2018 ESC SYNCOPE GUIDELINES

SUMMARY

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GUIDELINES

OVERVIEW OF UPDATED RECOMMENDATIONS SINCE 2009

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2018 EUROPEAN SOCIETY OF CARDIOLOGY
SYNCOPE GUIDELINES

Goals of 2018 Task Force[1]

Reducing Cost & Admissions:
Focus of recommendations is on the need to reduce hospital admissions and unnecessary system costs.

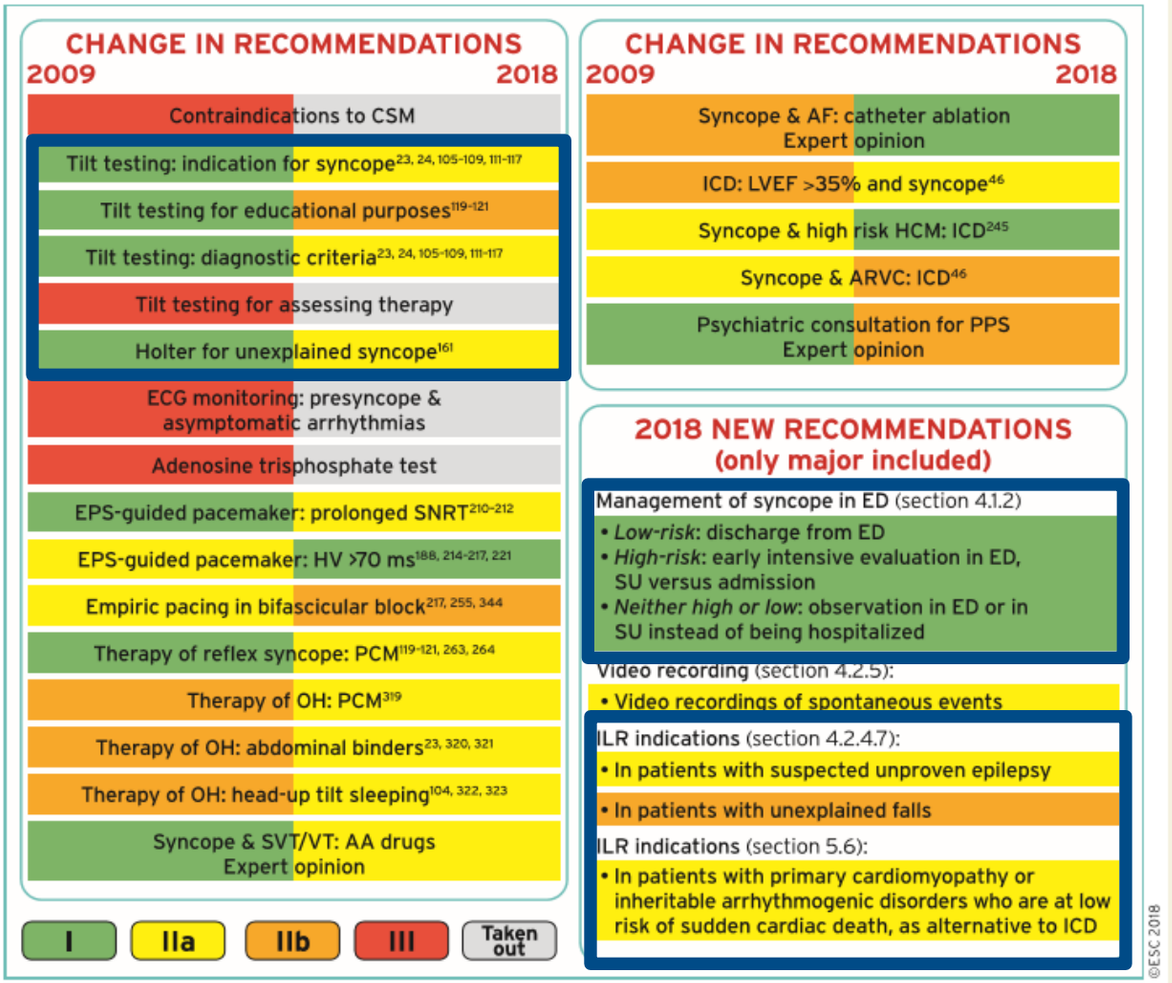
Providing Practical Guidance:
Guidelines include clinical recommendations and a separate *practical instructions guide* to drive implementation.

Driving Multidisciplinary Approach:
Most multidisciplinary syncope guidelines task force to date — must engage across specialties to better manage syncope patients (ED, cardiology, neurology, internal medicine, geriatrics, nursing).

[1] Brignole M, et al. *Eur Heart J*. 2018;39:1883-1948.

2018 EUROPEAN SOCIETY OF CARDIOLOGY
SYNCOPE GUIDELINES

New Concepts in 2018 Guidelines[1]



Extensive changes based on new evidence:

- Increased role of prolonged ECG monitoring with ILR
- Revised recommendation from Class I to Class II for Holter monitors and tilt tests
- Increased importance of risk stratification from ED and referral to syncope specialist

[1] Brignole M, et al. *Eur Heart J*. 2018;39:1883-1948. Figure I in Guidelines Introduction.

GUIDELINES RECOMMENDATION CLASSIFICATIONS[1]

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	*Weight of evidence/opinion is in favour of usefulness/efficacy.*	Should be considered
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion.*	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

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

Class I, Level of evidence "A" is HIGHEST recommendation

[1] Brignole M, et al. *Eur Heart J*. 2018;39:1883-1948. Table 1 and Table 2 in Guidelines Introduction.

COMPARISON OF CHANGES IN ILR RECOMMENDATIONS

2009 Guidelines[1]

Class I Level B

- Indicated in early phase evaluation in patients with recurrent syncope of uncertain origin, absence of high-risk criteria and a high likelihood of recurrence within battery longevity of the device
- Indicated in high-risk individuals in whom comprehensive evaluation did not demonstrate a cause of syncope or lead to a specific treatment

Class IIa Level B

- Considered in patients with suspected or certain reflex syncope presenting with frequent or traumatic syncopal episodes

2018 Guidelines[2]

Class I Level A

- Indicated in early phase evaluation in patients with recurrent syncope of uncertain origin, absence of high-risk criteria and a high likelihood of recurrence within battery longevity of the device
- Indicated in patients with high-risk criteria in whom a comprehensive evaluation did not demonstrate a cause of syncope or lead to a specific treatment, and who do not have conventional indications for primary prevention ICD or pacemaker

Class IIa Level B

- Considered in patients with suspected or certain reflex syncope presenting with frequent or severe syncopal episodes

Class IIb Level B — NEW!

Rule in or out arrhythmias in:

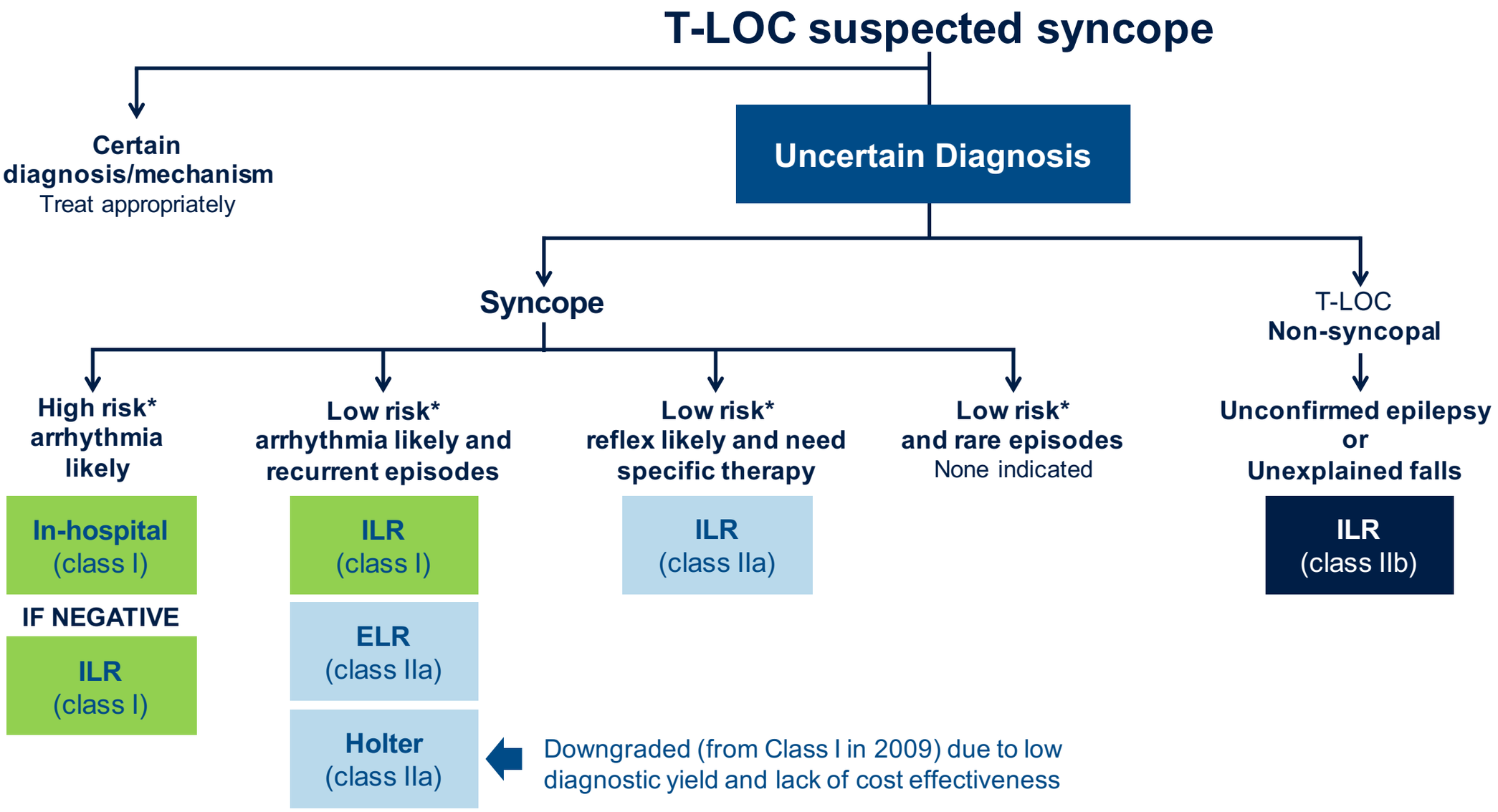
- Patients in whom epilepsy is suspected
- Patients with unexplained falls

Class IIb Level C — NEW!

ILR may be considered in patients with recurrent episodes of unexplained syncope who are at low risk for SCD and without a current indication for ICD.

[1] Moya A. *Eur Heart J*. 2009;30:2174-2176.
[2] Brignole M, et al. *Eur Heart J*. 2018;39:1883-1948.

T-LOC MONITORING RECOMMENDATIONS



Adapted from Ungar A. ECG Monitoring Role in Syncope 2018 ESC Guidelines. Presented at EHRA 2018.
*High Risk & Low Risk Recommendations Summarized on Slides 18 – 19.

EVIDENCE SUPPORT

RECOMMENDATIONS FOR DIAGNOSING UNEXPLAINED SYNCOPE

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EVIDENCE SUPPORT IN GUIDELINES

ILR is indicated in an **early phase of evaluation** in patients with recurrent syncope of uncertain origin, absence of high-risk criteria, and a high likelihood of recurrence within the battery life of the device.

2009		2018
Class I **LOE: B**	→	Class I **LOE: A**

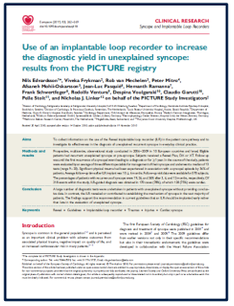
- **NEW — Meta-analysis: Five randomized clinical trials** comparing diagnostic yield of ICM monitoring to standard of care[1]

Study	Diagnostic yield		Relative probability	95% CI	P value
	ICM group n/N (%)	Control group n/N (%)			
RAST 2001	14/27 (52)	6/30 (20)	2.6	1.2-5.8	**0.01**
EaSyAS 2006	43/101 (43)	7/97 (7)	5.9	2.8-12	**0.001**
Da Costa 2013	15/41 (37)	4/37 (11)	3.4	1.2-9.3	**0.01**
FRESH 2014	18/39 (46)	2/39 (5)	9.0	2.2-3.6	**0.001**
EaSyAS II 2016	62/125 (50)	21/121 (17)	2.9	1.9-4.4	**0.001**
Total	**152/333 (46)**	**40/324 (12)**	**3.6**	**2.4-5.3**	**0.001**

3.6X **more likely to reach a diagnosis with ICM vs. standard of care**

- **NEW — Large non-randomized clinical trials**

PICTURE[2]



Use of an implantable loop recorder to increase the diagnostic yield in unexplained syncope: results from the PICTURE registry

570 patients

SPANISH REGISTRY[3]

Implantable Loop Recorder Allows an Etiologic Diagnosis in One-Third of Patients – Results of the Spanish Reveal Registry –

680 patients

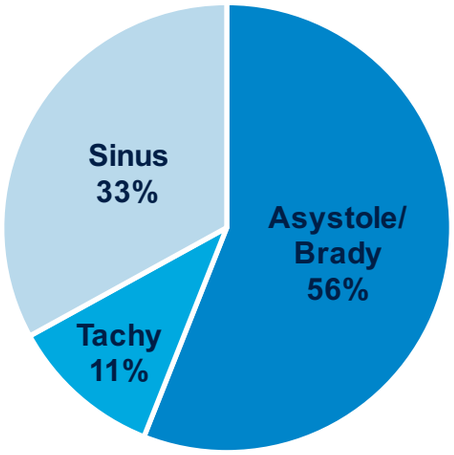
Strong evidence supports efficacy of early use of ICM in unexplained, recurrent syncope

[1] Brignole M, et al. *Eur Heart J*. 2018;39:1883-1948.
[2] Edvardsson N, et al. *Europace*. 2011:262-269.
[3] Lacunza-Ruiz FJ, et al. *Circ J*. 2013;77:2535-2541.

EVIDENCE SUPPORT IN GUIDELINES

ILR is indicated **in patients with high-risk** criteria in whom a **comprehensive evaluation did not demonstrate a cause of syncope** or lead to a specific treatment, and who do not have conventional indications for primary prevention ICD or pacemaker indication.

2009	2018
Class I **LOE: B**	Class I **LOE: A**



Pooled analysis of 9 studies (n = 509) — diagnostic yield after "extensive" workup[1]

- Diagnostic yield **35%** (176/506)
  - **67%** had arrhythmia associated with syncopal event

ILR monitoring in BBB patients w/ negative Electrophysiologic Study (EPS) to detect paroxysmal AVB

- NEW: DaCosta '13 — RCT
- NEW: Moya '11 — Large prospective trial (n = 323)

ILR diagnostic yield in syncope patients with BBB[2]

Study	N	ILR documented event	ILR documented arrhythmia	ILR documented AVB
Brignole 2001	52	24	22	12
Moya 2011	108	52	45	36
Da Costa 2013	41	15	15	11
Total	**201**	**91 (45%)**	**82 (41%)**	**59 (29%)**

Strong evidence to support ICM monitoring if comprehensive testing is inconclusive or does not meet current indications for a pacemaker

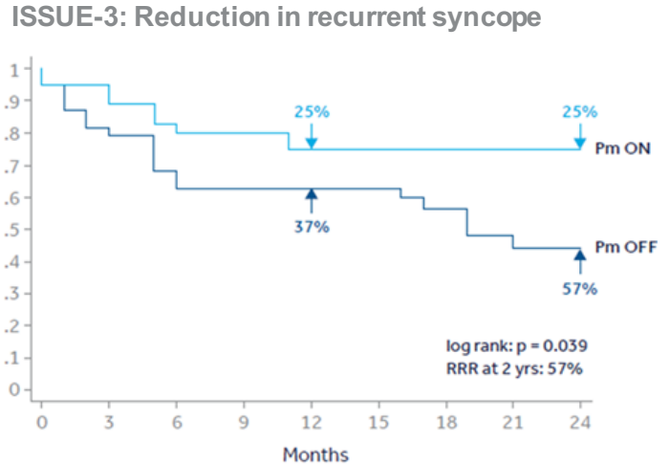
[1] Task Force members, et al. *Europace*. 2009;11:671-687.
[2] Brignole M, et al. *Eur Heart J*. 2018;39:1883-1948.

EVIDENCE SUPPORT IN GUIDELINES

	2009	2018
ILRs should be considered in patients with suspected or certain **reflex syncope** presenting with frequent or severe syncopal episodes.	Class IIa **LOE: B**	Class IIa **LOE: B**

ILR monitoring in reflex syncope patients to identify those that benefit from cardiac pacing[1-3]

- NEW: Brignole '12 (ISSUE – 3) — RCT-pacing on/off in reflex syncope patients with asystole (ICM detected)



- Dual-chamber pacemakers implanted in reflex syncope patients with ILR detected asystole (randomized to "on" or "off" pacing)
- 57% reduction in risk of recurrent syncope with pacing

- NEW: Brignole '15 (SUP2) — single arm — ICM detection as part of a diagnostic algorithm (asystole detected in reflex syncope patients response to pacing)
- Brignole '06 ISSUE2 — Therapy based on ICM monitoring effective in Neurally Mediated Syncope

Evidence is building for the need to identify asystole in reflex syncope patients as pacing therapy may be effective

[1] Brignole M, et al. *Circulation.* 2012;125:2566-2571.
[2] Brignole M, et al. *Eur Heart J.* 2015;36:1529-1535.
[3] Brignole M, et al. *Eur Heart J.* 2006;27:1085-1092.

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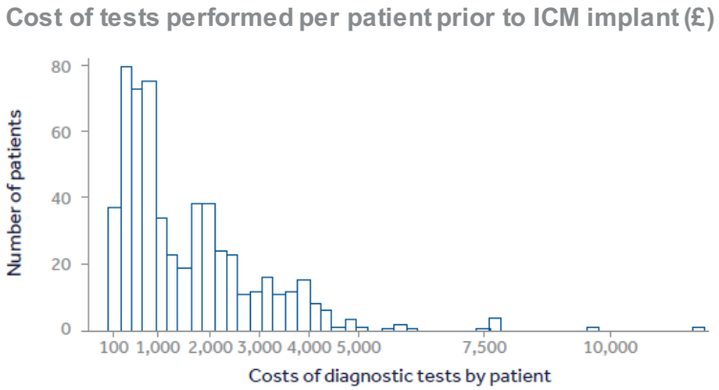
EVIDENCE SUPPORT IN GUIDELINES

	2009	2018
ILR is indicated in an **early phase of evaluation** in patients with recurrent syncope of uncertain origin, absence of high-risk criteria, and a high likelihood of recurrence…	Class I **LOE: B**	Class I **LOE: A**
Holter monitoring should be considered in patients who have frequent syncope or presyncope (> 1 episode per week).	Class I **LOE: B**	Class IIa **LOE: B**

2018 ESC Syncope Guidelines Task Force:

- "Holter monitoring in syncope is inexpensive in terms of setup costs, but **expensive in terms of cost per diagnosis**."[1]
- "ILR was **more cost-effective** than a conventional [monitoring] strategy"[2-5]
  - NEW: Edvardsson '11 and '15 PICTURE (n = 570) — prospective registry study



- Prior to ILR implant, patients saw an average of 3 specialists and received a median 13 tests (mean cost of testing: £1,613)
  - 10% of patients had tests exceeding £3,540
- ILR guided diagnosis in 78% of patients with syncopal recurrence

- Krahn '03 RAST — Cost per diagnosis was lower in the ILR group ($5,852 CAD) vs. conventional testing ($8,414 CAD)
- Farwell '04 EaSyAS — Earlier diagnosis and treatment in the ILR group resulted in 67% lower costs for subsequent diagnostic testing and hospitalization (ILR: £406 vs. conventional testing: £1,210)

[1] Brignole M, et al. *Eur Heart J*. 2018;39:1883-1948.
[2] Edvardsson N, et al. *Europace*. 2011;13:262-269.
[3] Farwell DJ, et al. Eur Heart J. 2004;25:1257-1263.
[4] Krahn AD, et al. *J Am Coll Cardiol*. 2003;42:495-501.
[5] Edvardsson N, et al. *Europace*. 2015;17:1141-1148.

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EVIDENCE SUPPORT

EXPANDED RECOMMENDATIONS FOR DIAGNOSING T-LOC

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EVIDENCE SUPPORT IN GUIDELINES

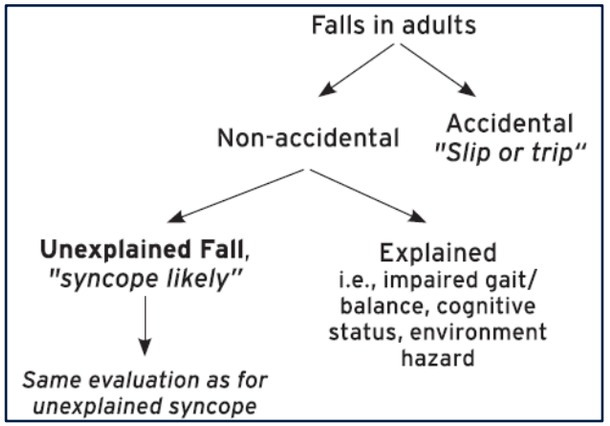
NEW 2018

ILR may be considered in patients with **unexplained falls**.

Class IIb
LOE: B

- "Despite the lack of controlled trials and an overall modest quality of studies, there is strong consensus that the management of unexplained falls should be the same as that for unexplained syncope"[1]

Suggested flow diagram to identify unexplained falls



- Pooled analysis of 5 studies with an ILR in the unexplained falls population[1]

Study	ILR patients	ILR documented event	ILR documented arrhythmia
Armstrong 2003	6	3 (50%)	1 (15%)
Ryan 2010	71	48 (68%)	3 (4%)
Maggi 2014	29	16 (55%)	7 (24%)
Bhangu 2016	70	56 (80%)	14 (20%)
Total	**176**	**123 (70%)**	**25 (14%)**

70% of patients had a recurrent fall while monitored with an ILR

14% of patients had an arrhythmia response for fall

Evidence is growing to support prolonged monitoring in patients with unexplained falls

[1] Brignole M, et al. *Eur Heart J*. 2018;39:1883-1948.

EVIDENCE SUPPORT IN GUIDELINES

NEW 2018

ILR may be considered in patients in whom **epilepsy was suspected** but the treatment has proven ineffective.

Class IIb
LOE: B

- "Syncope and Epilepsy have similar clinical features, including abrupt T-LOC without warning, abnormal limb movements such as myoclonic jerks or tonic-clonic activity"[1]
- Pooled analysis of 6 studies with an ILR in the unconfirmed epilepsy population[1]

Study	ILR patients	ILR documented event	ILR documented arrhythmia
Simpson 2000	1	1 (100%)	0 (0%)
Kanjwal 2009	3	3 (100%)	3 (100%)
Zaidi 2000	10	2 (20%)	2 (20%)
Ho 2006	14	6 (43%)	0 (0%)
Petkar 2012	103	69 (67%)	28 (27%)
Maggi 2014	28	17 (61%)	8 (29%)
Total	**201**	**98 (62%)**	**41 (26%)**

62% of patients had a T-LOC event captured during ILR monitoring

1 in 4 (26%) of patients had an arrhythmia response for T-LOC

ILR monitoring in the unconfirmed epileptic population can lead to appropriate diagnosis and therapy for T-LOC

[1] Brignole M, et al. *Eur Heart J*. 2018;39:1883-1948.

EVIDENCE SUPPORT IN GUIDELINES

NEW 2018

*Instead of an ICD, an ILR may be considered in patients with recurrent episodes of unexplained syncope who are at **low risk for SCD** and without current indication for ICD.*

Class IIb
LOE: C

- Unexplained syncope in this population is defined as “suspected arrhythmic syncope”
- No studies are available to support this specific guideline (LOE: C — *expert opinion)*
- ILRs are recommended to complete the diagnostic investigation in those not indicated for therapy devices and at “low risk” for SCD[1]
  - Structural heart disease is the most important predictive factor for a cardiac cause of syncope, with a sensitivity of > 90% and a specificity of ~50%
  - In many patients with CMP/IAD, individual risk stratification can be difficult due to atypical symptoms

While there is an absence of specific trials to support long-term cardiac monitoring in this population, the expert opinion is to continue cardiac monitoring in low-risk, non-ICD indicated patients

[1] Brignole M, et al. *Eur Heart J*. 2018;39:1883-1948.

2018 ESC SYNCOPE GUIDELINES: CONCLUSIONS

- The increasing need to reduce inappropriate admissions & tests and new evidence led to creation of the 2018 ESC Syncope Guidelines[1]
- ILR recommendation upgraded from a Class I/Level B to a Class I/Level A for unexplained syncope as meta-analysis shows 3.6X more patients were diagnosed compared to conventional tests[1]
- Holter monitors and tilt testing recommendations were revised from Class I to Class II due to lack of new evidence and cost implications[1-5]
- ILR recommendation expanded to patients with unexplained falls, unproven epilepsy, and patients at low-risk for SCD[1]

[1] Brignole M, et al. *Eur Heart J*. 2018;39:1883-1948.
[2] Edvardsson N, et al. *Europace*. 2011;13:262-269.
[3] Farwell DJ, et al. *Eur Heart J*. 200425:1287-1263.
[4] Krahn AD, et al. *J Am Coll Cardiol*. 2003;42:495-501.
[5] Edvardsson N, et al. *Europace*. 2015;17:1141-1148.

*RISK ASSESSMENT RECOMMENDATIONS[1]

Assessment of Syncopal Event

Low risk	High risk (red flag)
1. Associated with prodrome typical of reflex syncope (e.g., light-headedness, feeling of warmth, sweating, nausea, vomiting) 2. After unexpected unpleasant sight, sound, smell, or pain 3. After prolonged standing or crowded, hot places 4. During a meal or postprandial 5. Triggered by cough, defecation, or micturition 6. With head rotation or pressure on carotid sinus 7. Standing from supine/sitting position	**Major** 1. New onset of chest discomfort, breathlessness, abdominal pain, or headache 2. Syncope during exertion or when supine 3. Sudden onset palpitation immediately followed by syncope **Minor** (high risk only if associated with SHD or abnormal ECG): 1. No warning symptoms or short (< 10 s) prodrome 2. Family history of SCD at young age 3. Syncope in the sitting position

Past Medical History

Low risk	High risk (red flag)
1. Long history of recurrent syncope with low-risk features with the same characteristics of the current episode 2. Absence of structural heart disease	**Major** 1. Severe structural or coronary artery disease (heart failure, low LVEF, or previous myocardial infarction)

[1] Brignole M, et al. *Eur Heart J*. 2018;39:1883-1948.

*RISK ASSESSMENT RECOMMENDATIONS[1]

Physical Examination

Low risk	High risk (red flag)
1. Normal examination	**Major** 1. Unexplained systolic BP in the ED < 90 mmHg 2. Suggestion of gastrointestinal bleed on rectal examination 3. Persistent bradycardia (< 40 bpm) in awake state and in absence of physical training 4. Undiagnosed systolic murmur
1. Normal ECG	**Major** 1. ECG changes consistent with acute ischaemia 2. Mobitz II second- and third-degree AV block 3. Slow AF (< 40 bpm) 4. Persistent sinus bradycardia (< 40 bpm) 5. Bundle branch block or IVCD 6. Q waves consistent with CAD or cardiomyopathy 7. Sustained and non-sustained VT 8. Dysfunction of a pacemaker or ICD 9. Type 1 Brugada pattern 10. Long QT **Minor** 1. ECG changes consistent with acute ischaemia 2. Mobitz II second- and third-degree AV block 3. Slow AF (< 40 bpm) 4. Persistent sinus bradycardia (< 40 bpm) 5. Bundle branch block or IVCD 6. Q waves consistent with CAD or cardiomyopathy 7. Sustained and non-sustained VT 8. Dysfunction of a pacemaker or ICD 9. Type 1 Brugada pattern 10. Long QT

[1] Brignole M, et al. *Eur Heart J*. 2018;39:1883-1948.

Brief Statement
See the device manual for detailed information regarding the instructions for use, the implant procedure, indications, contraindications, warnings, precautions, and potential adverse events. If using an MRI SureScan™ device, see the MRI SureScan technical manual before performing an MRI. For further information, contact your local Medtronic representative and/or consult the Medtronic website at www.medtronic.com.

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