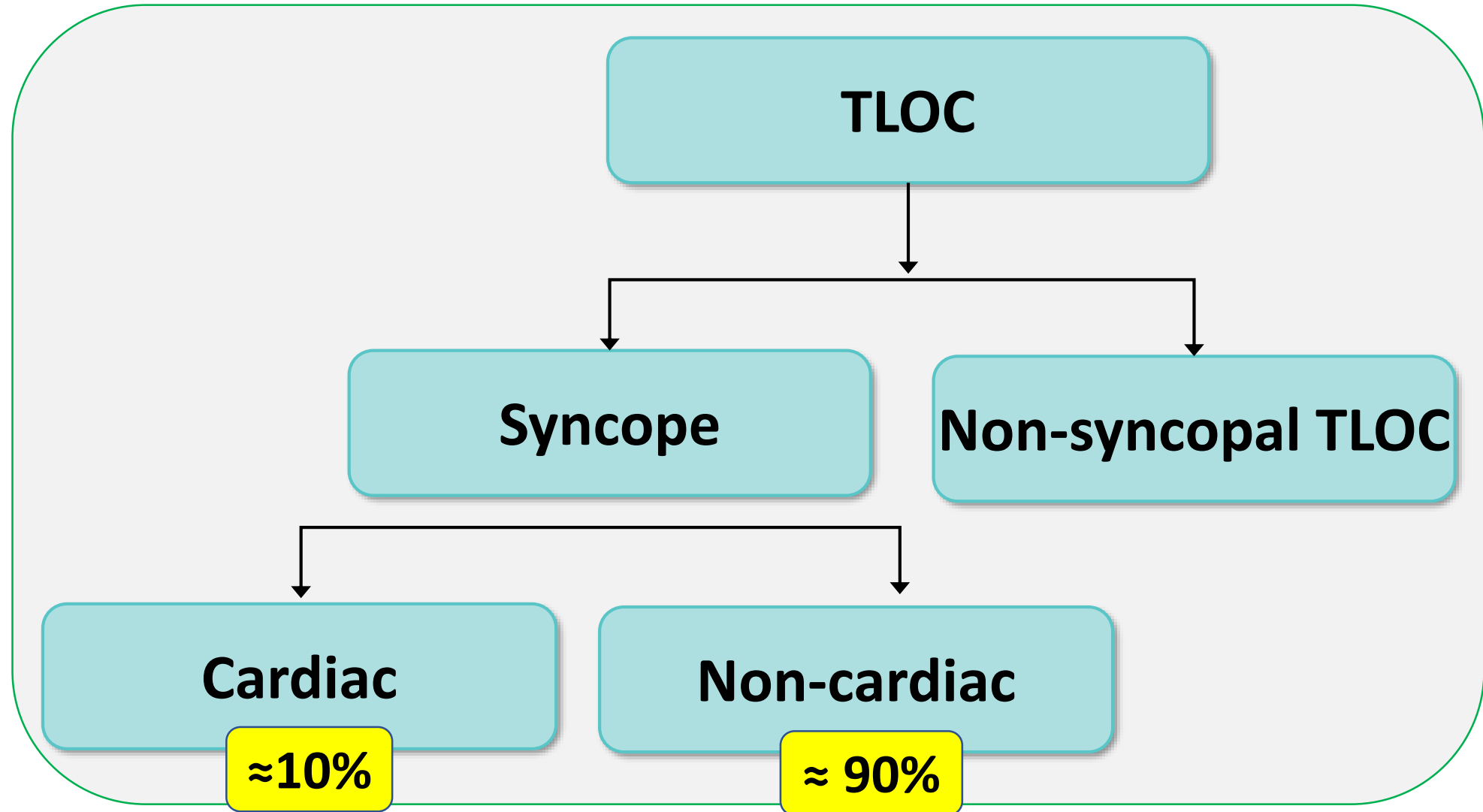




***CORSO TEORICO-PRATICO GIMSI-SIIA
“GESTIONE DEL PAZIENTE IPERTESO
CON SINCOPE”***

**L'inquadramento della
sincope**
Michele Brignole

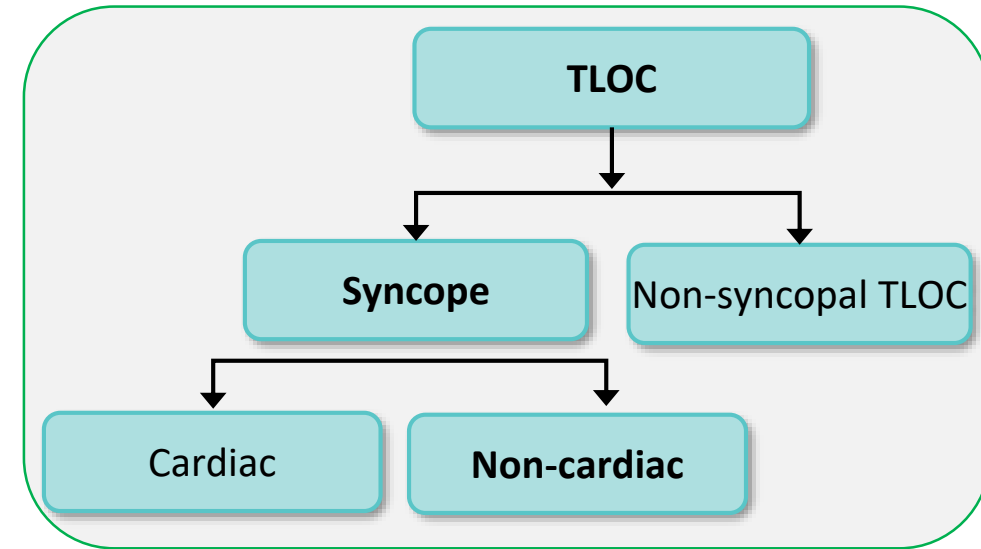
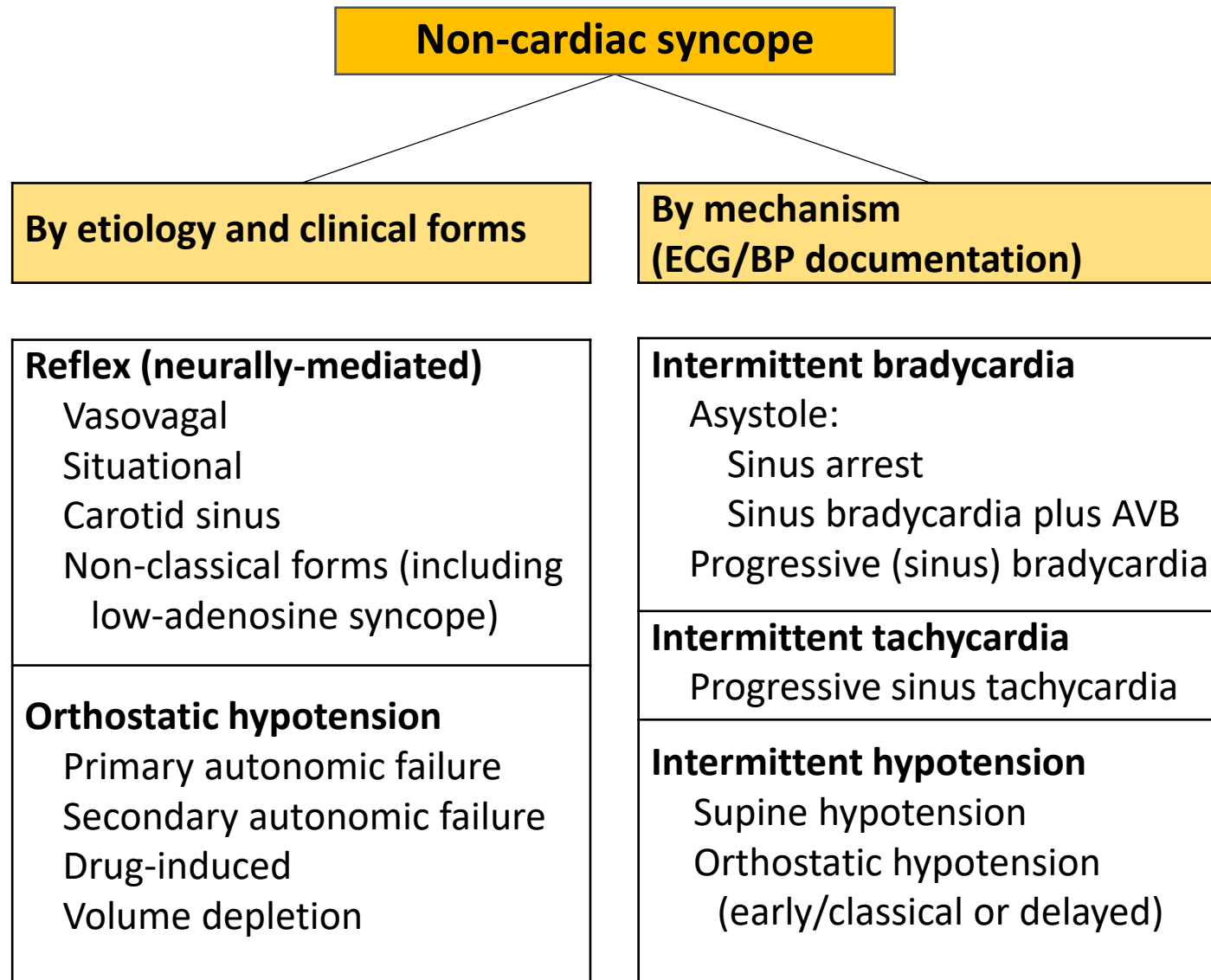
Classification of TLOCs



Cardiac likely

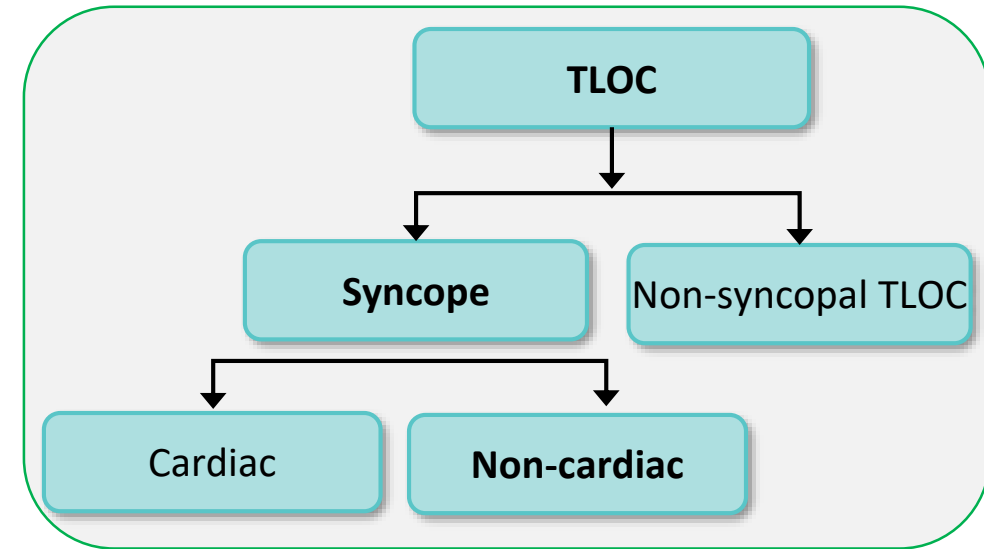
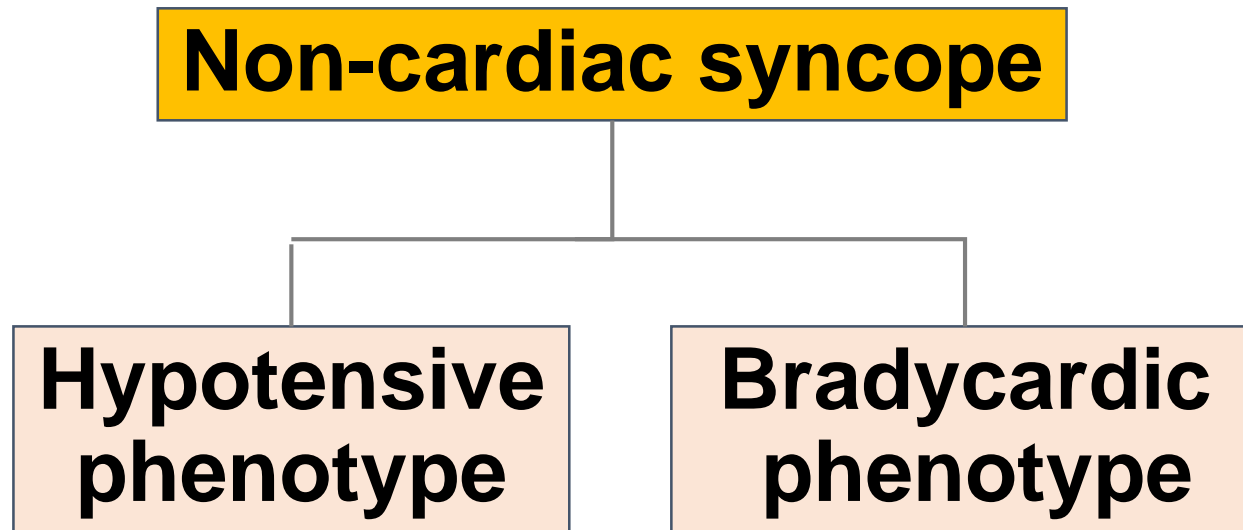
Cardiac syncope established	Cardiac syncope possible (to be confirmed by further investigations)
<p>Arrhythmic syncope is highly probable when the ECG shows:</p> <ul style="list-style-type: none">• Persistent sinus bradycardia <40 b.p.m. or sinus pause >3 s;• Mobitz II second- and third-degree AV block;• 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. <p>Cardiac ischaemia-related syncope is highly probable when syncope presents with evidence of acute myocardial ischaemia with or without myocardial infarction</p> <p>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.</p>	<p>ECG findings suggesting arrhythmic syncope:</p> <ul style="list-style-type: none">• 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 <p>Historical findings suggesting cardiac syncope:</p> <ul style="list-style-type: none">• 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

Classification of non-cardiac syncope



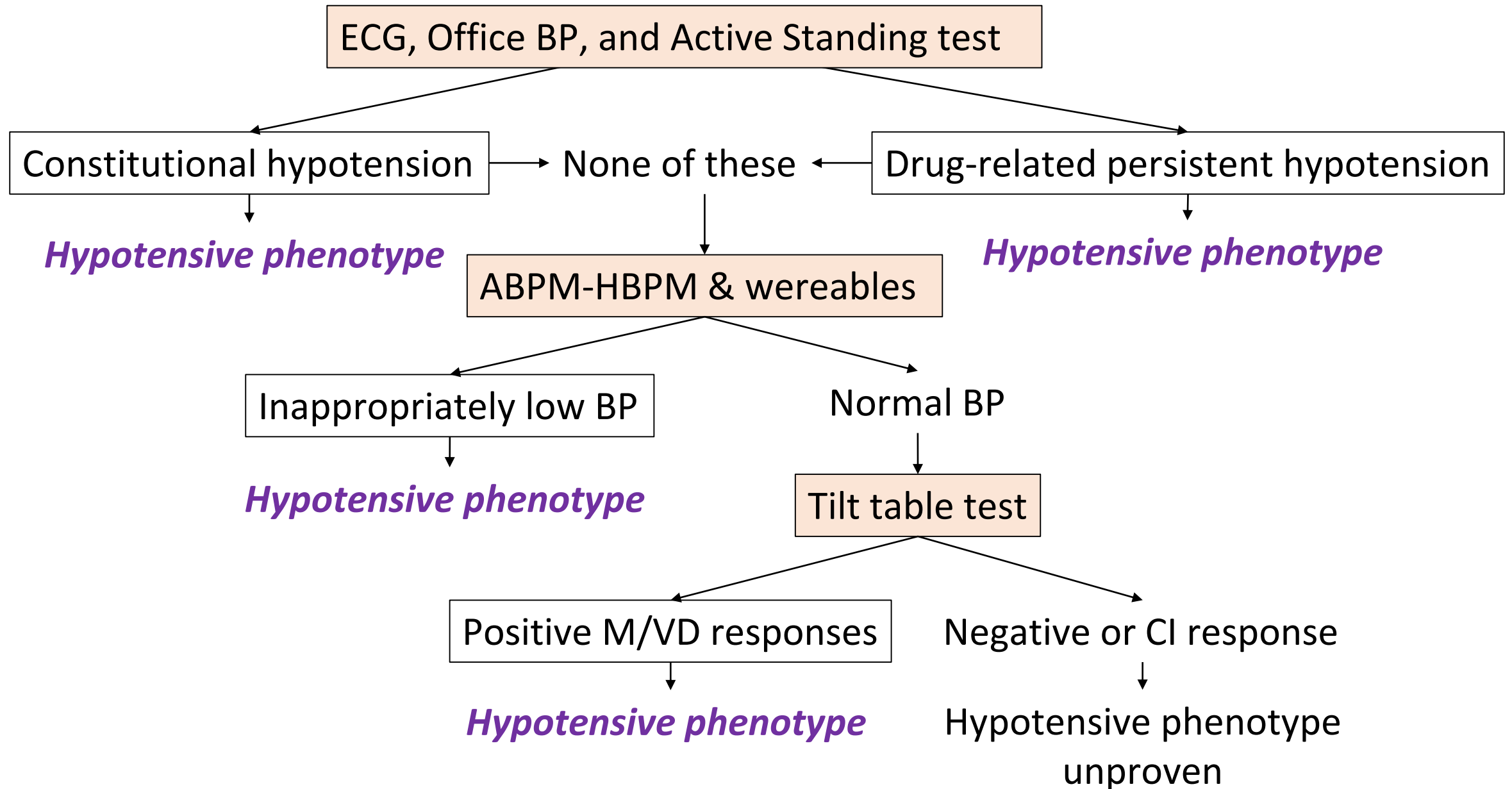
The efficacy of therapy is largely determined by the mechanism of syncope rather than its aetiology or clinical presentation

Mechanisms of non-cardiac syncope

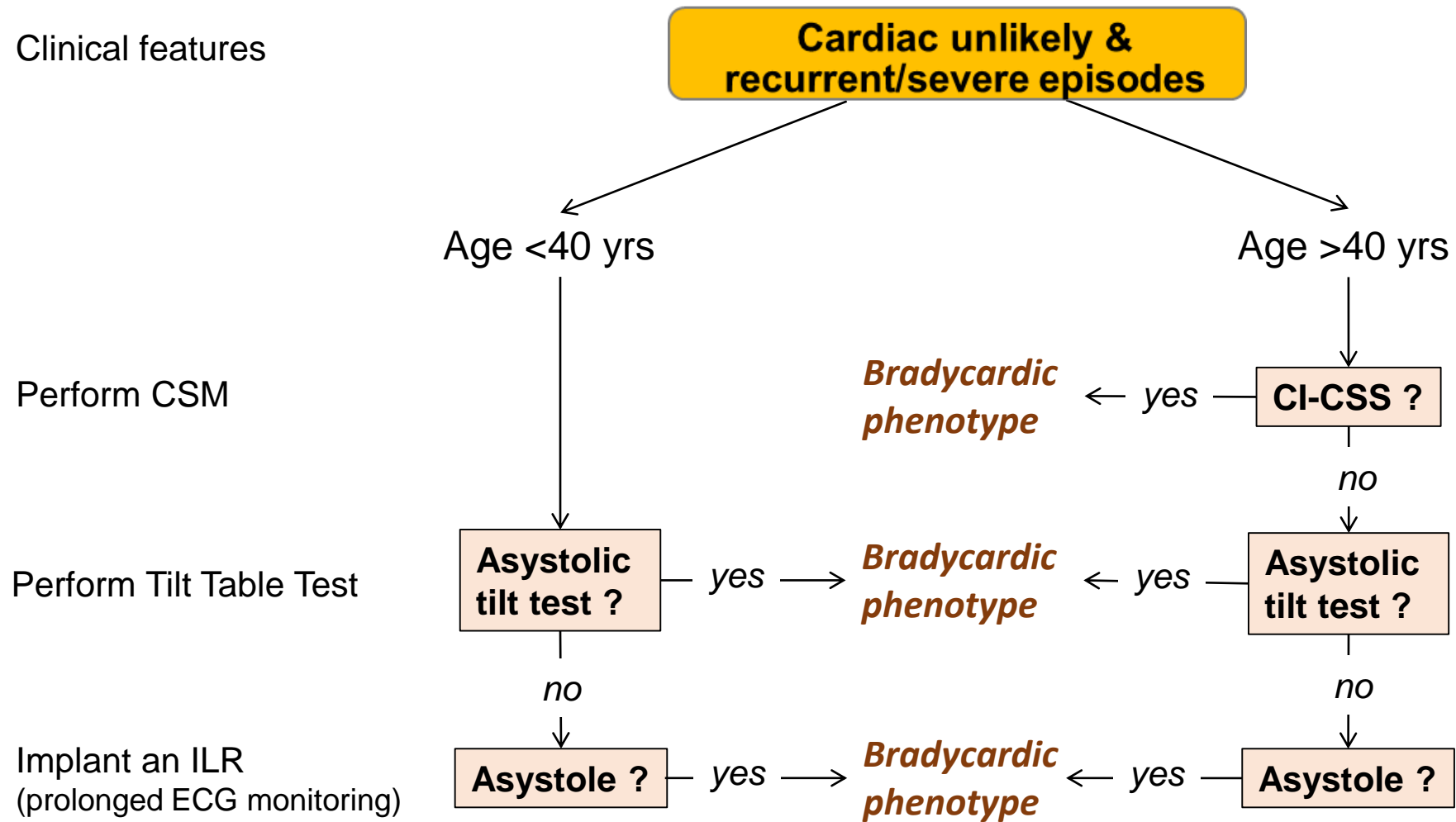


The efficacy of therapy is largely determined by the mechanism of syncope rather than its aetiology or clinical presentation

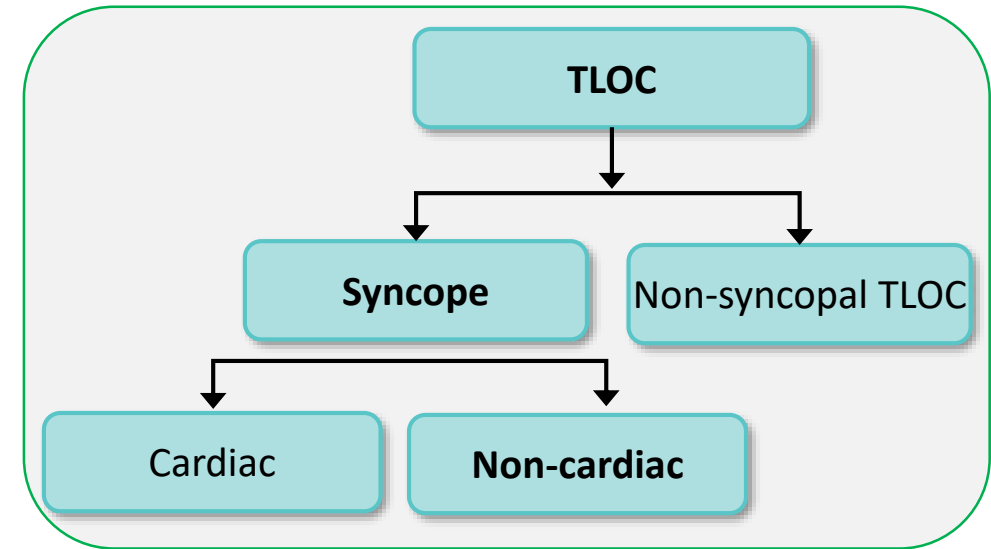
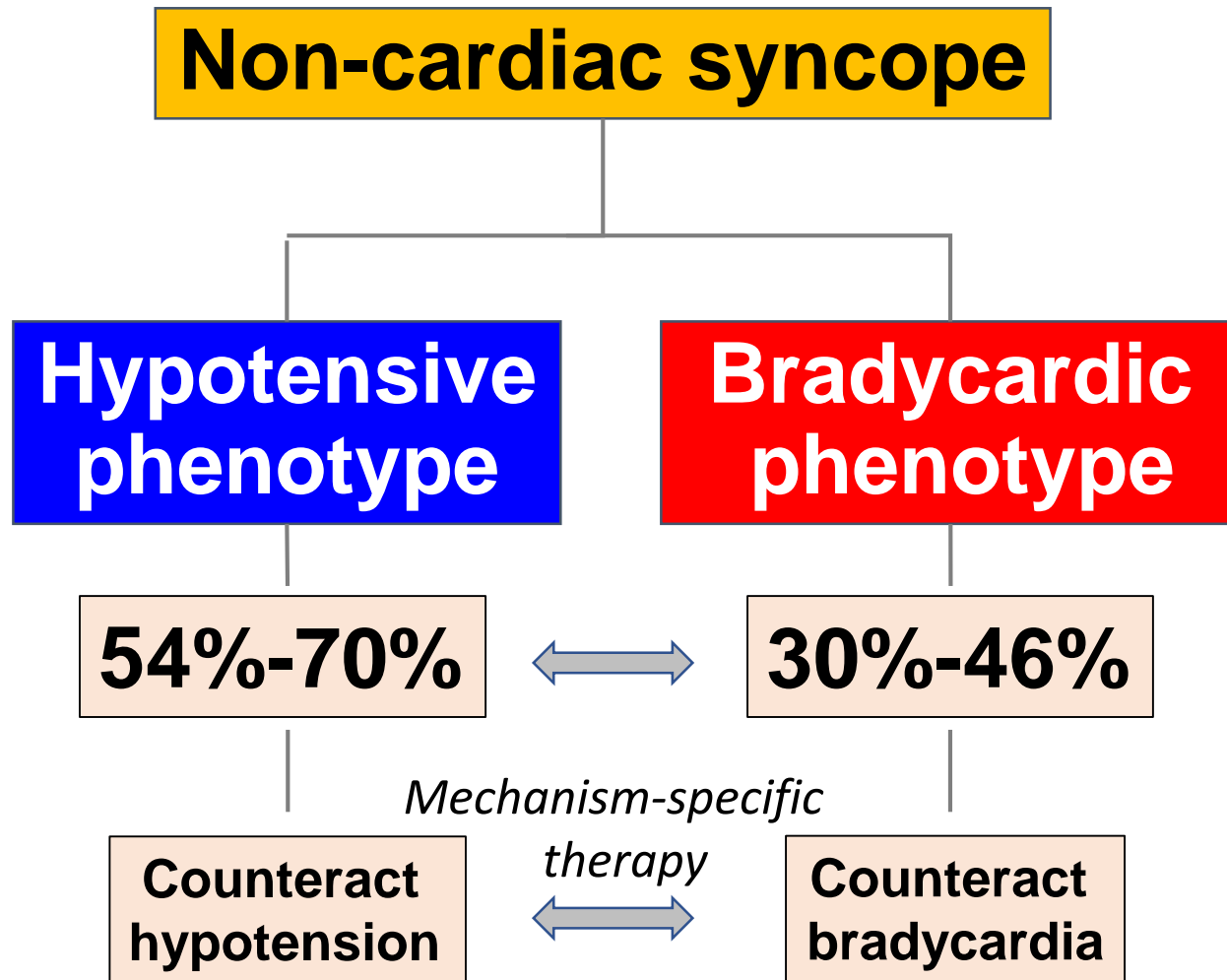
Hypotensive Phenotype: diagnostic work-up



How to identify patients with non-cardiac syncope and *Bradycardiac Phenotype*?



Mechanisms of non-cardiac syncope



Syncope 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 pts >40 years:
Cardiac pacing
(Class IIa/IIb)

In pts <40 years:
- Atomoxetine
- Cardioneuroablation
- Cardiac pacing

- Theophylline
- Caffeine

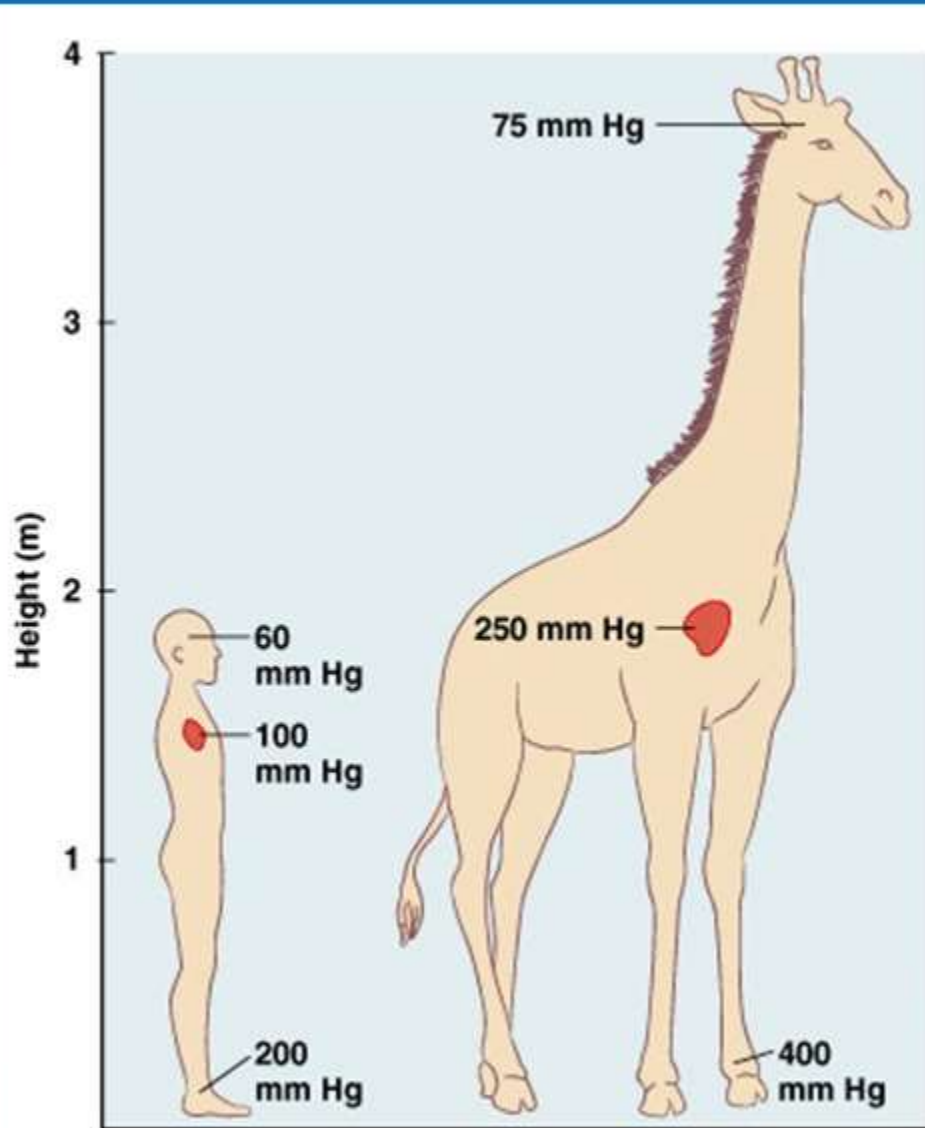
In the elderly:
- Compression garments
- Head-up tilt sleeping
(Class IIa)

Guideline-based established therapies

Emerging evidence-based new therapies

Il fenotipo ipotensivo

Why giraffe does not faint?



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- *Very tall animals (e.g. giraffe) must be able to pump blood up to the head*
- *They could also have difficulty with blood pooling in the feet, and peripheral edema*

Background question

Why some individuals with similar demographic characteristics develop reflex syncope and others not?

Low-blood pressure phenotype underpins the tendency to reflex syncope

Michele Brignole^a, Giulia Rivasi^b, Richard Sutton^c, Rose Anne Kenny^d, Carlos A. Morillo^e, Robert Sheldon^e, Satish R. Raj^e, Andrea Ungar^b, Raffaello Furlan^f, Gert van Dijk^g, Mohamed Hamdan^h, Viktor Hamrefors^{i,j}, Gunnar Engströmⁱ, Chloe Park^k, Davide Soranna^l, Antonella Zambon^{l,m}, Gianfranco Parati^{a,n,*}, and Artur Fedorowski^{i,o,*}

J Hypertension 2021; 39: 1319-1325

STUDY HYPOTHESIS: the patients with reflex syncope have a different cardiovascular physiology than in the general population

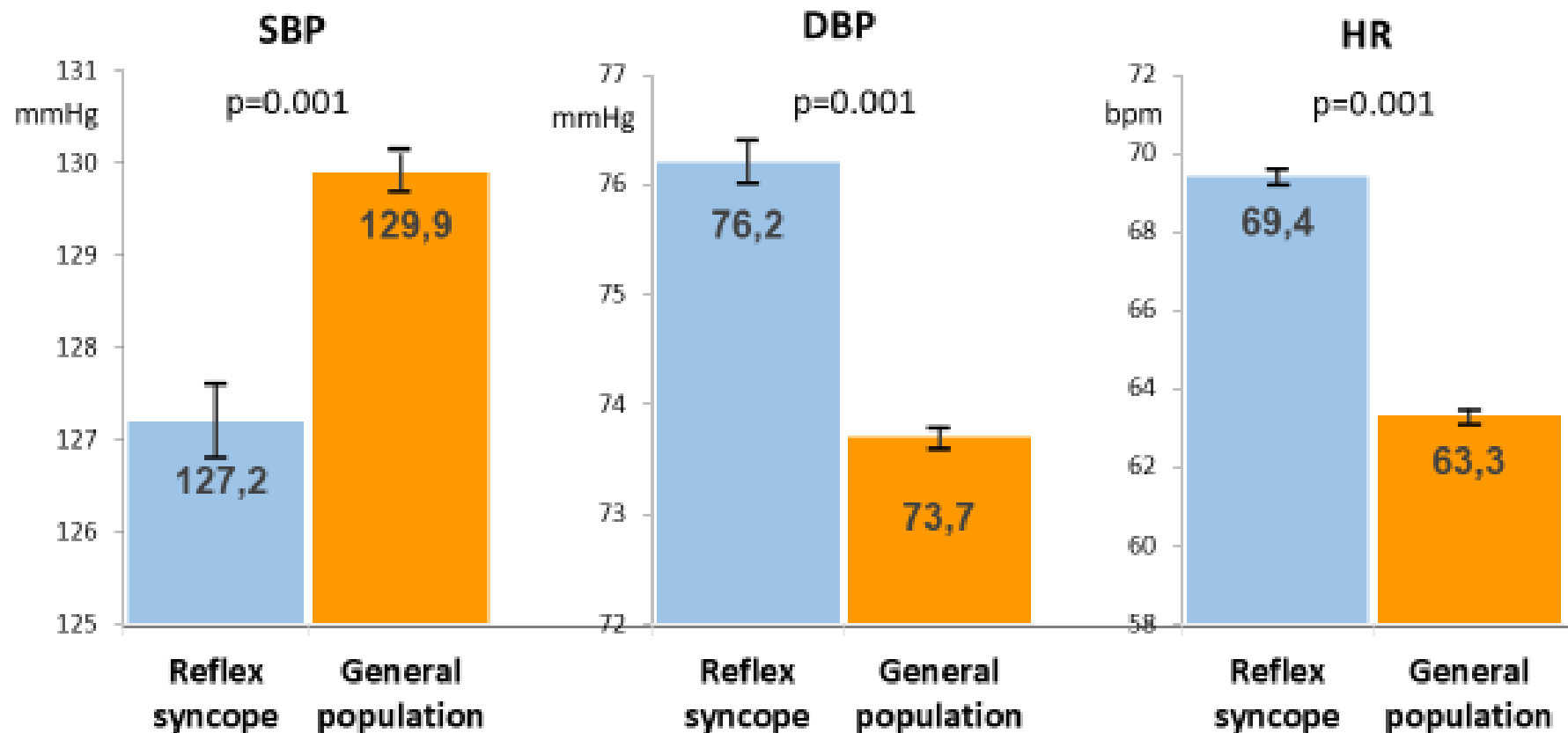
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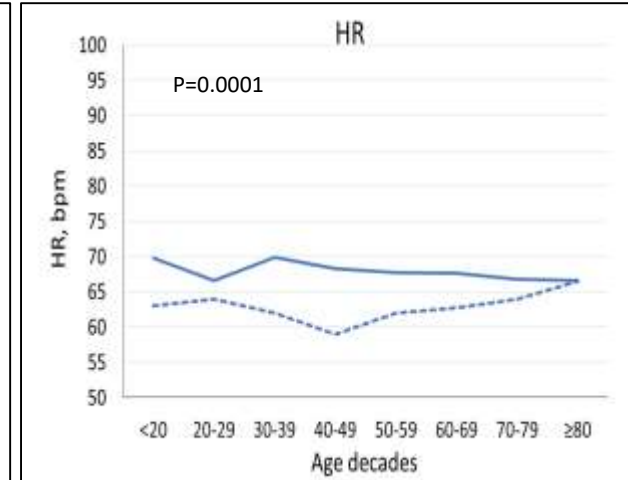
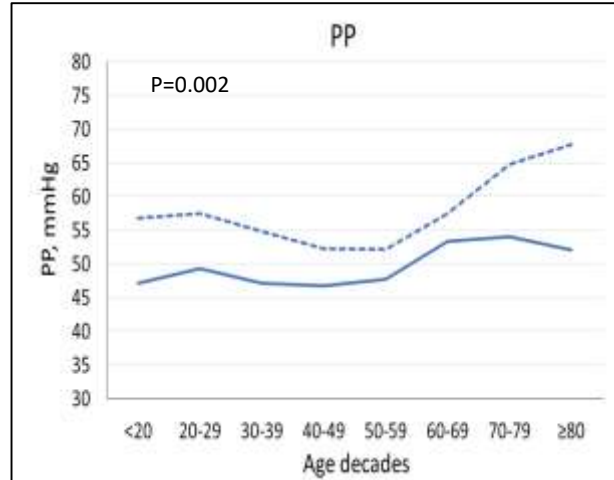
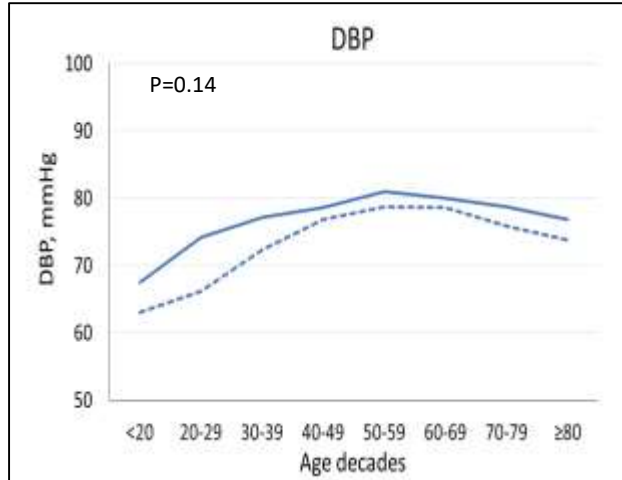
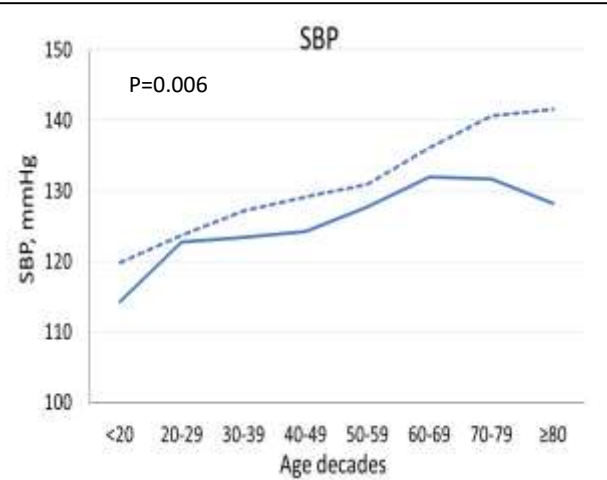
	Reflex syncope (6 studies)	General population (6 studies)
Total patients	6,516	64,968
Mean age	54±19	50±21
Females	56%	55%

Patients with reflex syncope have a different cardiovascular physiology than in the general population

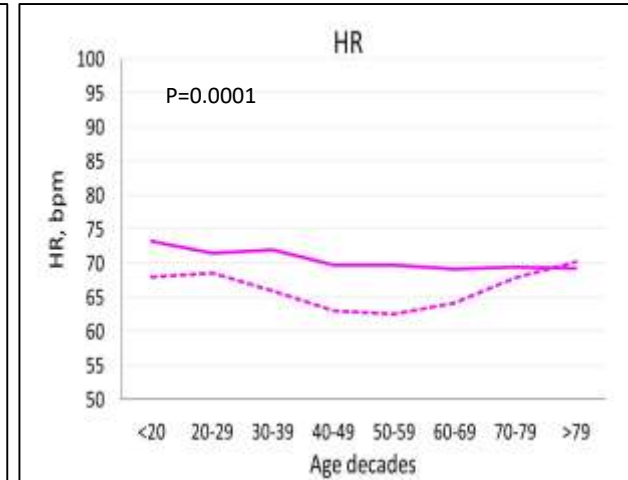
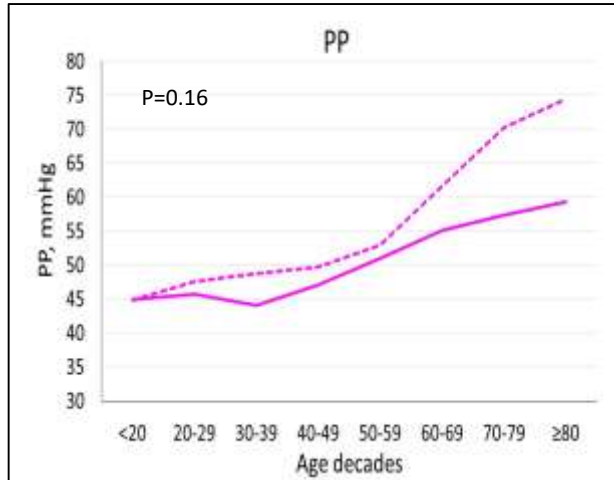
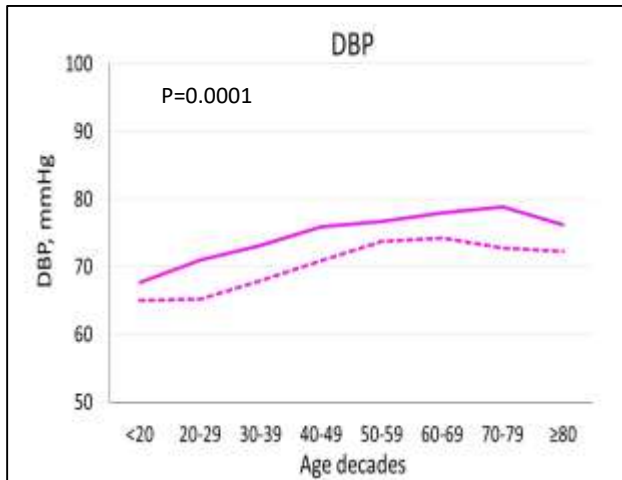
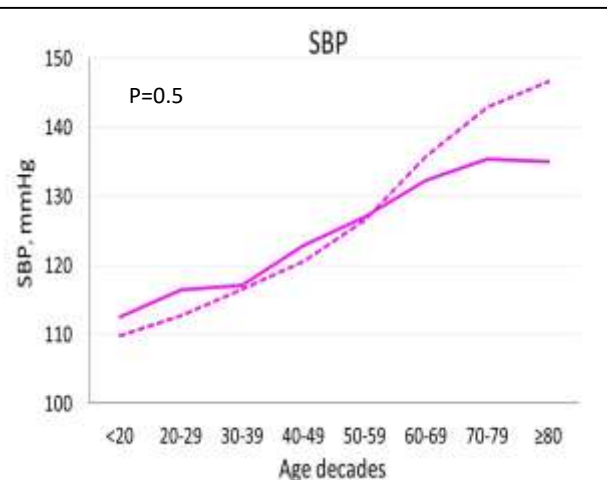


Patients with reflex syncope have a different cardiovascular physiology than in the general population (*J Hypertension* 2021)

Males



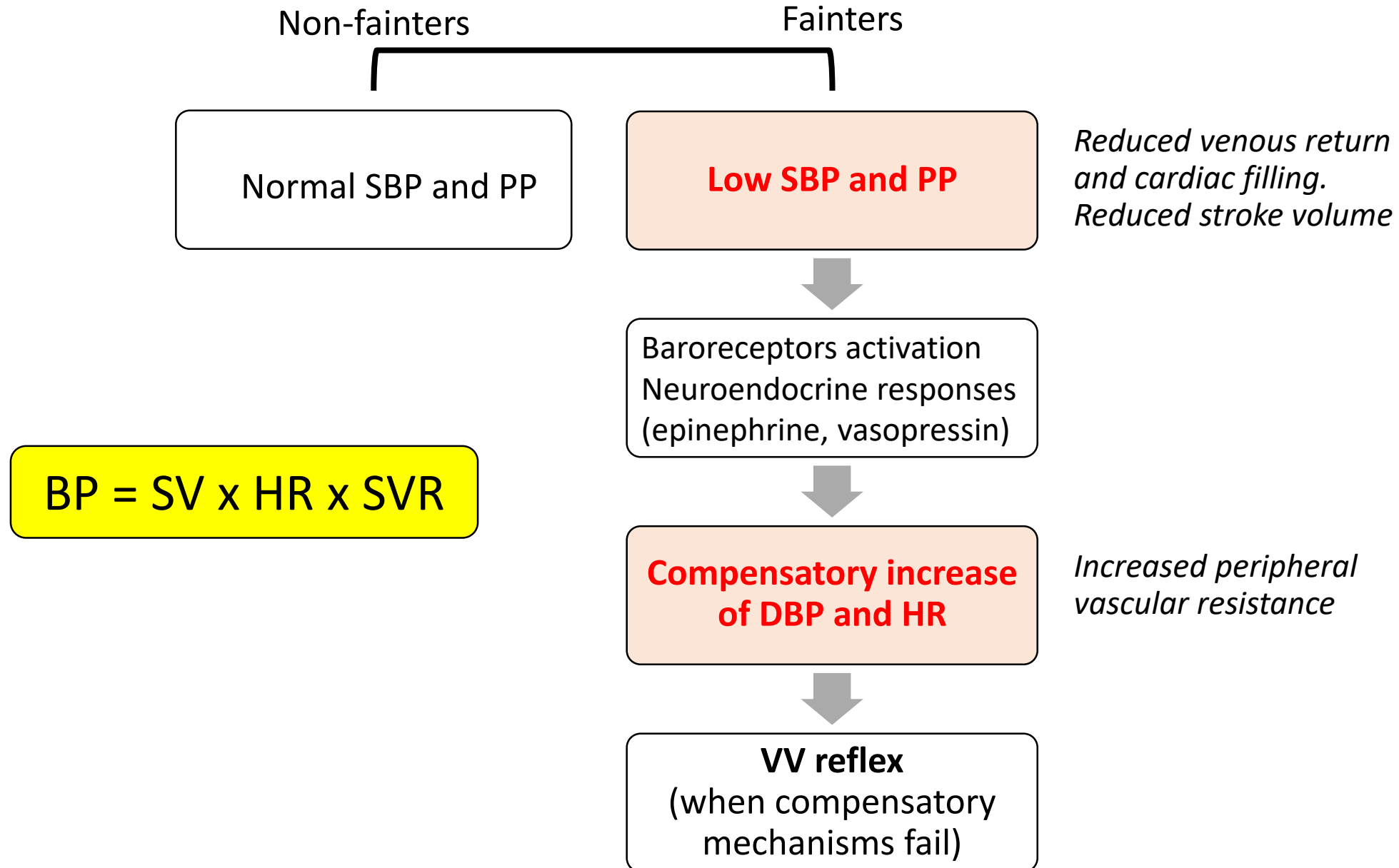
Females



— Syncope

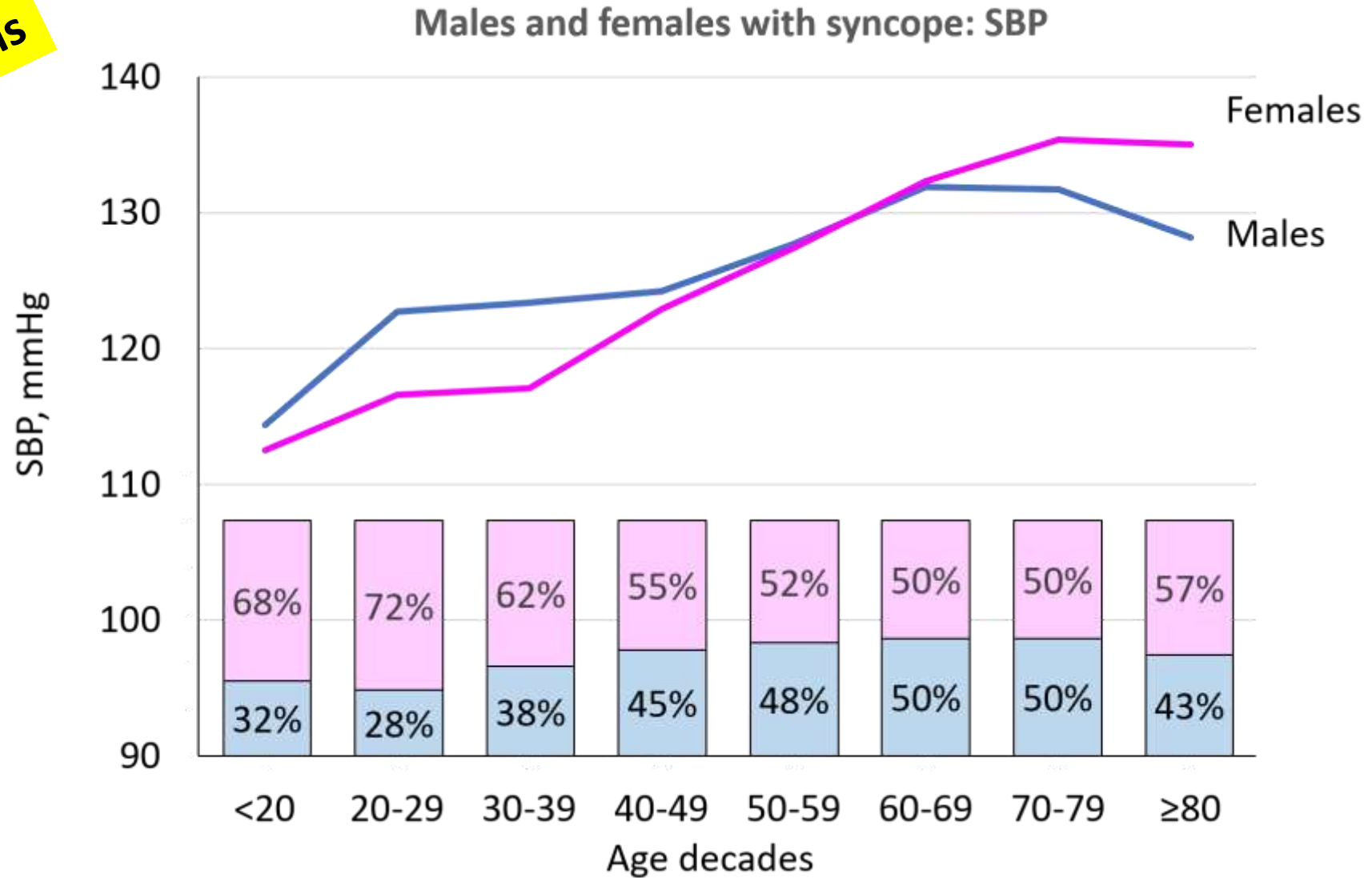
- - - General population

Patients with reflex syncope have a different cardiovascular physiology than in the general population (*J Hypertension 2021*)



Patients with reflex syncope have a different cardiovascular physiology than in the general population (*J Hypertension* 2021)

Confirmatory analysis



Low resting BP predisposes to positive response to tilt test

Hypertension protects from positive response to tilt test

Confirmatory analysis

	Total syncope population (n=5236) n (%)	Tilt-positive patients (n=3129) n (%)	Univariable analysis p value	Multivariable analysis p value
Hypertension*				
Yes	1655	864 (52)	0.0001	0.0001
No	3581	2265 (63)		
Baseline SBP at the time of tilt testing				
>128 mmHg	2443	1358 (56)	0.0001	0.0001
≤128 mmHg	2793	1771 (63)		

*Fedorowski A et al. Underlying hemodynamic differences are associated with a positive response during tilt testing. **Scientific Report 2021: 11: 17894***

Low BP predisposes to hypotensive episodes revealed by ABPM

Confirmatory analysis

Hypotensive episode = SBP drops >20 mmHg AND <100 mmHg

	Overall sample (<i>n</i> = 91)	Hypotensive episodes on ABPM (<i>n</i> = 50)	No hypotensive episodes on ABPM (<i>n</i> = 41)	<i>p</i>
ABPM				
ABPM: 24 h SBP, mean ± SD	121.5 ± 14.9	113.2 ± 10.7	131.5 ± 13.2	<0.001
ABPM: 24 h DBP, mean ± SD	68.0 ± 10.9	62.6 ± 8.9	74.5 ± 9.7	<0.001
ABPM: daytime SBP, mean ± SD	123.0 ± 15.9	114.1 ± 12.1	134.0 ± 12.7	<0.001
ABPM: daytime DBP, mean ± SD	70.3 ± 11.8	64.5 ± 10.2	77.3 ± 9.7	<0.001
ABPM: night-time SBP, mean ± SD	119.8 ± 16.1	112.2 ± 12.5	129.2 ± 15.1	<0.001
ABPM: night-time DBP, mean ± SD	65.7 ± 11.6	60.6 ± 9.3	72.0 ± 11.1	<0.001
ABPM: daytime SD, mean ± SD	13.4 ± 3.6	13.8 ± 3.5	12.8 ± 3.8	0.186
Nocturnal dipping, <i>n</i> (%)				
Dippers	26 (28.6)	14 (28.0)	12 (29.3)	0.894
Non-dippers	35 (38.5)	14 (28.0)	21 (51.2)	0.023
Reverse dippers	30 (33.0)	22 (44.0)	8 (19.5)	0.013

Patients with reflex syncope have lower 24-hour SBP than matched controls

Confirmatory analysis

	Syncope patients (n=50)	Controls (n=100)	P-Value
Age (years \pm SD)	45.5 \pm 14.6	45.5 \pm 14.5	-
Females, n (%)	35 (70)	70 (70)	-
Antihypertensive therapy, n (%)	4 (8)	13 (13)	0.352
Mean office SBP (mmHg \pm SD)	115.5 \pm 11.3	119.7 \pm 16.3	0.105
ABPM parameters:			
Mean 24h SBP (mmHg \pm SD)	112.9 \pm 12.6	119.3 \pm 11.5	0.002*
Mean Daytime SBP (mmHg \pm SD)	116.7 \pm 12.9	122.2 \pm 11.3	0.082
Mean Night-time SBP (mmHg \pm SD)	101.3 \pm 11.6	103.1 \pm 11.4	0.370
Mean 24h DBP (mmHg \pm SD)	85.2 \pm 9.6	79.1 \pm 10.6	<0.001*
Mean 24h PP (mmHg \pm SD)	27.7 \pm 7.6	40.3 \pm 9.0	<0.001*

Is VVS a chronic disease?



Syncope is intermittent

Low BP phenotype is chronic



The reflex syncope cascade

Predisposing condition

Preparatory stage

Syncopal stage

