomic function testing. The facility should also have access to echocardiography, invasive electrophysiological testing, stress testing, cardiac imaging, computed tomography and magnetic resonance imaging and electroencephalography.

Patients should have preferential access to hospitalisation and to any eventual therapy for syncope, namely pacemaker and ICD implantation, catheter ablation of arrhythmias, etc.

Dedicated rooms for assessment and investigation are required.

Setting

The majority of syncope patients can be investigated as out-patients or day cases. Indications for hospital admission are defined in another section (see part 4 ''Need for hospitalisation'').

The role of a local integrated syncope service is to set standards for the following in keeping with the objectives of the Guidelines on Syncope of the European Society of Cardiology and other appropriate guideline publications:

- The diagnostic criteria for causes of syncope
- The preferred approach to the diagnostic work-up in subgroups of patients with syncope
- Risk stratification of the patient with syncope
- Treatments to prevent syncopal recurrences

A major objective of the syncope facility is to reduce the number of hospitalisations by offering the patient a well defined, quick, alternative evaluation pathway.

Driving and syncope

An ESC Task Force report on driving and heart disease was published in 1998 which is the present reference standard for Europe[46] (Table 5). Two groups of drivers are defined. Group one comprises drivers of motorcycles, cars and other small vehicles with and without a trailer. Group two includes drivers of vehicles over 3.5 metric tonnes (3,500 kilos) or passengers carrying vehicles exceeding eight seats excluding the driver. Drivers of taxicabs, small ambulances and other vehicles form an intermediate category between the ordinary private driver and the vocational driver.

This Task force has the benefit of further publications that are relevant. Data suggest that the risk for car accident related to syncope is low.[46–49] Repeat tilt testing to assess any therapy probably has no predictive value. There is no evidence that allowing three asymptomatic months to elapse provides any confirmation that attack will not recur. To date, the evidence in favour of drug therapy remains unconvincing. Neurological review in syncopal patients is of little value. Modified disqualifying criteria according to 2004 Syncope Task Force are also reported in Table 5.

Appendix A. ESC Task Force on Guidelines on management (diagnosis and treatment) of syncope

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Recommendations. Syncope management facilities

Guidelines 2001	Update 2004
No recommendations	• A cohesive, structured care pathway — either delivered within a single syncope facility or as a more multi-faceted service — is recommended for the global assessment of the patient with syncope • Experience and training in key components of cardiology, neurology, emergency and geriatric medicine are pertinent • Core equipment for the facility include: surface ECG recording, phasic blood pressure monitoring, tilt table testing equipment, external and internal (implantable) ECG loop recorder systems, 24 h ambulatory blood pressure monitoring, 24 h ambulatory ECG and autonomic function testing. • Preferential access to other tests or therapy for syncope should be guaranteed and standardised • The majority of syncope patients should be investigated as out-patients or day cases

Table 5 Suggested recommendations for driving rules in patients suffering from syncope (modified after Task Force Report of the European Society of Cardiology on Driving and Heart Disease[46])

	Group 1 (private drivers)		Group 2 (vocational drivers)	
Diagnosis	Disqualifying criteria according to 1998 ESC document	Modified disqualifying criteria according to 2004 Syncope Task Force	Disqualifying criteria according to 1998 ESC document	Modified disqualifying criteria according to 2004 Syncope Task Force
Cardiac arrhythmias				
(a) Cardiac arrhythmias, medical treatment	Any disturbance of cardiac rhythm which is likely to cause syncope	Until successful treatment is established	Driving will not be permitted if the arrhythmia (i.e. non-sinus bradycardia, significant conduction defect, atrial flutter or fibrillation narrow or broad complex tachycardia) has caused or is likely to cause syncope. Once the arrhythmia has been controlled (re-) licensing may be permitted provided that left ventricular ejection fraction is >0.40, ambulatory electrocardiography excludes ventricular tachycardia, and exercise requirements can be met.	Until successful treatment is established
(b) Pacemaker implant	Within one week	No change	Any persistent symptoms	Until appropriate function is established.
(c) Successful catheter ablation			(Re-)licensing may be permitted after at least 6 weeks has elapsed, and provided that there is no disqualifying condition	Until long-term success is confirmed, usually 3 months
(d) ICD implant	Within 6 months if no arrhythmia recurrence and no disabling symptoms at time of ICD discharge. For drivers receiving prophylactic ICD implant no restrictions are imposed	Low risk, controversial opinions, tendency to shorten the time of restriction	Permanent	No change

(*Continued on next page*)

Table 5 (*continued*)

Diagnosis	Group 1 (private drivers)		Group 2 (vocational drivers)	
	Disqualifying criteria according to 1998 ESC document	Modified disqualifying criteria according to 2004 Syncope Task Force	Disqualifying criteria according to 1998 ESC document	Modified disqualifying criteria according to 2004 Syncope Task Force
Neurally-mediated syncope				
(a) Vasovagal:				
— Single/mild	No restrictions	No change	Specialist evaluation including neurological review	No restriction unless it occurred during high risk activity ([a])
— Severe ([a])	Until symptoms controlled	No change	Until symptoms controlled. (Re-) licensing after three months and possibly negative tilt-test; careful follow-up mandatory	Permanent restriction unless effective treatment has been established
(b) Carotid sinus:				
— Single/mild	No restrictions	No change	No restrictions	No restriction unless it occurred during high risk activity ([a])
— Severe ([a])	Until symptoms controlled	No change	Until symptoms controlled	Permanent restriction unless effective treatment has been established
(c) Situational:				
— Single/mild	No restrictions	No restrictions	No restrictions	No restriction unless it occurred during high risk activity ([a])
— Severe ([a])	—	Until appropriate therapy is established	—	Permanent restriction unless effective treatment has been established
Syncope of uncertain cause				
— Single/mild	—	No restrictions unless it occurred during high risk activity ([a])	—	Until diagnosis and appropriate therapy is established
— Severe ([a])	In case of severe syncope until cause identified especially in patients with heart disease or at least 3 months without symptoms before (re-)licensing	Until diagnosis and appropriate therapy is established	Requires specialist evaluation including a neurological review if appropriate. Following unexplained syncope, provocation testing and investigation for arrhythmia must be implemented, especially also in patients with heart disease. If the results are satisfactory (re-)licensing may be permitted after 3 months. Careful follow-up is mandatory	Until diagnosis and appropriate therapy is established

[a] Neurally-mediated syncope is defined as severe if it is very frequent, or occurring during the prosecution of a 'high risk' activity, or recurrent or unpredictable in ''high risk'' patients (see part 3, treatment).

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