Sincope: «Hot topics» 2022

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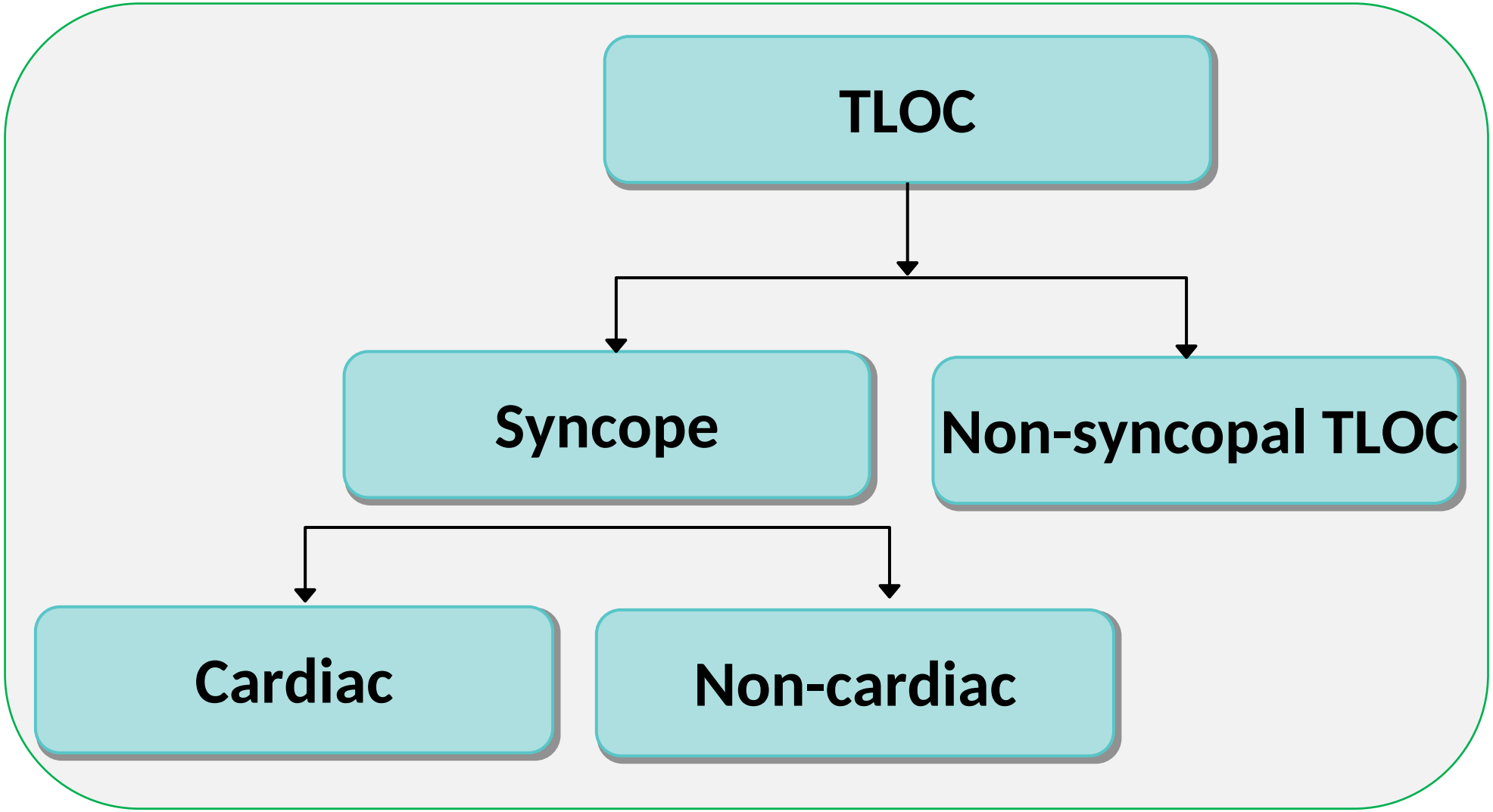
Classification of TLOCs



Brignole M, Rivasi G. New insights in diagnostics and therapies in syncope: a novel approach to non-cardiac syncope. ***Heart*** *2021;107:864–873*

Cardiac likely

Cardiac syncope established	Cardiac syncope possible (to be confirmed by further investigations)
Arrhythmic syncope is highly probable when the ECG shows: • Persistent sinus bradycardia <40 b.p.m. or sinus pause >3 s; • Mobitz II second- and third-degree AV block; • Alternating left and right BBB; • VT or rapid paroxysmal SVT; • Non-sustained episodes of polymorphic VT and long or short QT interval; • Pacemaker or ICD malfunction with cardiac pauses. **Cardiac ischaemia-related syncope** is highly probable when syncope presents with evidence of acute myocardial ischaemia with or without myocardial infarction **Syncope due to structural cardiopulmonary disorders** is highly probable when syncope presents in patients with prolapsing atrial myxoma, left atrial ball thrombus, severe aortic stenosis, pulmonary embolus, or acute aortic dissection.	**ECG findings suggesting arrhythmic syncope**: • Bifascicular block • Other intraventricular conduction abnormalities (QRS duration ≥0.12 s) • Mobitz I second-degree AV block and 1 degree AV block with markedly prolonged PR interval • Asymptomatic mild inappropriate sinus bradycardia (40–50 b.p.m.) or slow atrial fibrillation (40–50 b.p.m.) • Non-sustained VT • Pre-excited QRS complexes • Long or short QT intervals • ST-segment elevation with type 1 Brugada pattern • Negative T waves in right precordial leads, epsilon waves suggestive of ARVC • Left ventricular hypertrophy suggesting hypertrophic cardiomyopathy **Historical findings suggesting cardiac syncope:** • Syncope during exertion or when supine • Sudden onset palpitation immediately followed by syncope • Family history of unexplained sudden death at young age • Presence of structural heart disease or coronary artery disease

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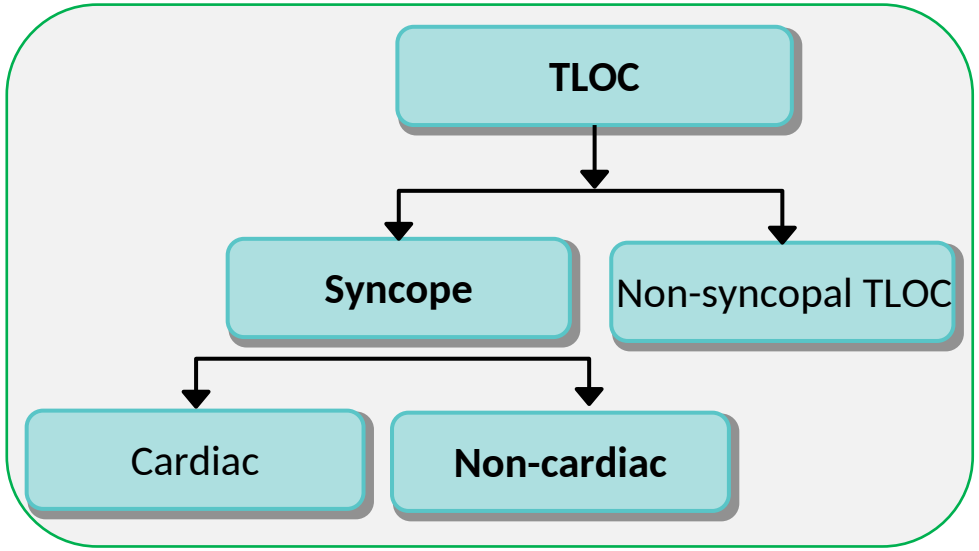
Classification of non-cardiac syncope

Non-cardiac syncope

By etiology and clinical forms	**By mechanism (ECG/BP documentation)**
Reflex (neurally-mediated) Vasovagal Situational Carotid sinus Non-classical forms (including low-adenosine syncope)	**Intermittent bradycardia** Asystole: Sinus arrest Sinus bradycardia plus AVB Progressive (sinus) bradycardia
Orthostatic hypotension Primary autonomic failure Secondary autonomic failure Drug-induced Volume depletion	**Intermittent tachycardia** Progressive sinus tachycardia
	Intermittent hypotension Supine hypotension Orthostatic hypotension (early/classical or delayed)



The efficacy of therapy is largely determined by the mechanism of syncope rather than its aetiology or clinical presentation

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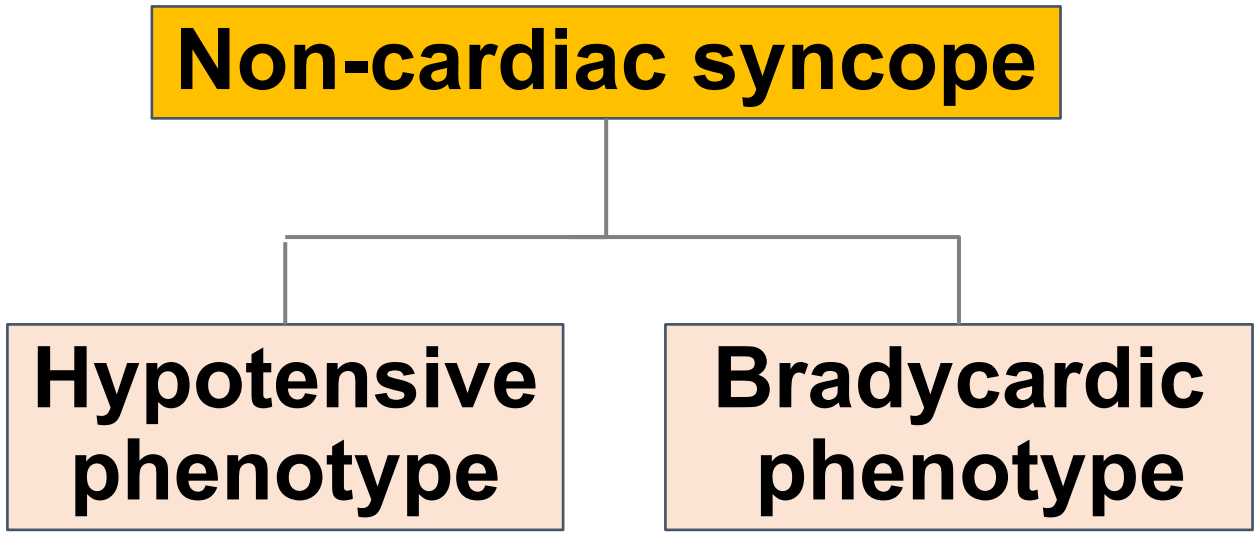
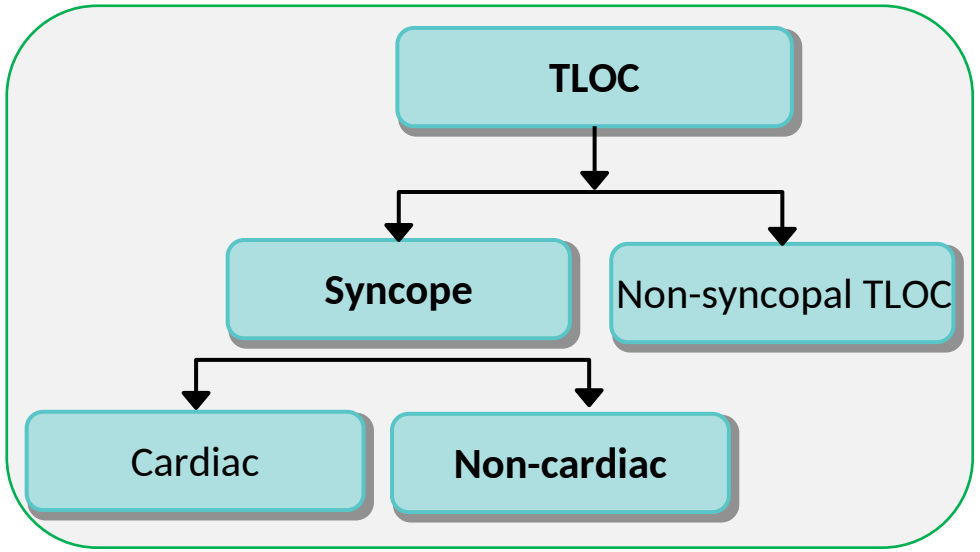
Mechanisms of non-cardiac syncope





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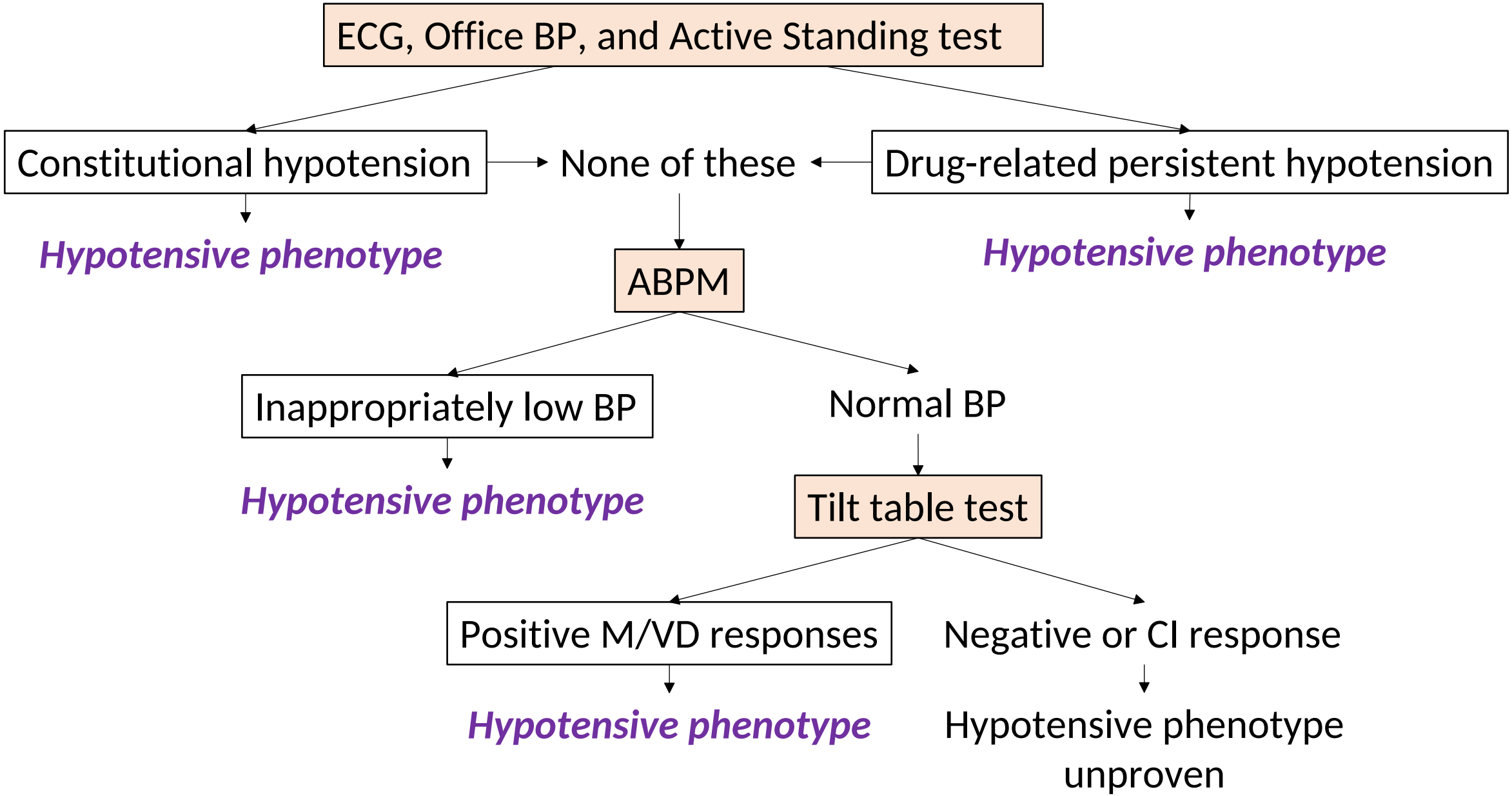
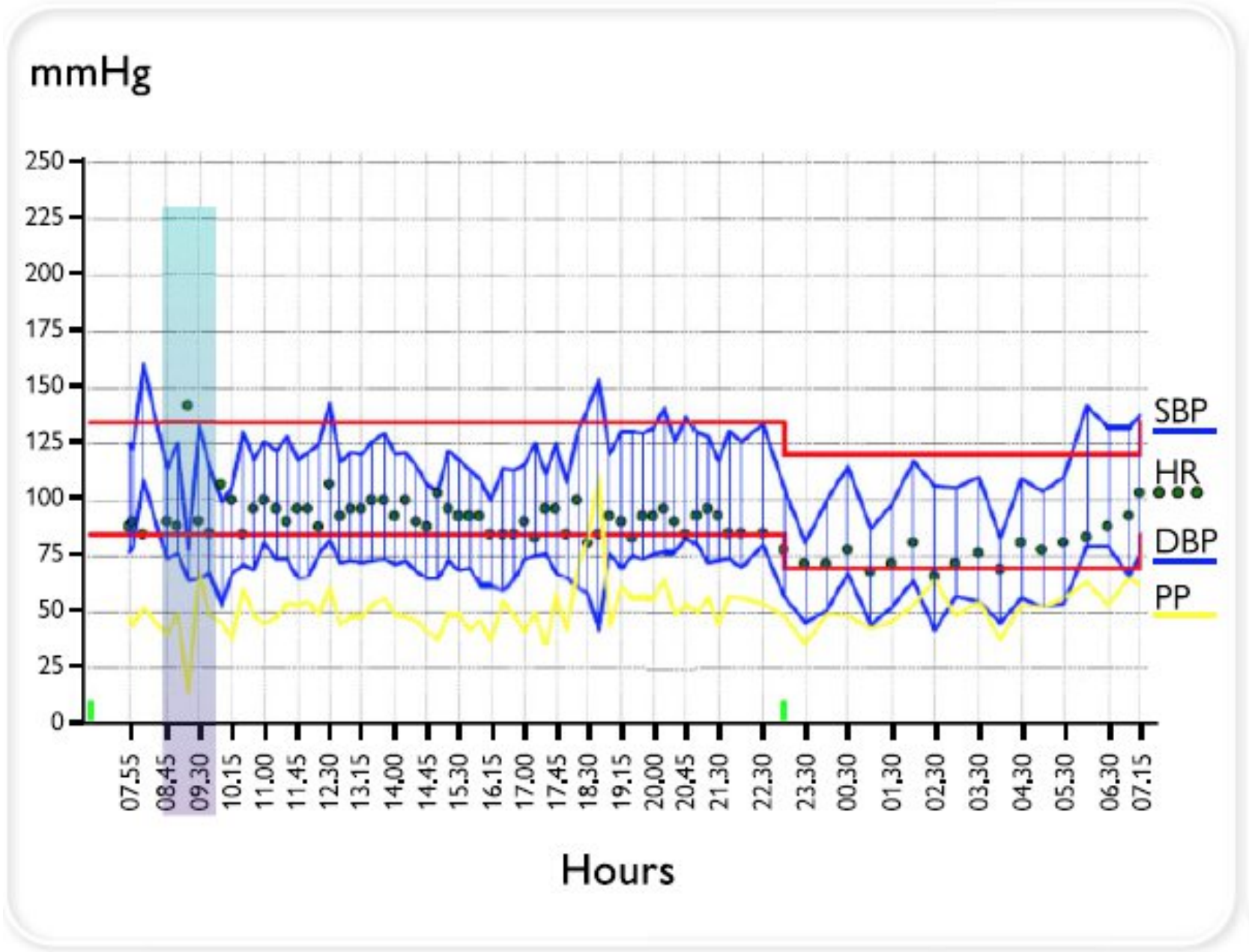
Hypotensive Phenotype: diagnostic work-up



Heart 2021;107:864–873

ABPM

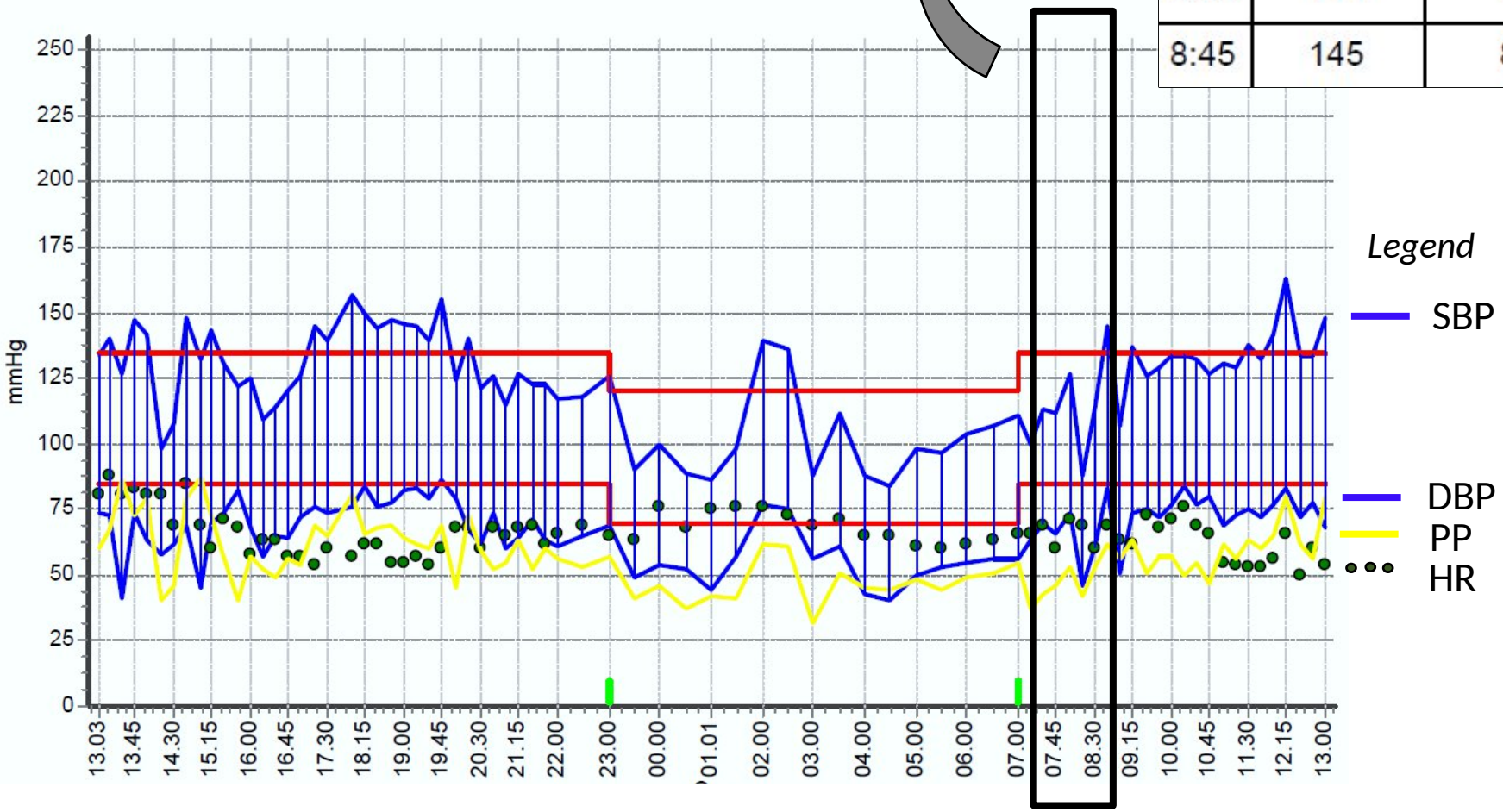
Intermittent hypotension



ABPM

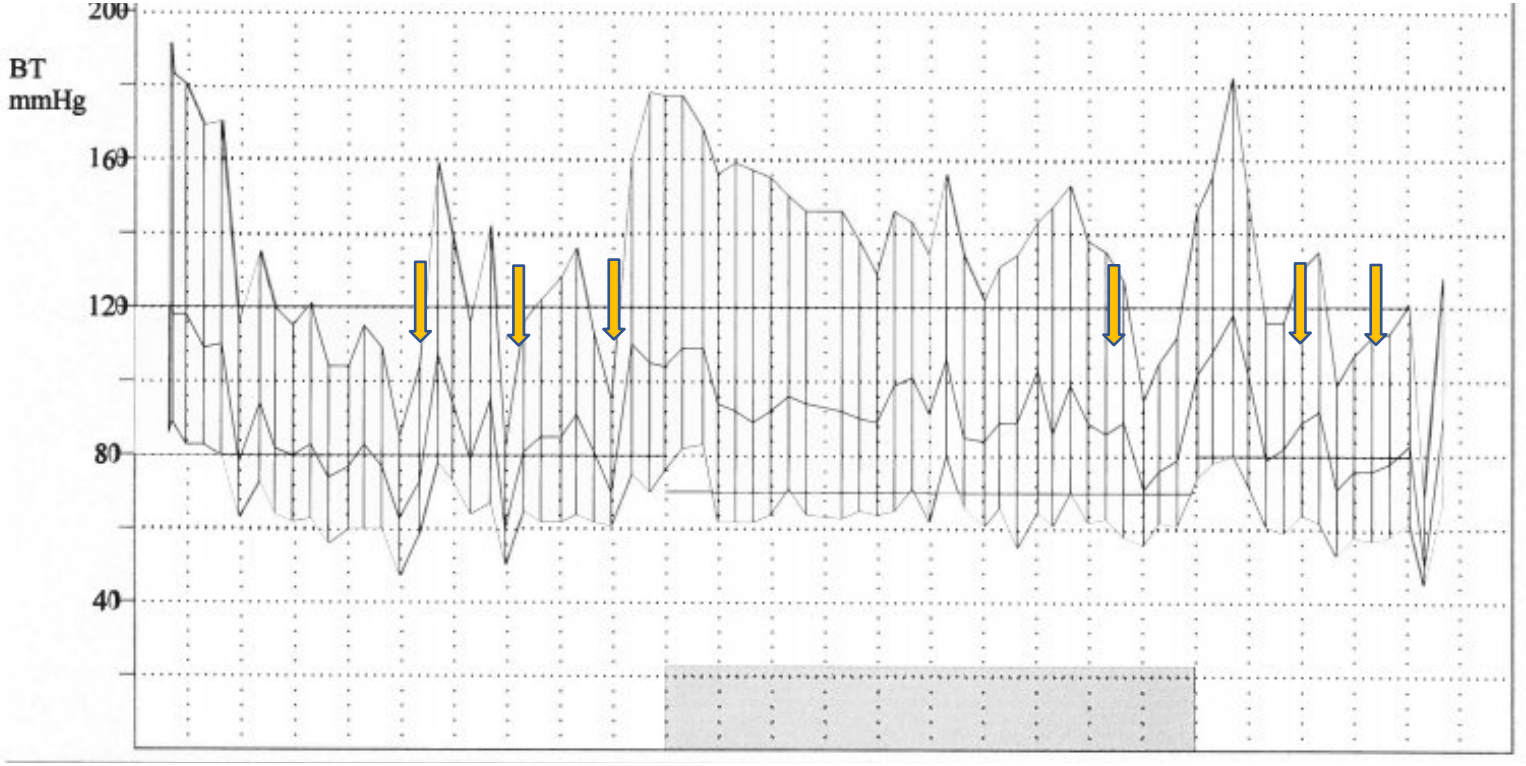
Intermittent hypotension

	Systolic BP	Diastolic BP	Mean BP	Pulse Pressure	Heart Rate
7:45	112	66	81	46	60
8:00	127	74	91	53	71
8:15	88	46	60	42	69
8:30	114	61	78	53	60
8:45	145	83	103	62	69



ABPM

Tid	Sys	Dia	MAP	PT:	HF
12:40 Tis	191	86	121	105	52
12:42	191	88	119	103	52
12:44	183	89	118	94	52
12:59	180	83	118	97	48
13:19	169	83	109	86	50
13:39	170	80	110	90	56
13:59	116	63	78	53	61
14:22	135	73	94	62	57
14:39	120	64	82	56	54
14:59	115	62	80	53	60
15:19	121	63	83	58	55
15:39	104	56	74	48	61
16:02	104	60	77	44	57
16:19	115	60	83	55	50
16:39	109	60	77	49	47
16:59	85	47	63	38	56
17:22	104	59	73	45	53
17:42	159	78	107	81	47
17:59	139	73	94	66	48
18:19	116	64	79	52	51
18:42	142	67	95	75	48
18:59	82	50	60	32	61
19:19	116	65	81	51	58
19:39	122	62	85	60	50
20:02	128	62	85	66	47
20:19	136	64	91	72	47
20:39	113	62	81	51	50
20:59	95	61	70	34	61
21:22	160	75	110	85	47
21:42	178	70	105	108	48
21:59	177	76	104	101	48
22:19	177	82	109	95	48
22:42	168	83	109	85	52
22:59	156	62	94	94	53



PS, m, 86 yrs

ESC European Society of Cardiology
European Heart Journal (2022) **00**, 1–12
https://doi.org/10.1093/eurheartj/ehac347

CLINICAL RESEARCH
Hypertension

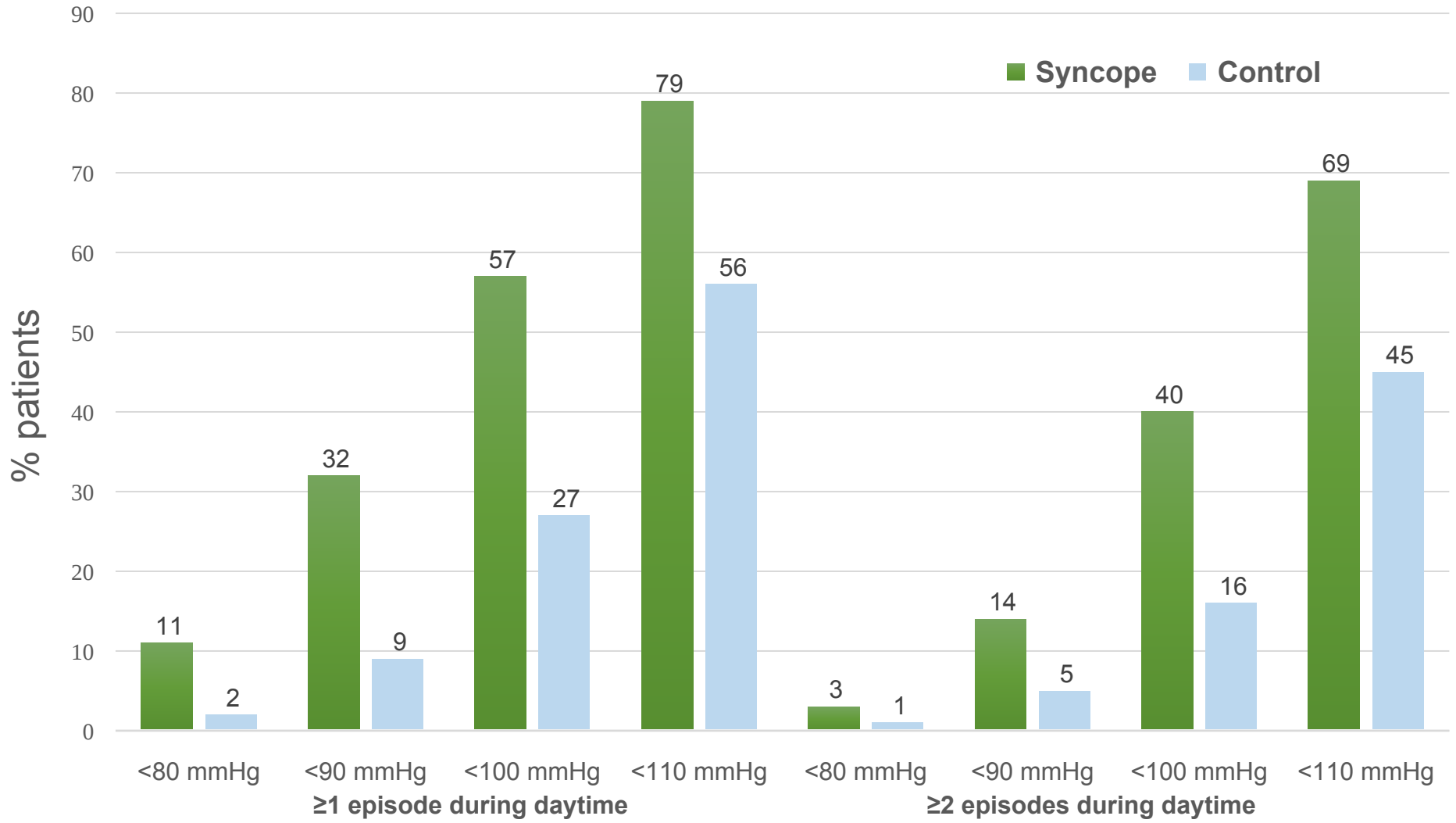
Association between hypotension during 24 h ambulatory blood pressure monitoring and reflex syncope: the SynABPM 1 study

Giulia Rivasi [1]*, Antonella Groppelli[2], Michele Brignole [2], Davide Soranna[3], Antonella Zambon[3,4], Grzegorz Bilo [2], Martino Pengo [2], Bashaaer Sharad[5], Viktor Hamrefors [5], Martina Rafanelli[1], Giuseppe Dario Testa [1], Ciara Rice[6], Rose Anne Kenny[6,7], Richard Sutton [5,8], Andrea Ungar[1], Artur Fedorowski [5,9†], and Gianfranco Parati [2†]

European Heart Journal (2022) *ahead of print*
https://doi.org/10.1093/eurheartj/ehac347

Characteristics of the study groups after matching procedure

	Derivation sample		Validation sample	
	Syncope n=158	*Controls n=329*	*Syncope n=164*	*Controls n=164*
Median age	62	58	66	62
Females, %	95	192	91	89
ABPM, median, mmHg				
24-hour SBP	123	124	129	129
Daytime SBP	127	130	132	134
Night-time SBP	112	114	118	114
Mean BP	89	92	93	93



Rivasi G et al. SynABPM study: Eur Heart J 2022, ahead of print

Cut-off values of SBP achieving the best diagnostic value for hypotensive syncope

	Sensitivity (95% CI)	**Specificity** (95% CI)	Odds ratio	P value*
Daytime SBP <90 mmHg, ≥1 episode	**32** (26-36)	**91** (88-93)	4.6	<0.001
Daytime SBP <100 mmHg, ≥2 episodes	**40** (34-46)	**84** (81-87)	3.5	<0.001

Rivasi G et al. SynABPM study: Eur Heart J 2022, ahead of print

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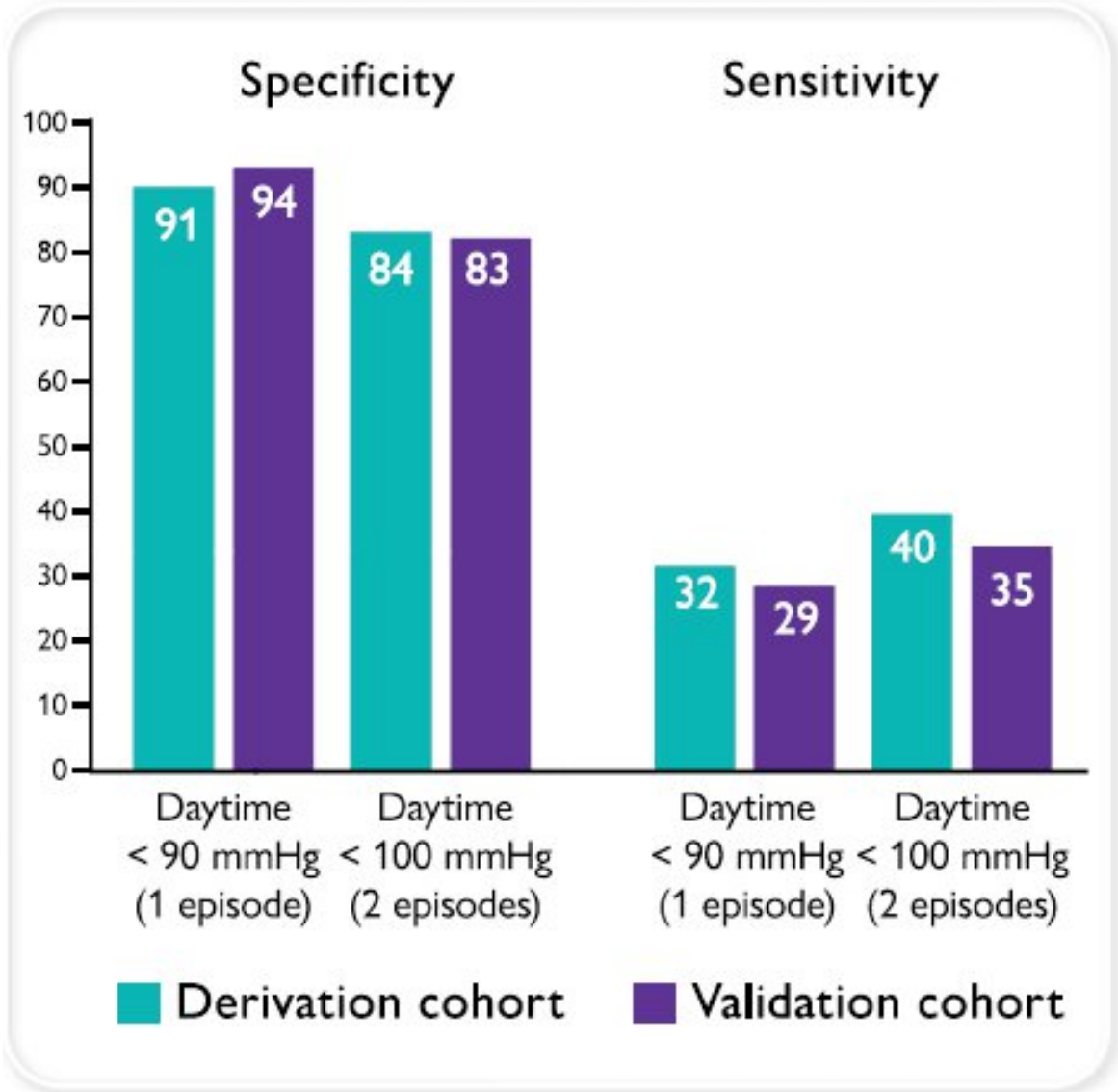
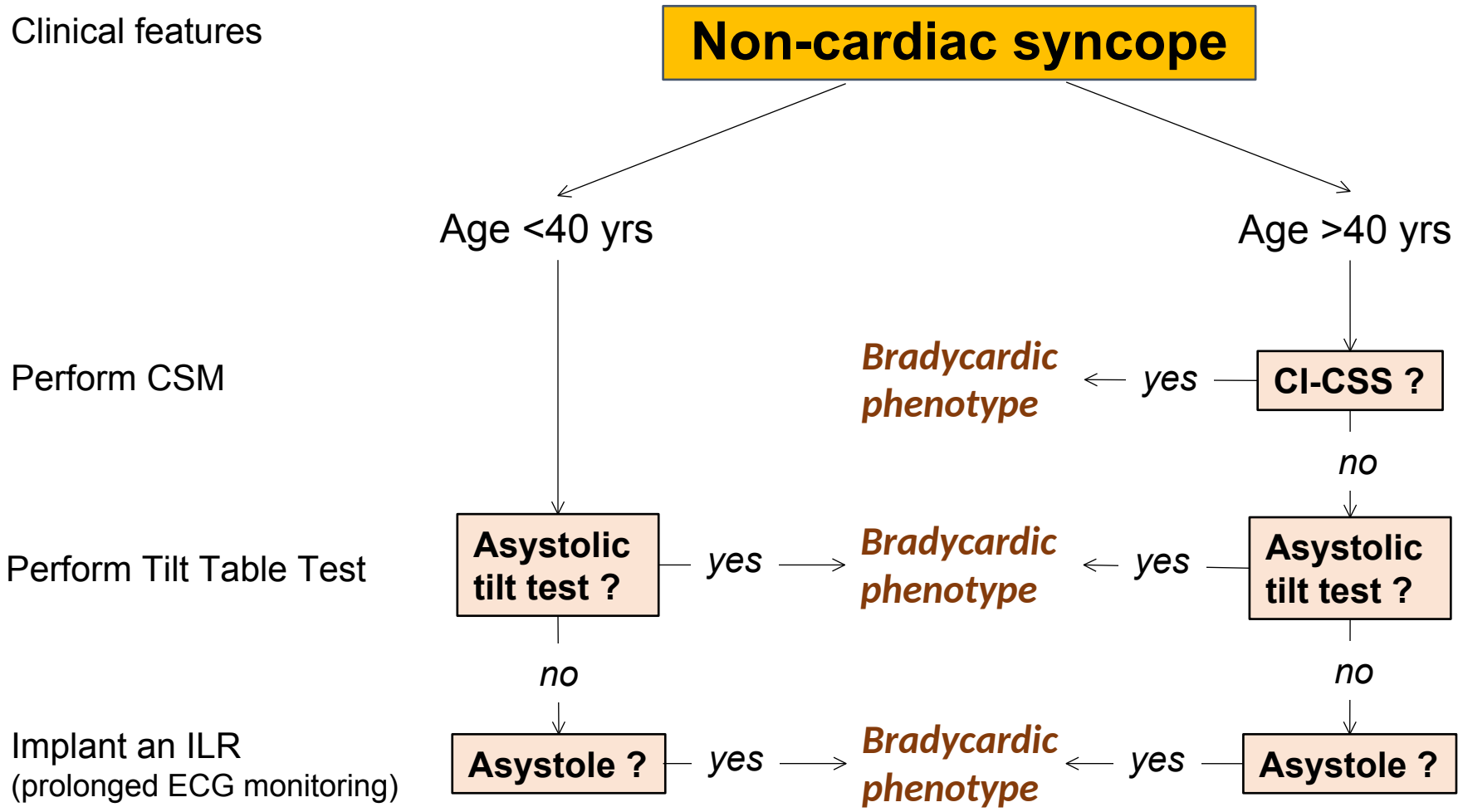


Bradycardiac Phenotype: diagnostic work-up



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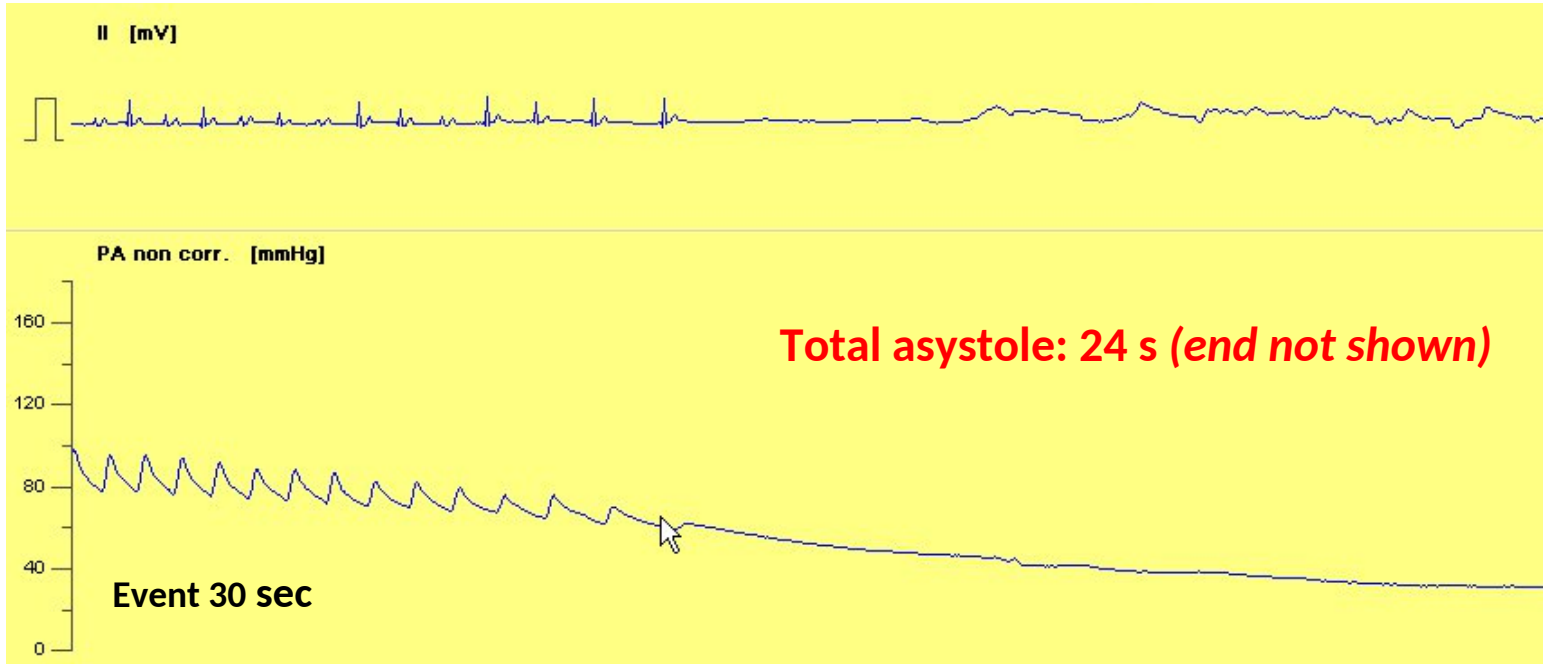
Bradycardiac phenotype:

Induced and spontaneous event in the same patient

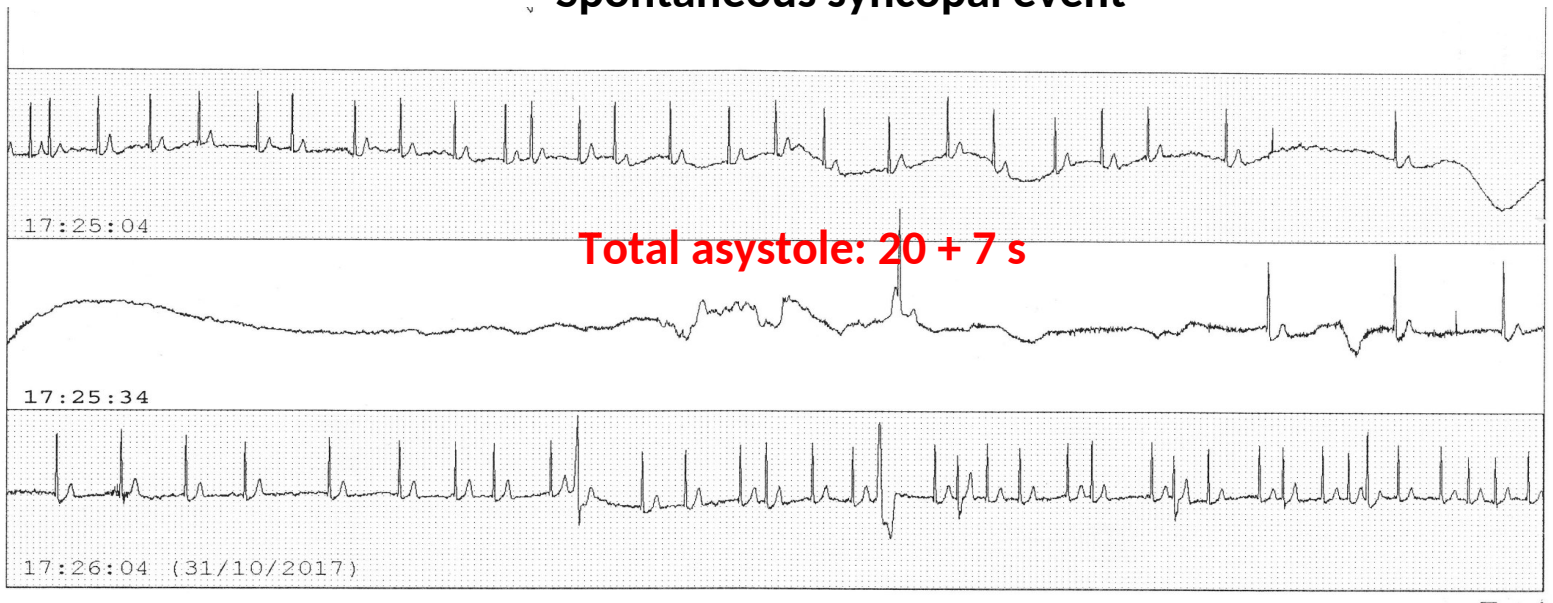
Tilt testing

ECG monitoring

Tilt-induced syncopal event

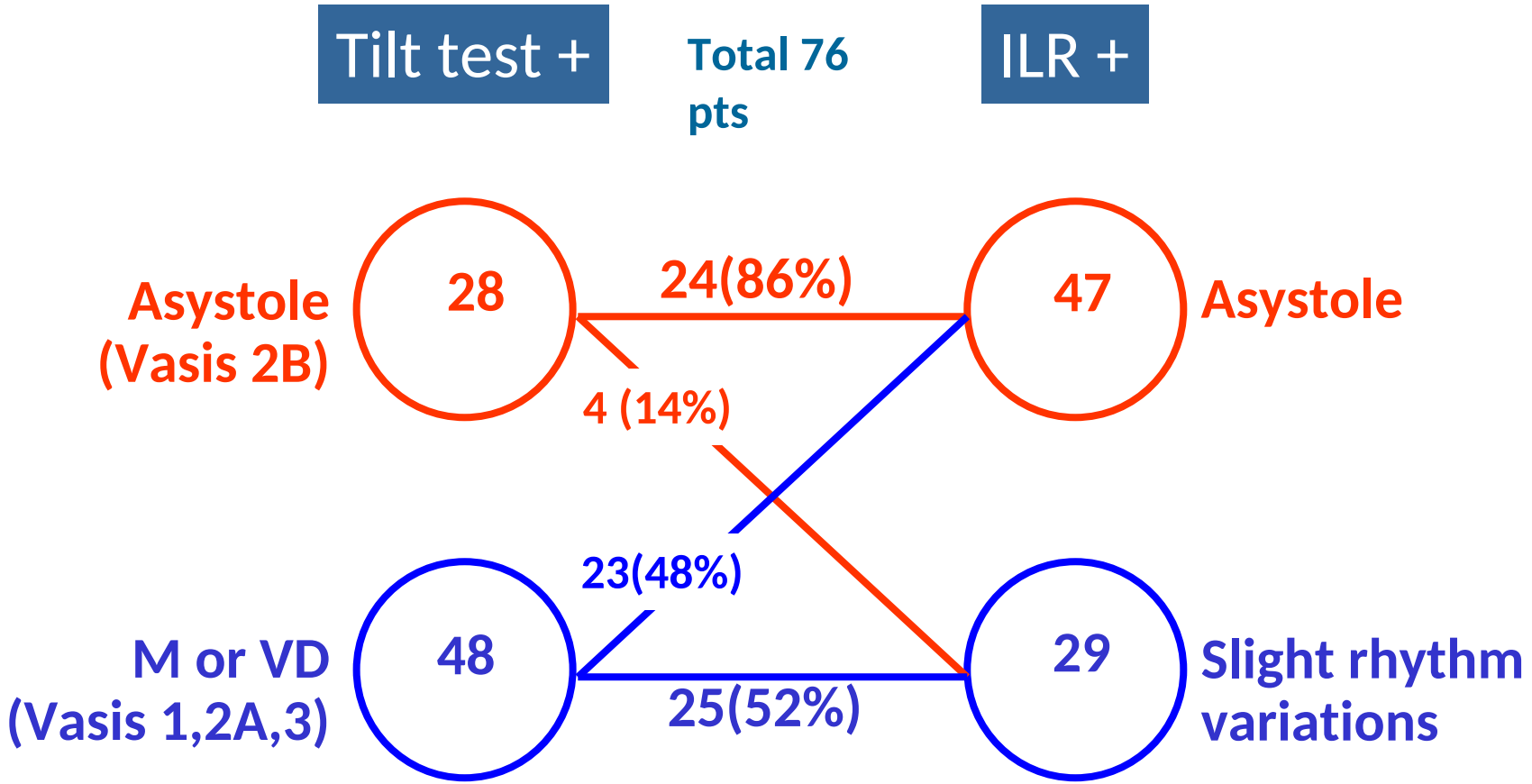


Spontaneous syncopal event



FN, f, ITA108-005

Correlation between tilt test responses and ILR-documented mechanism



Positive predictive value of asystolic tilt: 0.86 (95% CI 0.70-0.95)

Brignole M et al. Circ Arrhythm Electrophysiol 2013

Tilt testing: «The Italian protocol»

'The Italian Protocol': a simplified head-up tilt testing potentiated with oral nitroglycerin to assess patients with unexplained syncope

A. Bartoletti[1], P. Alboni[2], F. Ammirati[3], M. Brignole[4], A. Del Rosso[5], G. Foglia Manzillo[6], C. Menozzi[7], A. Raviele[8] and R. Sutton[9]

Europace 2000; 2: 339-342

Methodology

1. *Stabilization phase* of 5 min in the supine position;
2. *passive phase* of 20 min at a tilt angle of 60 degrees;
3. *provocation phase* of further 15 min after 3-400 g NTG sublingual spray.
4. *Test interruption* when the protocol is completed in the absence of symptoms, or there is occurrence of syncope

Prevalence of asystole during tilt-test induced vasovagal syncope may depend on test methodology.

Russo,... Brignole. Europace 2022, *in press*

Data from 16 studies for a total of 8514 positive tests (nitroglycerine protocols).

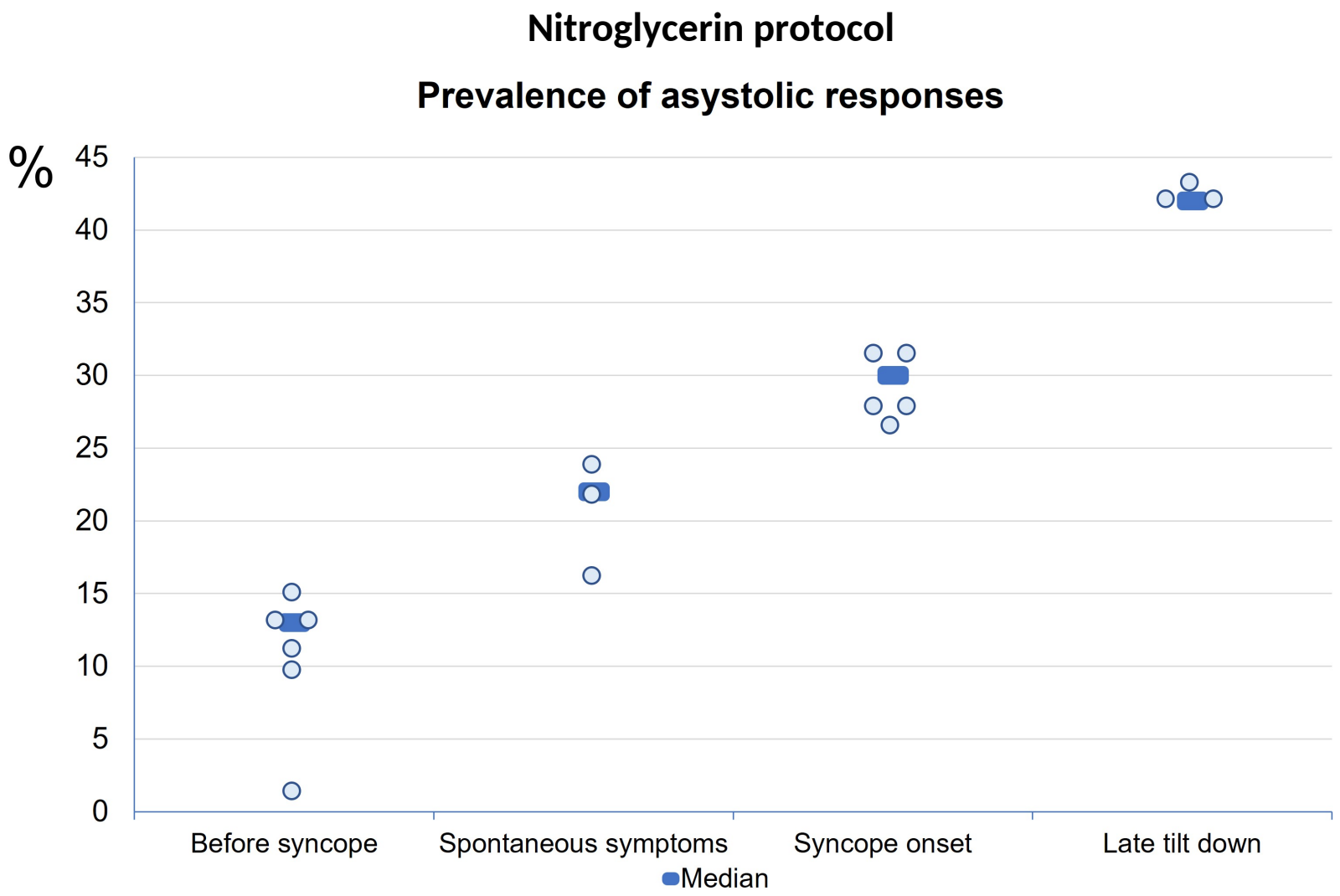
<u>Timing of tilt-down</u>:

1) Before syncope (vasovagal patterns or presyncope)

2) Induced symptoms recognized by the patient as its own

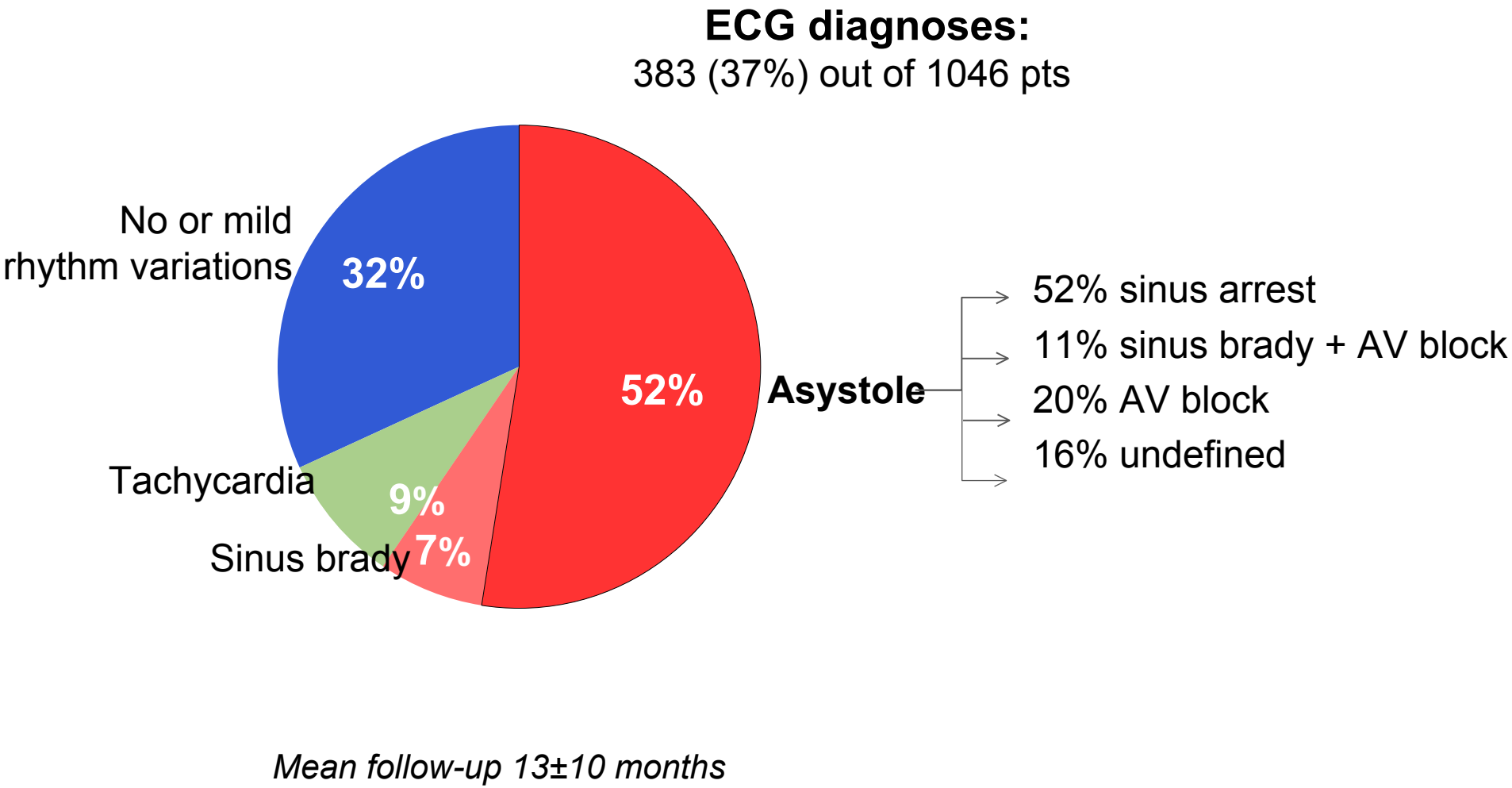
3) Syncope onset

4) Established LOC (lack of response to vocal stimuli, loss of muscular tone, jerking movements)



A meta-analysis of implantable loop recorder studies

Europace 2018; 20: 1362-1366

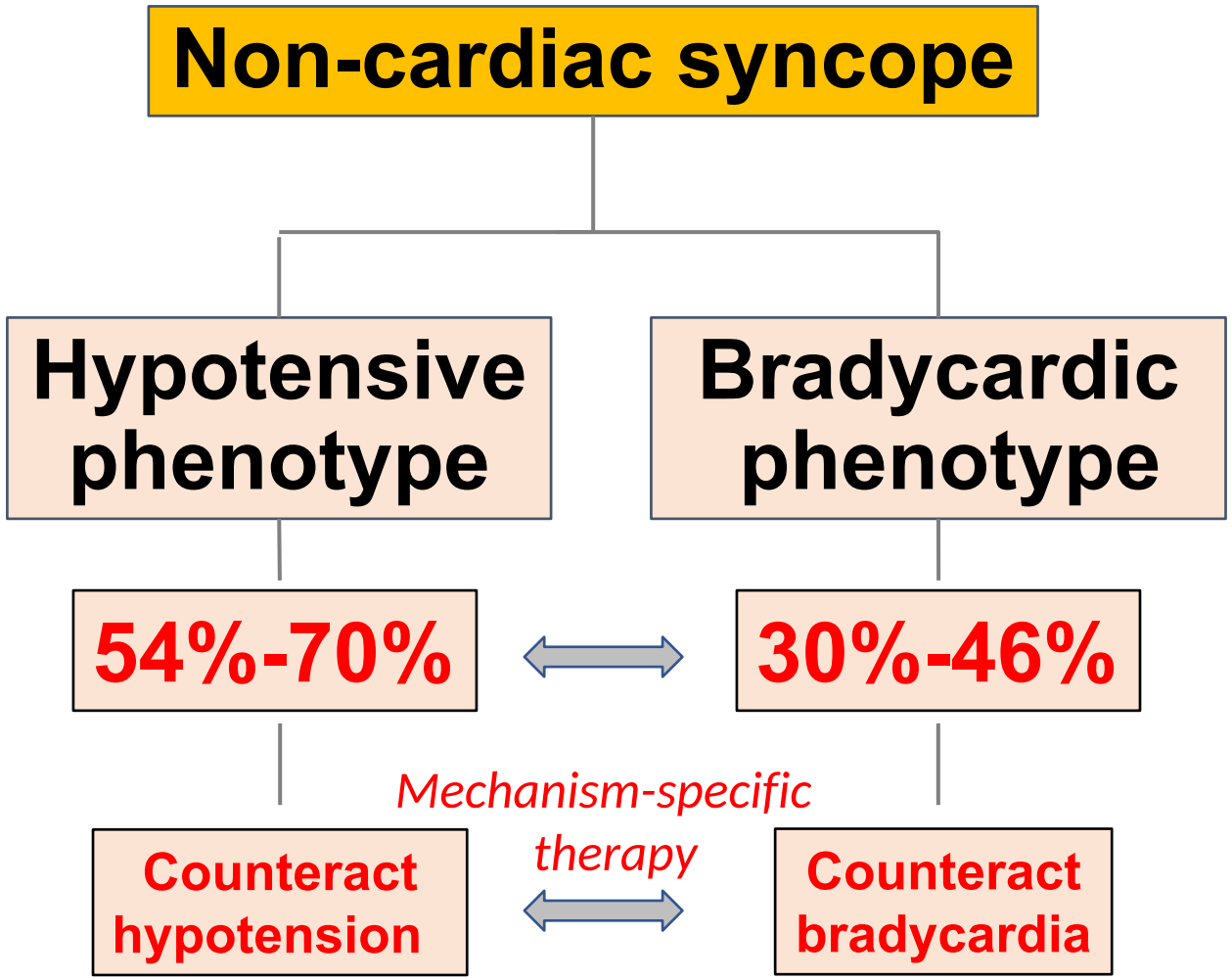


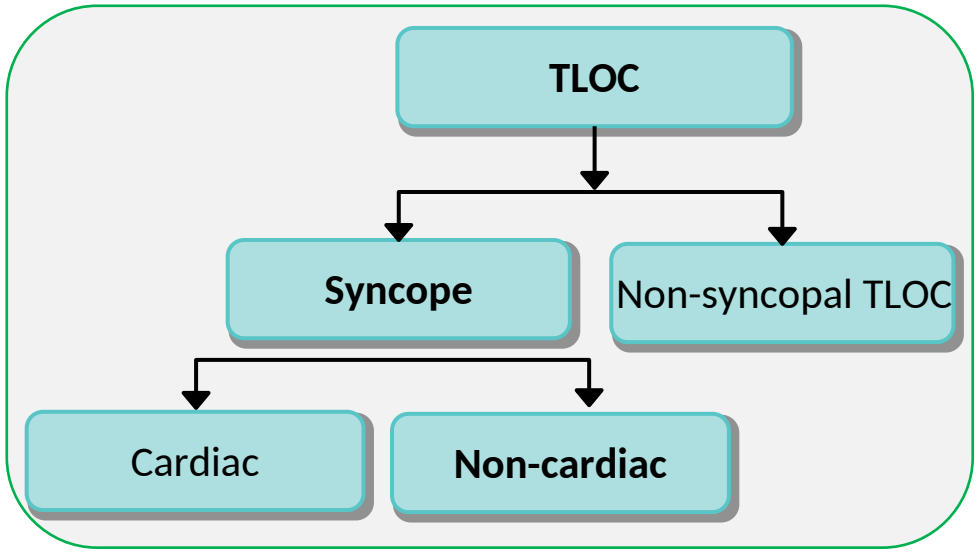
Mean follow-up 13±10 months

Source: *pooled data from ISSUE-2, ISSUE-3, SUP-2 and USA-FU trials*

(Eur Heart J 2006, Circulation 2012, Eur Heart J 2015, Heart Rhythm 2017)

Mechanisms of non-cardiac syncope





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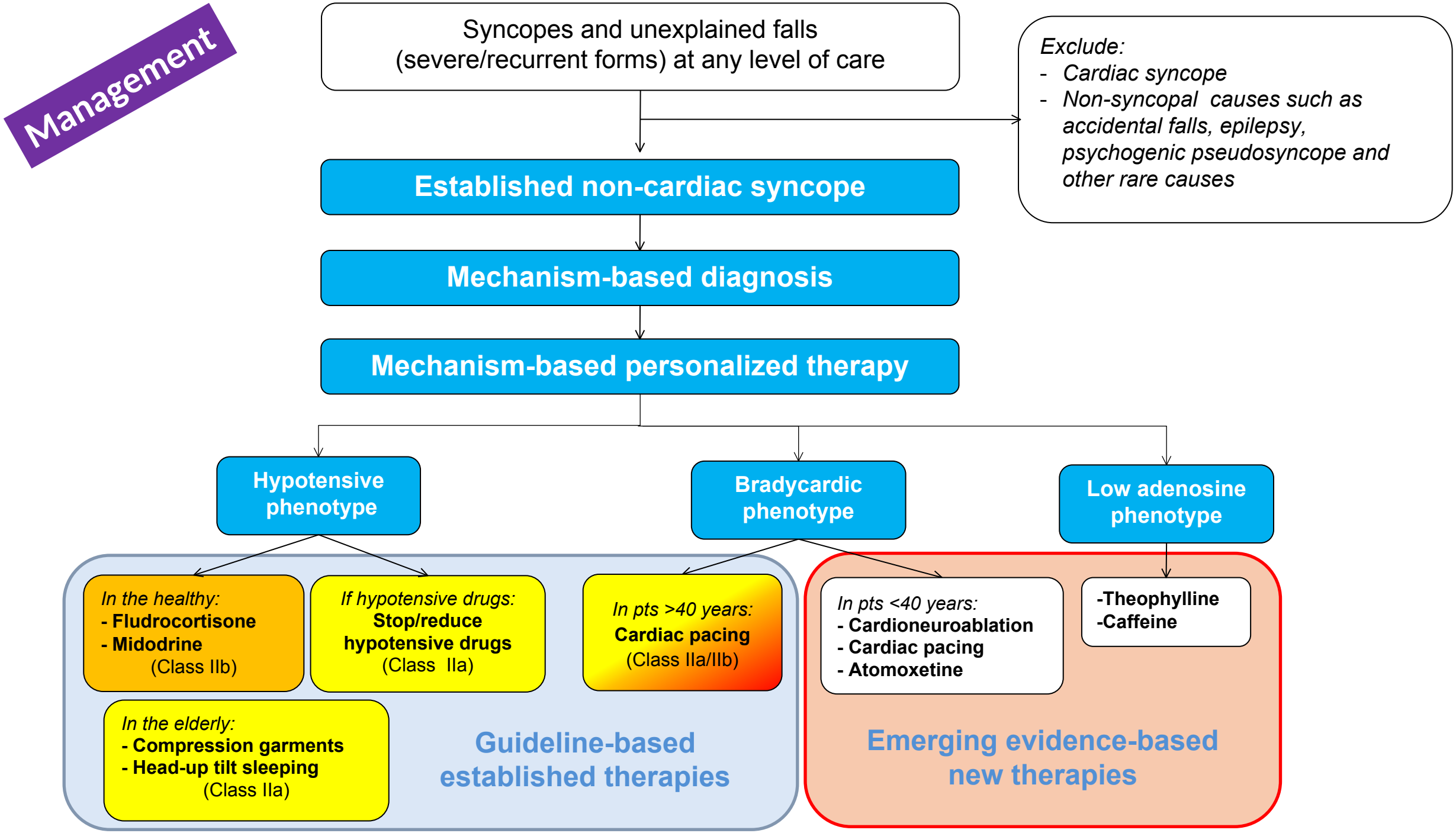
Management
Syncopes and unexplained falls
(severe/recurrent forms) at any level of care
Exclude:
- Cardiac syncope
- Non-syncopal causes such as accidental falls, epilepsy, psychogenic pseudosyncope and other rare causes
Established non-cardiac syncope
Mechanism-based diagnosis
Mechanism-based personalized therapy
Hypotensive phenotype
Bradycardic phenotype
Low adenosine phenotype
In the healthy:
- Fludrocortisone
- Midodrine
(Class IIb)
If hypotensive drugs:
Stop/reduce hypotensive drugs
(Class IIa)
In the elderly:
- Compression garments
- Head-up tilt sleeping
(Class IIa)
In pts >40 years:
Cardiac pacing
(Class IIa/IIb)
Guideline-based established therapies
In pts <40 years:
- Cardioneuroablation
- Cardiac pacing
- Atomoxetine
-Theophylline
-Caffeine
Emerging evidence-based new therapies