



# La stratificazione del rischio in ambito lavorativo del paziente con sincope e disautonomia cardiovascolare

SIML, Sezione territoriale lombarda  
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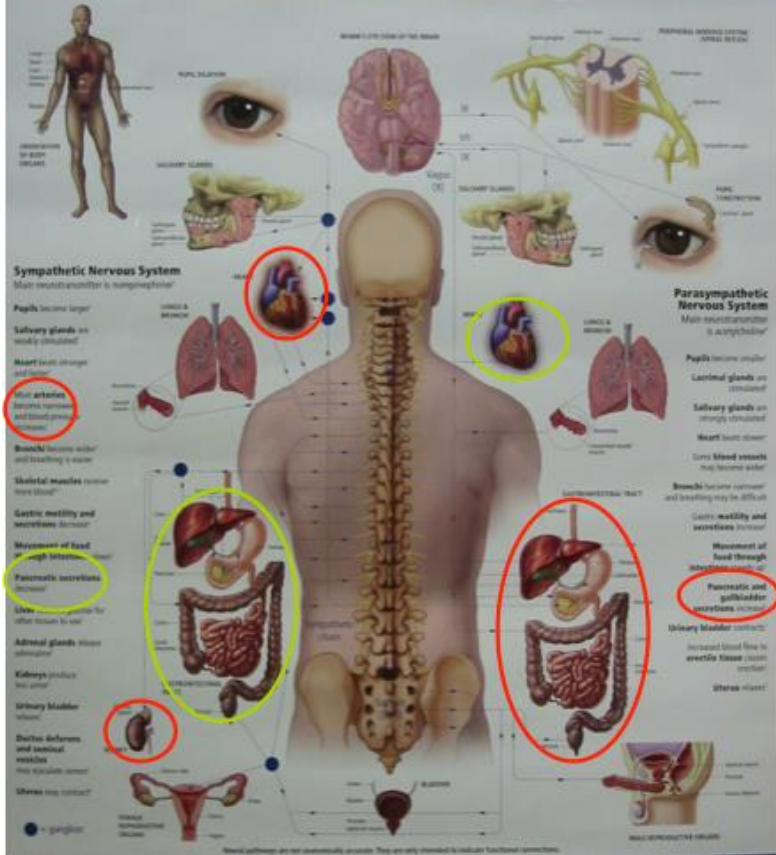
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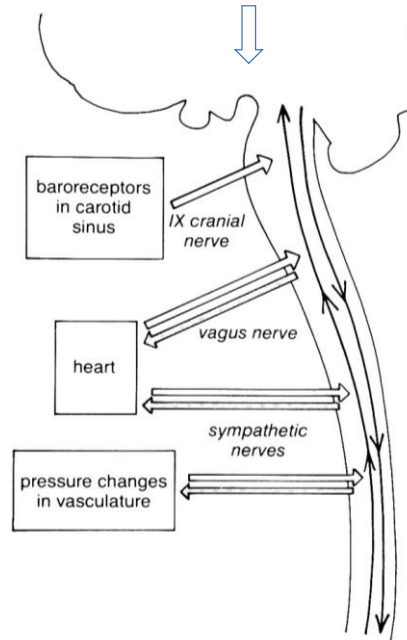
# Outline

- 1. Sincope neuromediata e stratificazione del rischio in ambito lavorativo**
2. Disautonomia cardiovascolare e work ability
3. Sindrome disautonomica post-Covid19: incidenza e work ability

# Autonomic Nervous System Anatomy & Physiology



## Cortical and sub-cortical



Modified by Pagani et al, 1992; 13: 50

The sympathetic and parasympathetic balanced activity is crucial to control visceral functions such as:

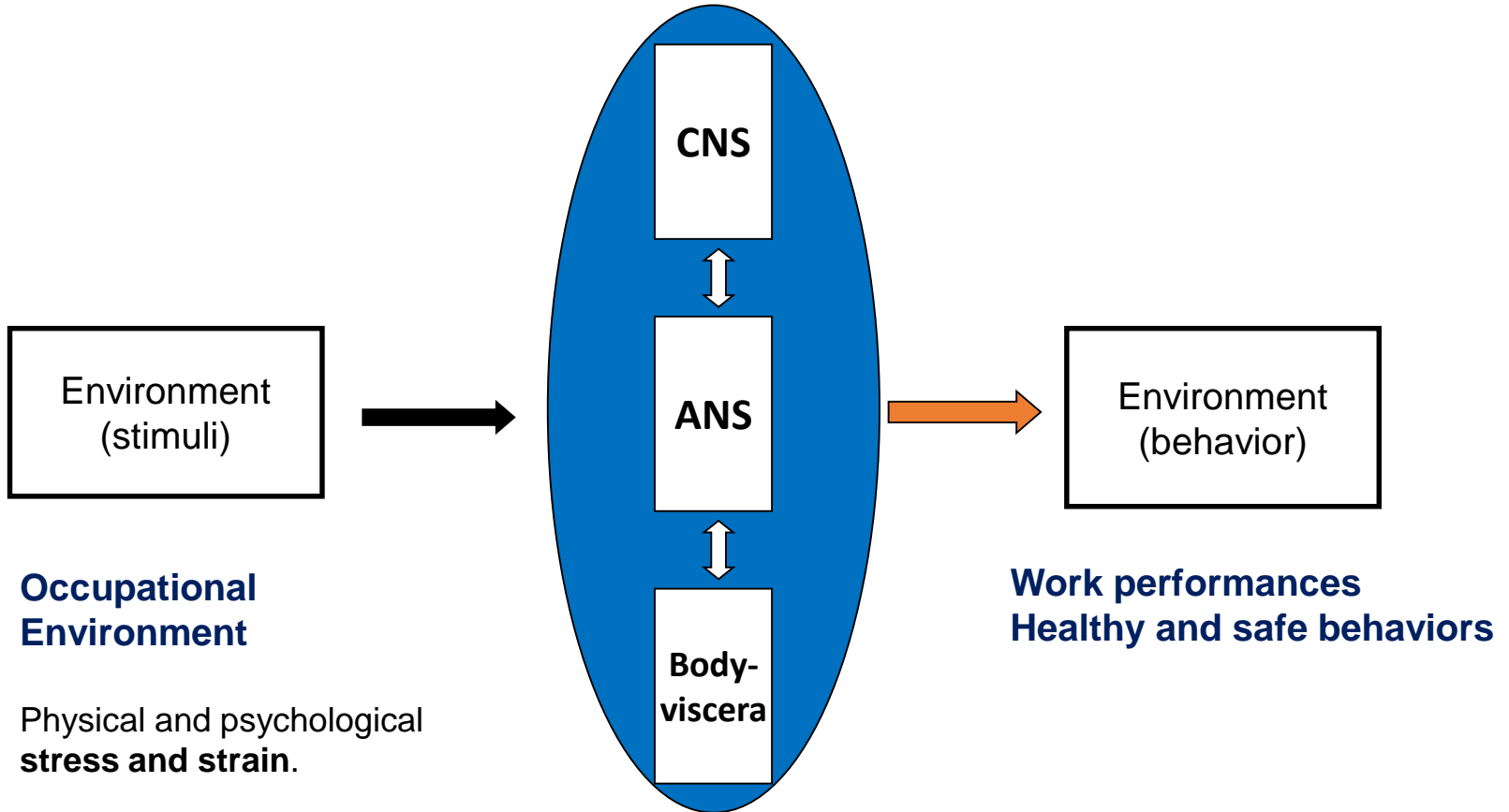
- Heart rate/stroke volume
- Blood pressure
- Gastroenteric motility and secretion
- Body temperature
- Energy expenditure
- Other essential functions

Unbalance of ANS functioning may impair responses to environmental stimuli and promote acute and chronic diseases.

**OUT**

**IN**

**OUT**



**Orthostatic stress, irregular shifting schedule**, changes of environmental temperature, noise.

The transient loss of consciousness associated with the inability to maintain postural tone may turn in a life-threatening condition for the fainter and for the bystanders when occurring during hazardous jobs.





# Bin lorry crash driver suspended as inquiry hears history of blackouts

FROM PAGE ONE

First Bus following repeated sick days prior to his blackout in April 2010.

Paramedics examined him on the bus and he refused to accompany them to hospital, instead returning to the depot where he informed his managers about

The toll of a temple bell marked the

Gerard McKaig, that he fainted 'at work, in canteen, hot environment, no warning signs'.

Later, he visited a second GP, Dr John Langan, who was giving evidence at the FAI yesterday, and repeated his claim that he fainted in the work canteen but then told him he had felt light-headed beforehand.

Mr Clarke was signed off as fit

record: 'Dr Langan has dictated a letter saying fit to drive as had warning signs and reasons for attack.'

First Bus medical officer Dr Kenneth Lyons wrote in a letter that the incident happened on 'a stationary bus' and that Mr Clarke 'had no particular warning of the event although he was aware of feeling warm'.

DVLA evidence indicates

blackout with no external cause (provocation), no warning signs (prodromal) and were sitting or lying at the time (posture) should be referred for further examinations before driving, outlined in 'box three'.

Dorothy Bain QC, representing the family of Jacqueline Morton, 51, who was killed in the crash, cross-examined Mr Lyons at the FAI yesterday.



FRANCIS PAGE 25

# Council suspends death crash driver

Francis  
August

AMY WATSON

THE driver of a bin lorry that crashed killing six people in Glasgow city centre has been suspended from work.

Glasgow City Council said it has suspended Harry Clarke 'on a precautionary basis' ahead of a full investigation.

After the crash Mr Clarke returned to work at the Shieldhall waste depot but did not resume driving duties.

His suspension came after a fatal ac-

## Authority acts after bin lorry tragedy inquiry hears health record evidence

cident inquiry (FAI) that is taking place into the tragedy was told that Mr Clarke did not disclose his medical history when completing a health questionnaire when he applied to work for the council.

A spokeswoman for Glasgow City Council said 'The council can confirm that it has suspended Mr Harry Clarke on

a precautionary basis pending a full disciplinary investigation.

'A number of allegations have been made during the inquiry in regard to Mr Clarke's conduct before and at the point where he commenced employment with the council. These allegations have yet to be put to Mr Clarke and he has not

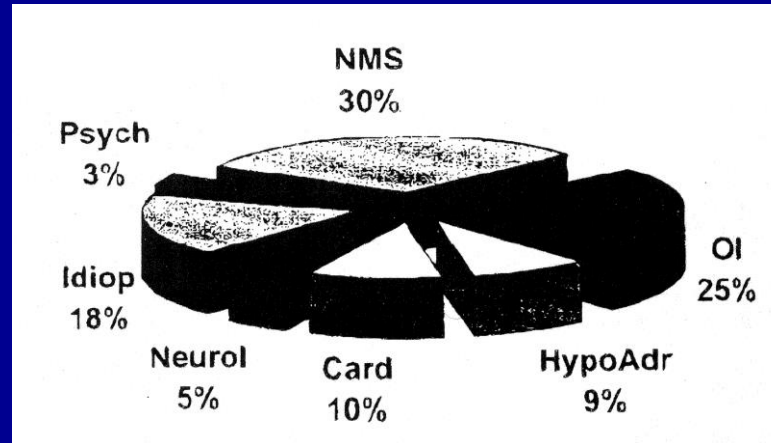
yet had the opportunity of responding to them. The internal investigation will therefore take place at the conclusion of the FAI.'

It comes after the inquiry was told that Mr Clarke did not disclose his medical history when completing a health questionnaire when he applied to work for the council.

Yesterday, the FAI into the crash heard that Mr Clarke was 'on his last legs' at

CONTINUED ON PAGE 4

Reflex Syncope is the most frequent type of syncope particularly in working age (young and old).



Mosqueda-Garcia et al. Circulation 2000;102:289

The High Risk Activities are common in occupational environment and include the professional driving.

*The rate of Unexplained Syncope is about 25 % in people discharged from ED and has been decreased thanks to dedicated Syncope Unit.*

# An approach to the evaluation and management of syncope in adults

Steve W Parry, Maw Pin Tan

BMJ | 27 FEBRUARY 2010 | VOLUME 340

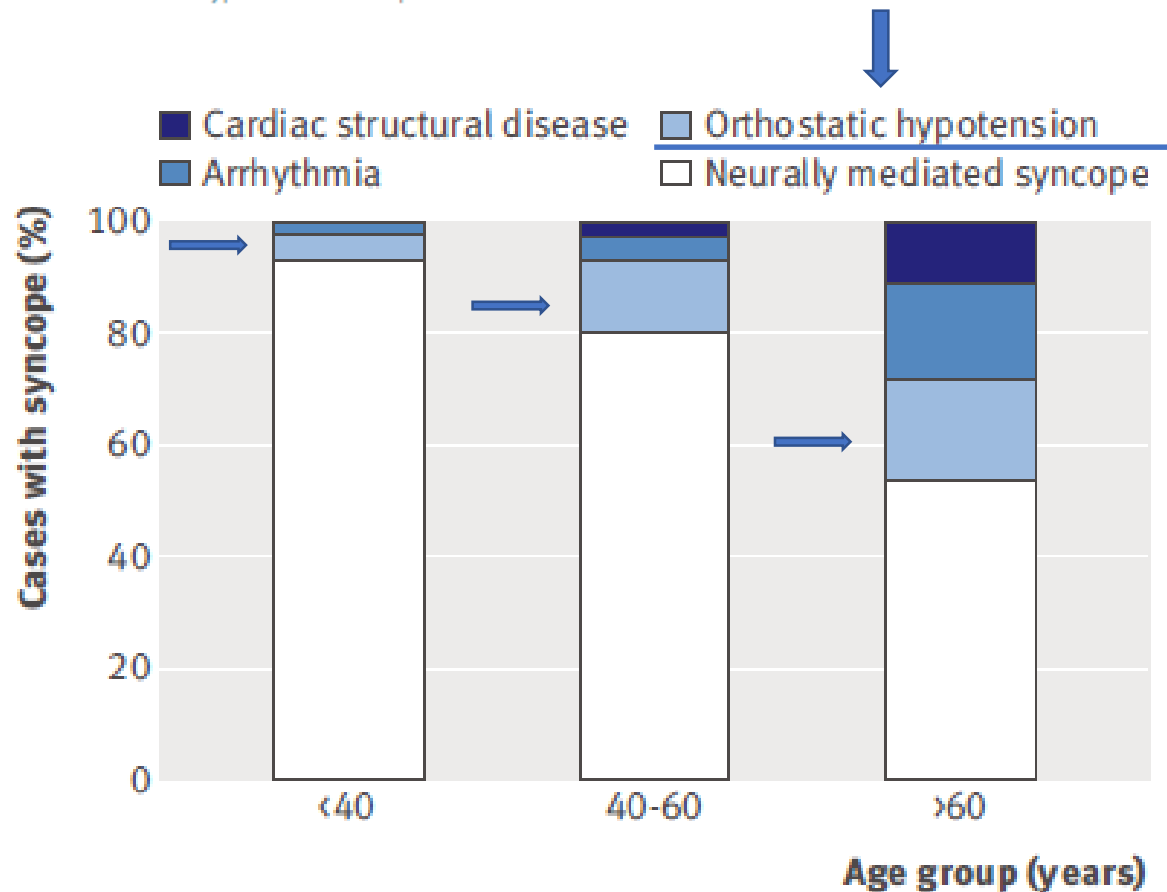


Fig 1 | Causes of syncope by age



# Definition of OH

Consensus definition of Orthostatic Hypotension (OH):

Reduction of systolic blood pressure (SBP) of at least 20 mmHg or diastolic pressure (DBP) of at least 10 mmHg within 3 minutes of active standing or head-up tilt at an angle of at least 60 degrees.

These values are associated with 5% false positive.

A fall of SPB of 30 mmHg or more would reduce the false positive to 1%.

**Update on Management of Neurogenic Orthostatic Hypotension**

**Phillip A. Low and Wolfgang Singer**

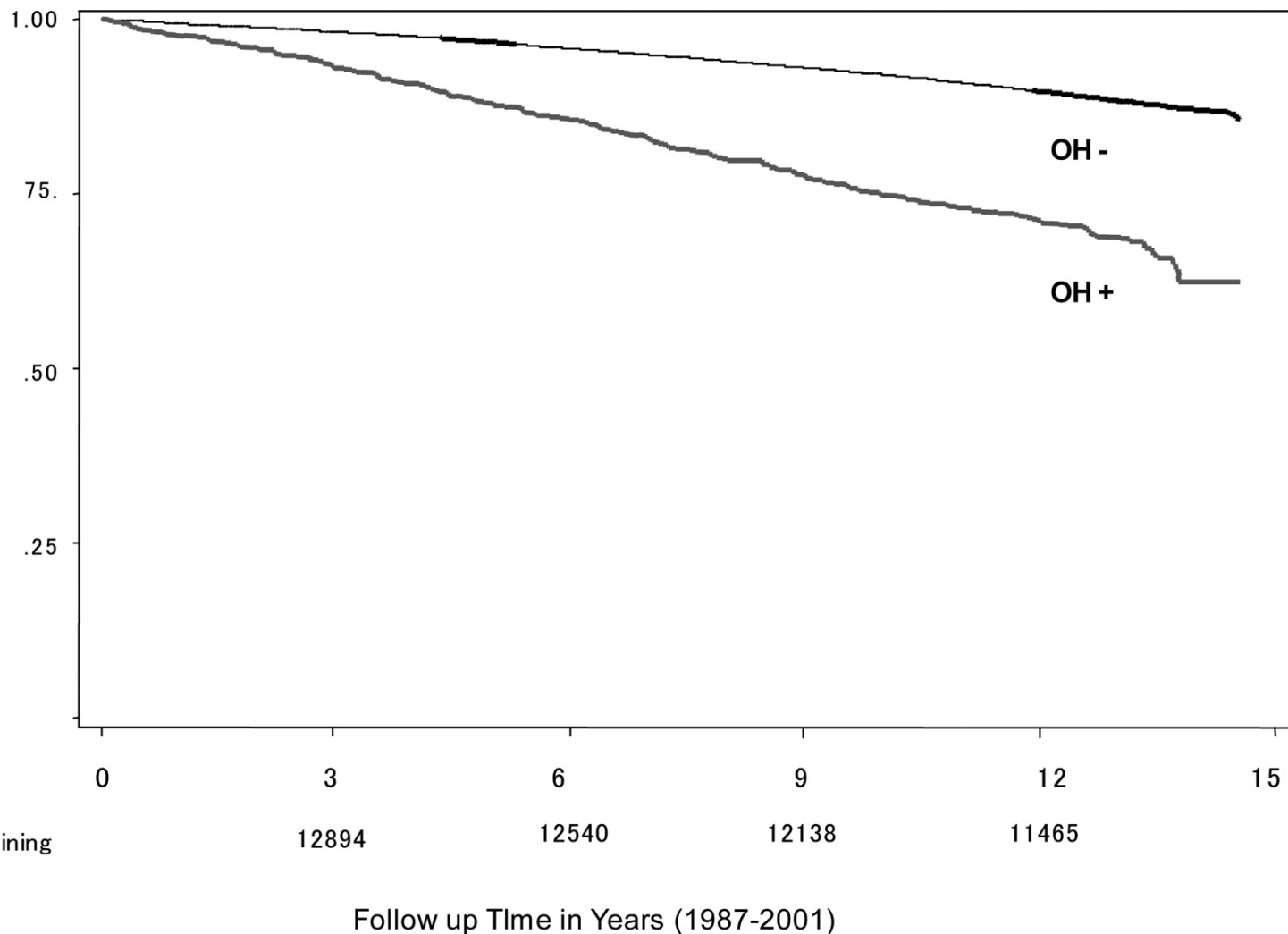
*Lancet Neurol.* 2008 May ; 7(5): 451–458. doi:10.1016/S1474-4422(08)70088-7.

Orthostatic hypotension affects about 6% of subjects in the middle age and it is associated to an increase of mortality and cardiovascular acute events independently of the presence of other traditional risk factors.

*(ARIC Study, Rose KM et al. Circulation 2006;114: 630-636 )*

*(Fedorowski et al. European Heart Journal 2010; 31: 85-9)*

# Kaplan-Meier survival curves by OH status



Participants Remaining

12894

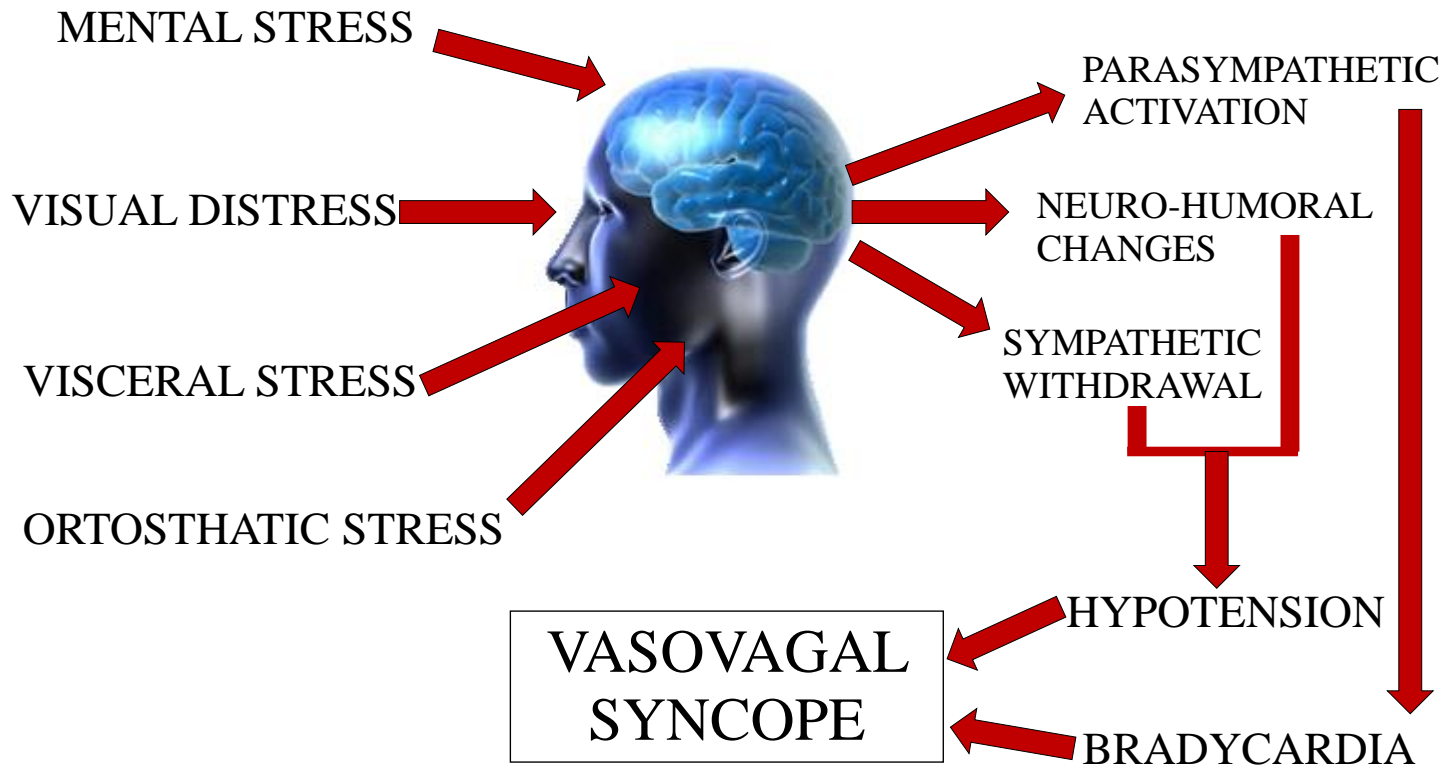
12540

12138

11465

Follow up Time in Years (1987-2001)

# Central and peripheral initiating factors of Vasovagal Syncope



*R. Mosqueda-Garcia in «Vasovagal Syncope»; Ed P. Alboni, R. Furlan, Springer. 2015*

In susceptible individuals different stimuli potentially present in the work environment or during specific job task might promote reflex syncope.

Syncope events/visits per 1000 patient-years

**General population**  
**18.1 – 39.7**

**General practice**  
**9.3**

**Medico del  
Lavoro ?**

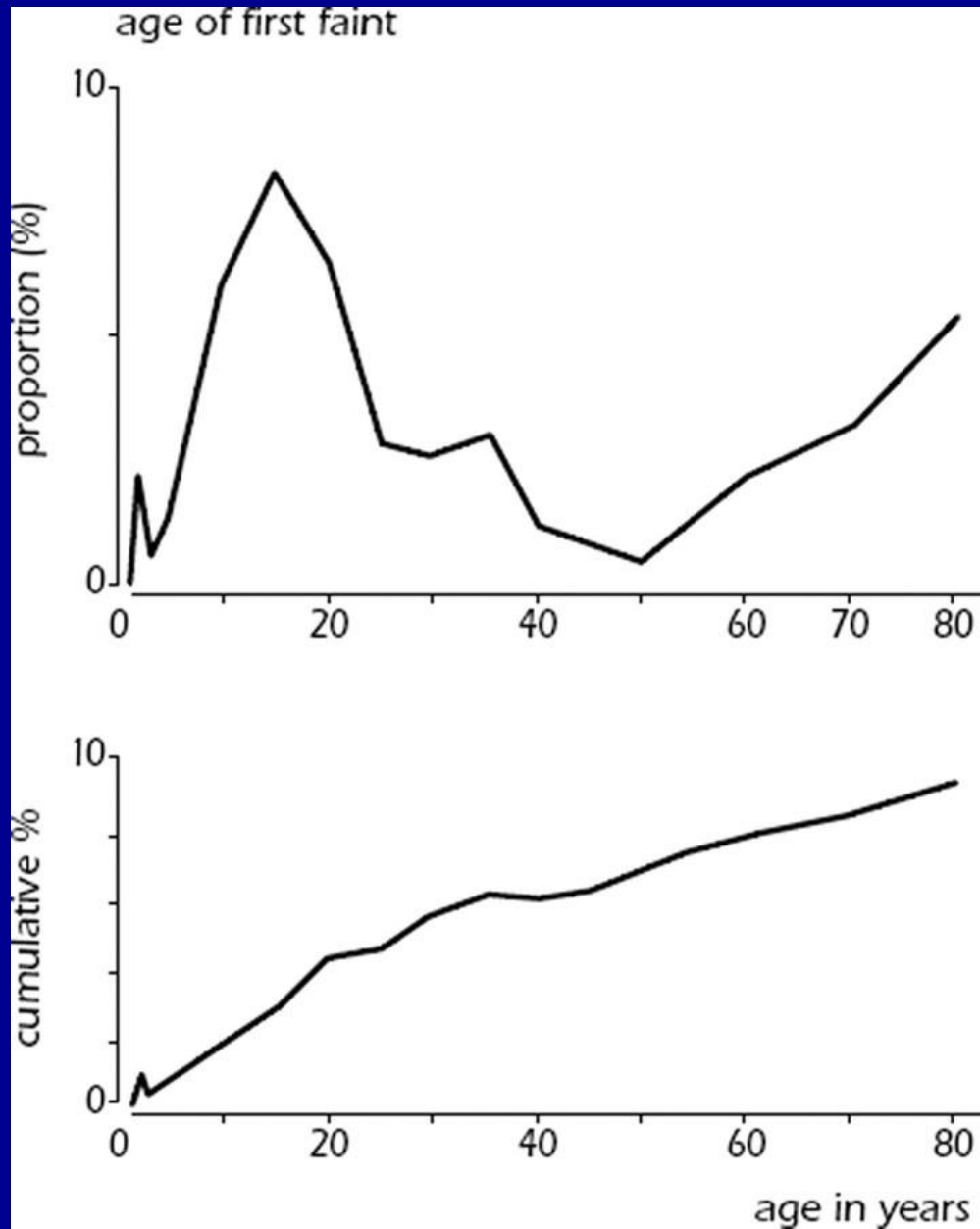
**ED**  
**0.7**

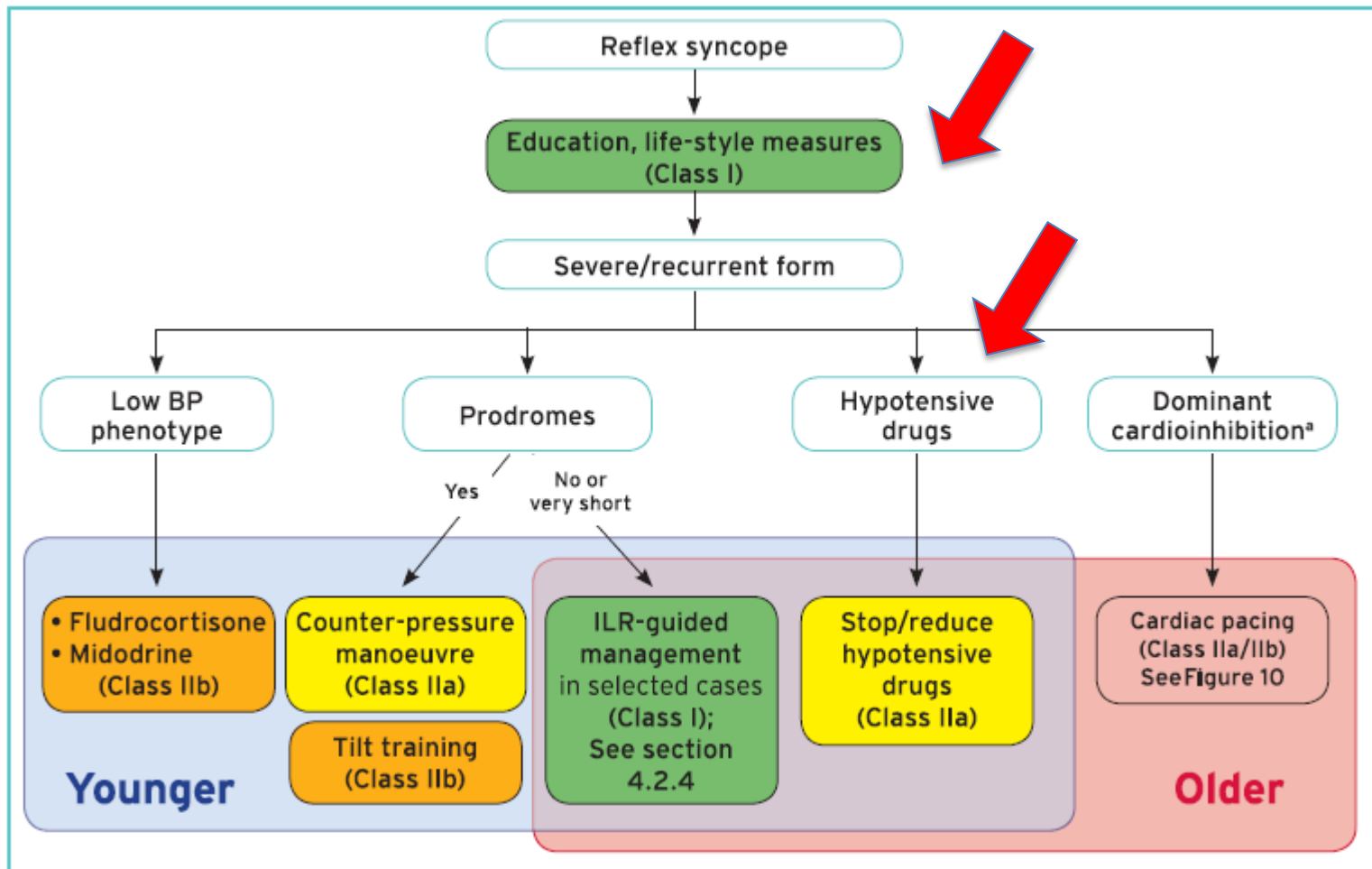
Half of the subjects admitted to ED for syncope are aged 18 to 65 and 84% of them are discharged *(Barbic et al. 2019 from STePS database)*.

Among workers who have lost consciousness 16 to 25% of them had syncope during work activity *(Gaggioli et al 2013; Barbic et al. 2019)*.

The working age is continuously extending, and the syncope incidence increases with age.







**2018 ESC Guidelines for the diagnosis and management of syncope**

*European Heart Journal*, Volume 39, Issue 21, 01 June 2018, Pages 1883–1948

- The problem: how we can manage patient suffering from reflex syncope in working place
- Multidisciplinary approach involving occupational physicians and experts on syncope to make a concrete proposal

**Table 1**

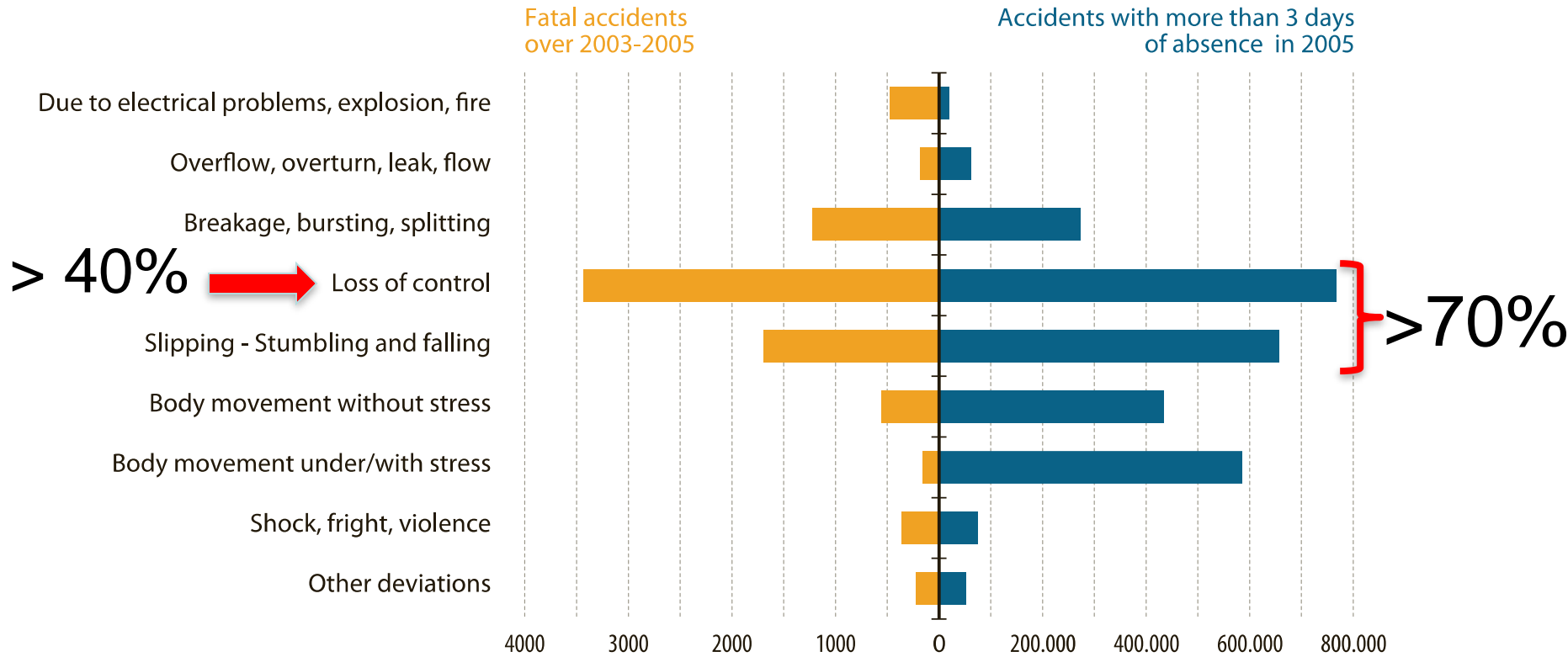
The 10 most dangerous jobs based on number of fatalities and the main cause of deaths by US Bureau of Labor Statistics ([www.bls.gov](http://www.bls.gov)) in 2012.

Job description	Main cause of death
Timber and Logging workers	Contact with objects and equipment
Fishermen and related fish industry workers	<u>Transportation incidents</u>
Aircraft pilot and flight engineers	<u>Transportation incidents</u>
Structural iron and steel workers	Contact with objects and equipment
Farmers and ranchers	Transportation incidents
Roofers and Linemen	Falls
Electrical power-line installers and repairers	Harmful substances exposure / environment
Drivers and truck drivers	<u>Transportation incidents</u>
Refuse and recyclable material collectors	<u>Transportation incidents</u>
Military and Police Personnel	<u>Transportation incidents</u>
Construction laborers	<u>Falls</u>
Firefighters	Fires and explosions
Helpers, construction trades	<u>Falls</u>
Grounds maintenance workers	<u>Falls</u>

*Barbic et al, Autonomic Neuroscience: Basic and Clinical 184 (2014) 46-52*

The main cause of syncope while driving was, unexpectedly, neurally mediated (37,3%) (*Sorajia et al, Circulation 2009*)

**Figure 3.4:** Number of fatal accidents (left part) and accidents at work with more than 3 days of absence (right part) by deviation



Source: ESAW<sup>31</sup>



# Construction work

(scaffolding, ladders, deep excavation)





# Driving heavy vehicles



# Industrial work sites in extremely high temperature, or close to hot surfaces








# Working with suspension gear





*Article*

# Association of Occupational Distress and Low Sleep Quality with Syncope, Presyncope, and Falls in Workers

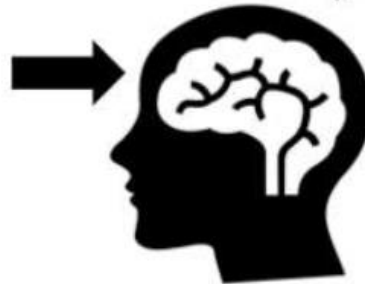
Nicola Magnavita <sup>1,2,3,\*</sup>, Reparata Rosa Di Prinzio <sup>1</sup>, Gabriele Arnesano <sup>1</sup>, Anna Cerrina <sup>3</sup>,  
Maddalena Gabriele <sup>3</sup>, Sergio Garbarino <sup>1,4</sup>, Martina Gasbarri <sup>3</sup>, Angela Iuliano <sup>1</sup>, Marcella Labella <sup>3</sup>,  
Carmela Matera <sup>3</sup>, Igor Mauro <sup>1</sup> and Franca Barbic <sup>1,5,6</sup>

*Int. J. Environ. Res. Public Health* **2021**, *18*, 12283



Occupational Environment

Mental Stress  
(Occupational distress and  
sleep disorders)  
Visual stress (environmental  
stimuli)  
Visceral stress (i.e. total body  
vibration; smells)  
Ortosthatic prolonged stress



Parasympathetic tone ↑

Neuro-humoral  
changes

Sympathetic  
tone ↓

**Vasovagal  
syncope or  
pre-syncope  
(falls)**

HYPOTENSION

BRADYCARDIA

**Table 4.** Association of episodes of syncope, presyncope and falls with occupational distress, poor sleep quality, impaired mental health, and metabolic syndrome (logistic regression models adjusted by age and sex).

Type of Problem	Distress OR (CI95%)	Bad Sleep OR (CI95%)	Low Mental Health OR (CI95%)	MetS OR (CI95%)
Syncope	1.62 (1.05; 2.52) *	1.79 (1.16; 2.77) ***	2.43 (1.52; 3.87) ***	0.61 (0.27; 1.39)
Recurrent syncope	2.11 (1.15; 3.88) *	2.19 (1.18; 4.04) *	3.88 (2.12; 7.08) ***	1.02 (0.40; 2.75)
Recent syncope	1.89 (0.71; 5.04)	1.68 (0.63; 4.45)	2.55 (0.96; 6.78)	1.81 (0.48; 6.78)
Presyncope	1.77 (1.25; 2.49) ***	2.95 (2.08; 4.18) ***	2.61 (1.78; 3.84) ***	1.21 (0.71; 2.04)
Fall unknown cause	1.00 (0.61; 1.66)	1.49 (0.91; 2.42)	1.69 (0.99; 2.87)	1.33 (0.67; 2.65)

**Notes.** OR: odds ratio; CI95%: confidence interval at 95%; distress: ERI > 1; bad sleep: PSQI  $\geq$  5; low mental health: GHQ-12  $\geq$  3; MetS: metabolic syndrome, three or more components (hypertension, hyperglycemia, low HDH cholesterol, hypertriglyceridemia, obesity).  
\*  $p < 0.05$ ; \*\*\*  $p < 0.001$ .

A global risk stratification seems to be appropriate for three major reasons:

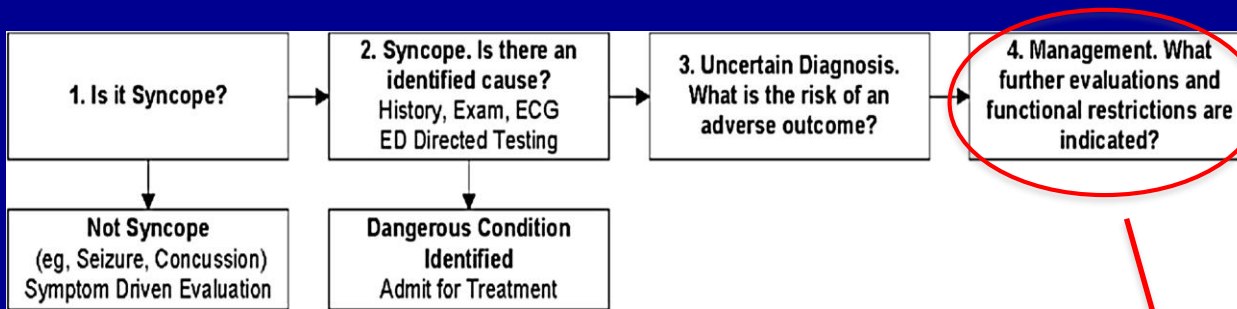
1. Working and driving are often a significant part of the patient's daily activities, are strictly related to their quality of life and may jeopardize safety. A recurrence of syncope could cause injuries for workers, drivers and for innocent bystanders.
2. Common triggers for syncope may be present in some work environments and tasks, and potentially increase the risk of syncope recurrence (*Ganzeboom et al 2006, Lind et al 1968, Burton J 2010, Kenny et al 2013, Keller et al 2009, Mosqueda-Garcia et al 1997*).
3. A lack of proper individualized medical advice regarding work safety might provoke unjustified loss of employment (*Linzer et al 1991, van Dijk et al 2007*). It could create accidents if the subject decides to return to a high risk job without the necessary precautions. Finally, this could increase global costs for the community (*Kenny et al 2013*).

*There are only a few published papers that support these statements, but occupational and ER physicians generally agree with this framework.*



# Priorities for Emergency Department Syncope Research

(First International Workshop on Syncope Risk Stratification in the Emergency Department, 2013)



Is it syncope?

- Use a symptoms-based definition: transient loss of consciousness, associated with inability to maintain postural tone and with immediate, spontaneous, and complete recovery.
- Exclude alcohol, illicit drugs, seizure, stroke/transient ischemic attack, head trauma, or hypoglycemia as presumptive cause.

Is a serious condition identified in the ED?

- Exclude such patients from subsequent risk-stratification research.

What is the risk of a serious outcome?

- Use standardized reporting guidelines for all future risk-stratification studies of syncope.
- Select outcomes that affect mortality and morbidity and that share a common pathophysiologic pathway (for composite outcomes).
- Measure outcomes for at least 30 days after the index syncope event.
- Include novel biomarkers and bedside diagnostics as candidate predictors.
- Generate continuous rather than binary risk estimates.
- Compare the risk-prediction tools with existing practice.
- Enroll large patient cohorts to generate stable risk-prediction tools.

What further evaluations and functional restrictions are required?

- Assess the safety of rapid observation protocols.
- Assess the role of specialty syncope units.
- Evaluate the effectiveness and cost-effectiveness of ambulatory cardiac monitoring.
- Develop risk-tailored driving recommendations.
- Develop risk-tailored work recommendations.

Sun BC et al *Annals of Emergency Medicine* DOI: (10.1016/j.annemergmed.2014.04.01)



European Heart Journal (2016) 37, 1493–1498  
doi:10.1093/eurheartj/ehv378



# Practical Instructions for the 2018 ESC Guidelines for the diagnosis and management of syncope

## 2.3.5 Risk of syncope during work

Syncope at work is a rare event and its impact in terms of injury is usually benign.<sup>71</sup> However, as syncope is associated with a loss of postural tone, even a benign vasovagal episode can be hazardous in high-risk working environments. Thus, in people with syncope, it is necessary to stratify the occupational risks of syncope recurrence, particularly if the time of exposure to hazardous conditions is significant.<sup>65,72</sup> Referral to occupational physicians may be recommended in these circumstances.



ESC

European Society  
of Cardiology

European Heart Journal (2018) 39, e43–e80

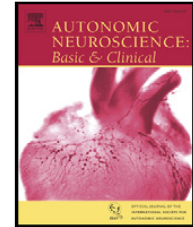
doi:10.1093/eurheartj/ehy071



Contents lists available at ScienceDirect

## Autonomic Neuroscience: Basic and Clinical

journal homepage: [www.elsevier.com/locate/autneu](http://www.elsevier.com/locate/autneu)



### Driving and Working with Syncope



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Vasovagal Syncope During Driving, Working and Exercise  
How to Manage Patients Who Are About to Resume Work  
*F. Barbic, R. Sheldon, R. Furlan*

*in “Vasovagal Syncope” P. Alboni, R. Furlan Editors; Springer 2015, Chapt 25, pag. 297-307*

## Risk Index for job task $(RI)_j$

$$\text{Time}(T) \times \text{Facilitating Features (FF)} \times \text{Expected Harm (EH)}$$

$$RI_{\text{worker}} = \textit{Recurrence Risk} \times \sum RI_j$$

More than one job task might be present in a normal working day

$$RI_N = RI_{\text{worker}} / RI_{\text{ref}} \text{ (white collar)}$$

# Facilitating Features

**Table 2**

Working features potentially promoting neurally mediated syncope recurrence.

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## Work features

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- Standing for long periods
  - Warm environment
  - Frequent temperatures changes
  - Frequent change of posture
  - Emotion/stress/high level job demand
  - Heavy protective clothing and equipment
  - Fatigue
-

# Expected Harm

**Table 4**

Estimated Expected Harm (EH) values for the worker and the third-party for 10 job tasks. Values are expressed as a median (1st-3rd quartile).







Job Task	EH worker	EH third-party
1. <u>Driving ambulance and emergency vehicles</u>	52.7 (20.0-77.4)	54.1 (22.6-78.1)
2. Driving trucks of merchandise and material on the highway and streets	48.8 (25.6-74.9)	50.0 (25.0-72.3)
3. Handling very high temperature materials with a risk of spreading and burns	45.9 (22.3-75.2)	17.3 (5.4-48.3)
4. Working in <u>high places with risk of fall</u>	60.5 (37.7-88.3)	2.5 (0.8-10.6)
5. Driving truck in construction area	36.0 (20.8-55.8)	26.5 (11.2-50.2)
6. Surgical or other medical invasive procedure with risk for operator and patient	17.2 (4-42.3)	30.2 (10-67.1)
7. Activity closed to <u>switch board at risk to electric shock</u>	40.1 (18.7-70.2)	5.0 (1.0-20.0)
8. Working <u>closed to machine risky for dragging</u>	39.2 (19.7-66.6)	3.8 (0.9-23.2)
9. Controller of machinery to move heavy materials	9.0 (2.2-21.9)	18.4 (7.8-44.7)
10. Activity in the office with no risk for safety	0.9 (0.25-3.8)	0.2 (0.1-0.6)



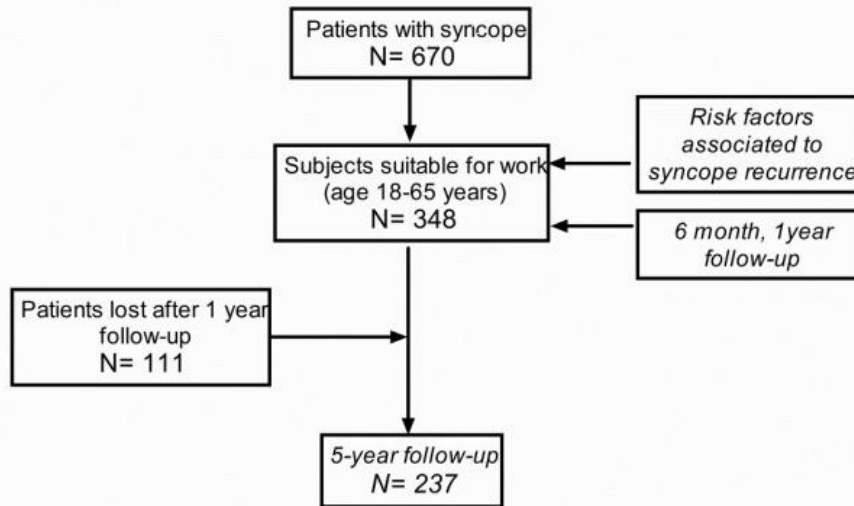
White collar (reference)



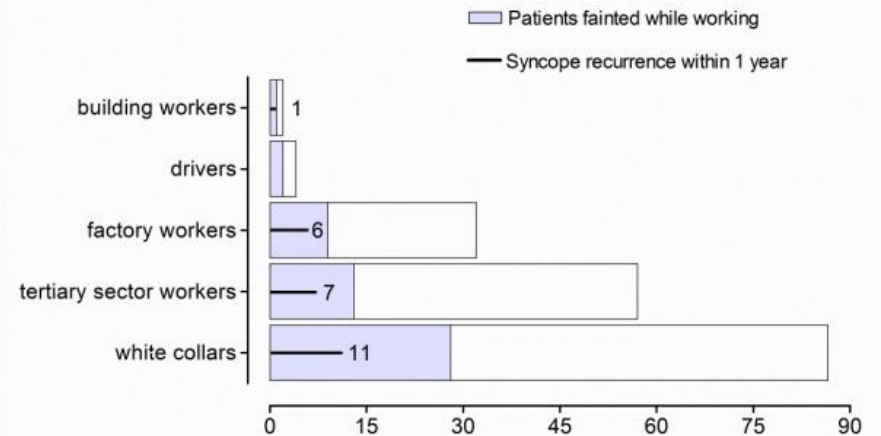
# Syncope in a Working-Age Population: Recurrence Risk and Related Risk Factors

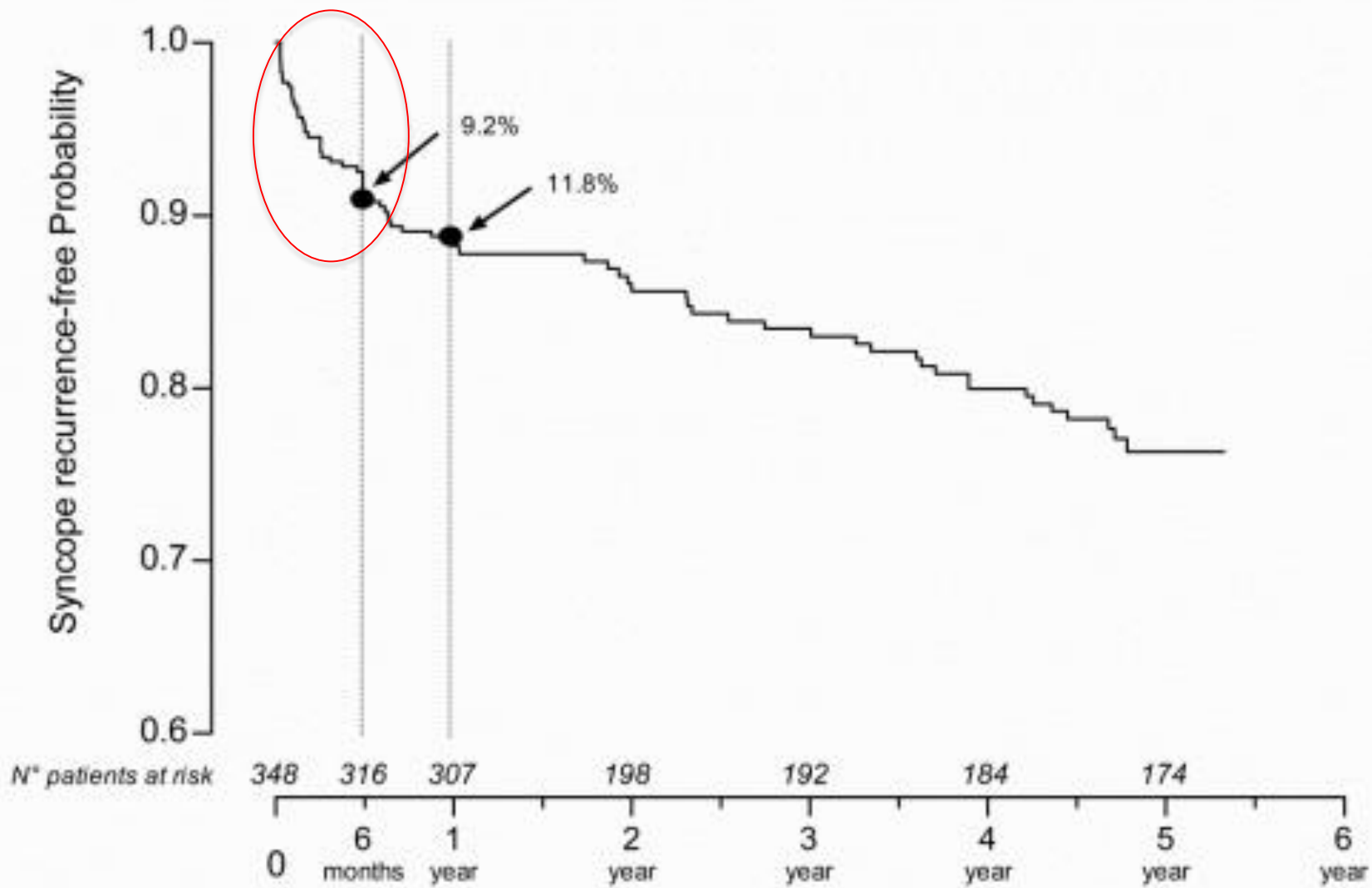
Franca Barbic <sup>1,\*</sup> , Franca Dipaola <sup>1</sup>, Giovanni Casazza <sup>2</sup> , Marta Borella <sup>3</sup>, Maura Minonzio <sup>1</sup> ,  
Monica Solbiati <sup>4</sup> , Satish R. Raj <sup>5</sup> , Robert Sheldon <sup>5</sup>, James Quinn <sup>6</sup>, Giorgio Costantino <sup>4</sup>   
and Raffaello Furlan <sup>1</sup>

A. Flow diagram of Studied Population



B. Occupational sector of active workers at the time of syncope





**Table 2.** Predictors of syncope recurrence within 6 months and 1 year from syncope index event.

	6-Months		1-Year			
	Univariable Analysis		Univariable Analysis		Multivariable Analysis	
	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>
Age > 40 “years”	1.84 (0.86–3.94)	0.12	1.49 (0.77–2.91)	0.24	-	
Gender	1.10 (0.53–2.31)	0.79	1.19 (0.61–2.33)	0.60	-	
No Hospital admission	2.82 (0.65–12.17)	0.17	1.71 (0.58–5.03)	0.33	-	
Abnormal ECG	1.53 (0.63–3.72)	0.35	2.14 (1.00–4.56)	0.05	-	
First syncopal episode	1.33 (0.62–2.86)	0.46	1.36 (0.69–2.7)	0.38	-	
→ Syncopal episodes ≥ 3	2.10 (0.99–4.42)	0.05	2.23 (1.14–4.38)	0.02	2.06 (1.03–4.10)	0.04
Trauma	1.85 (0.63–5.45)	0.27	1.54 (0.62–3.81)	0.35	-	
Absence of prodromal symptoms	1.43 (0.53–3.84)	0.48	1.28 (0.54–3.02)	0.57	-	
Cardiovascular Disease	1.74 (0.67–4.51)	0.25	1.25 (0.49–3.18)	0.64	-	
Neoplasm	1.67 (0.19–14.29)	0.64	1.25 (0.15–10.69)	0.84	-	
Neurological Disease	2.68 (0.84–8.57)	0.10	1.97 (0.62–6.20)	0.25	-	
COPD	2.95 (0.59–14.81)	0.19	2.2 (0.44–10.96)	0.34	-	
→ Diabetes	1.53 (0.43–5.46)	0.51	2.93 (1.08–7.91)	0.03	2.85 (1.04–7.83)	0.04
Hypertension	1.22 (0.50–2.95)	0.66	1.23 (0.56–2.73)	0.60	-	
→ Anemia	2.68 (0.84–8.57)	0.10	3.59 (1.30–9.94)	0.01	3.51 (1.25–9.83)	0.02

OR, Odds Ratio; CI, Confidence Interval; other abbreviations as in Table 1.

#### 4. Discussion

The main results of the current investigation are as follows:

1. In total, 51.9% of patients presenting to the ED because of syncope were of working-age (18–65 years) and proved to be healthier compared to unselected syncope patients of previous studies (19–22).
2. In total, 60.6% of the working age patients were active workers at that time and 25% of them fainted while working.
3. The risk of syncope relapse was higher within the first 6 months, i.e., 9.2%, after the index event compared to the remaining follow-up periods (3.5% per year).
4. Diabetes, anaemia, and  $\geq 3$  lifetime syncope episodes were risk factors independently associated with syncope recurrence at 1-year.

# The role of pre-syncope symptoms

If present (about 80% of patients in working age of STePS data base), prodromes may be crucial to reduce the risk of accidents because syncope.

To be helpful some features are mandatory:

- Consistent and repeatable
- Promptly recognized by the patient
- Last for an adequate amount of time to allow the worker to reach a safe position

# Summary

To promote a safe return to a risky job, the aspects to be considered are:

- The number of spells in the year preceding the syncope reference event, anemia and diabetes are independent risk factors for reflex syncope recurrence (*Sumner et al 2010, Sheldon et al 1996, Barbic et al 2019*).
- *The maximum risk of recurrence occurs in the first 6 months after the syncope reference event (Barbic et al , 2019)*
- The characteristics of the job task and the environmental working conditions potentially promoting syncope (*Barbic et al 2014; Magnavita et al 2020*)
- The capability to recognize symptoms preceding syncope, when present, and a specific training including physical countermeasures (*Wieling et al 2004*)
- The work environment interventions and additional safety devices (*J Burton, 2010, Canada, WHO Healthy Workplace Framework and Model*)



Emergency  
physicians

Other hospital  
ward physicians

General practitioners  
Occupational physicians



Is there a potential risk with a return to work?



Multidisciplinary Syncope Unit



Syncope recurrence risk and job tasks and environmental conditions evaluation.  
Individualized training on prodroms recognition and physical counter-manoevres.  
Additional safety device and environmental intervention.  
Temporary exclusion from high risky jobs  
Safe return to work avoiding unjustified loss of employment

Work accident prevention, community cost reduction, quality of  
life improvement

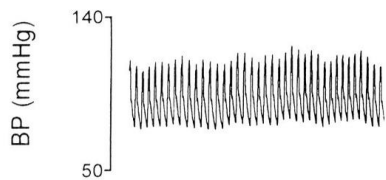
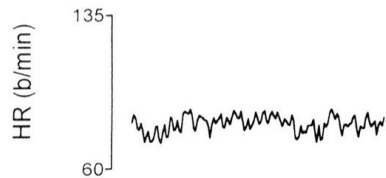
# Outline

1. Sincope neuromediata e stratificazione del rischio in ambito lavorativo
- 2. Disautonomia cardiovascolare e work ability: Postural Orthostatic Tachycardia Syndrome**
3. Sindrome disautonomica post-Covid19: incidenza e impatto sulla capacità lavorativa

# Autonomic disorders and work ability: POTS

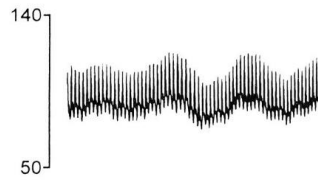
- Postural Orthostatic Tachycardia Syndrome (POTS) is a chronic condition characterized by dysfunction of autonomic control of the cardiovascular system (*Furlan R et al, 1998; Okamoto LE et al, 2012; Jacob G et al 2019 Sheldon RS et al, 2015; Schondorf L et al, 1993*)
- POTS is characterized by symptoms mirroring what was observed in some patients after COVID19.
- The onset of POTS often follows an acute viral infection.
- Recently it has been hypothesized that post-COVID19 syndrome might also involve the autonomic nervous system (*Goldstein, 2020; Dani M et al, 2021*).

## REST



Anxiety

## STAND



Palpitations  
Shortness of breath  
Lightheadness  
Dizziness  
Fatigue  
↓ Exercise tolerance  
Pre-syncope  
Syncope

## Definition

- Chronic symptoms of *orthostatic intolerance* (at least 6 months)
- Increased **HR  $\geq 30$  bpm ( $>40$  bpm 12-19 yrs)** in upright posture or **HR  $> 120$  bpm** during standing
- *Absence of orthostatic hypotension* (a decrease in BP  $<20/10$  mmHg).
- Absence of other overt causes of orthostatic tachycardia (drugs, bed rest, chronic debilitating disorders).

# Epidemiology

- Affects **women** >> men, **4-5:1**; age 15-50 years.
- About 0.2- 0.5% of the population are affected, under-diagnosed, often symptoms are cyclic.
- Appears after **viral infection** (EBV, CMV, Borrelia, others), trauma, **delivery**, prolonged surgery, anecdotal causes; mostly unknown cause.
- Usually is not a progressive illness and relief with aging.
- A frequent cause of **disability, loss of work**, no **school**.
- About 80% of female patients report an **exacerbation of symptoms around menstruation**.

# Clinical features

- Presyncope and lightheadedness are common in these patients, only a minority ( $\approx 30\%$ ) actually faint.
- Many patients have been co-diagnosed with irritable bowel syndrome
- Joint hypermobility (Ehlers-Danlos Syndrome type III) has been frequently associated with POTS
- A striking physical feature in  $\approx 50\%$  of patients with POTS is a dependent acrocyanosis.



# Autonomic disorders and work ability: POTS

We recently addressed the **impact of POTS on Work Ability.**

**Table 1.** Demographics and Clinical Characteristics of Postural Orthostatic Tachycardia Syndrome (POTS) patients and Controls.

Demographics and Clinical Characteristics	POTS Patients (n = 22)	Controls (n = 18)
Age (years)	36 ± 2	39 ± 3
Sex (Male/Female)	2/20	4/14
Body Mass Index (kg/m <sup>2</sup> )	21.2 ± 0.7	21.9 ± 1.0
Total WAI score	29.8 ± 1.4	45.6 ± 0.5 *
Coexisting diseases, n (%)	22 (100)	7 (39) *
Cardiovascular	7 (32)	-
Musculoskeletal	17 (77)	2 (11)
Gastrointestinal	13 (59)	-
Nervous System	11 (50)	-
Ehlers-Danlos syndrome	5 (23)	-
Fibromyalgia	3 (14)	-
Other	19 (86)	6 (27)
Drug assumption, n (%)	20 (91)	2 (11) *

WAI indicates the Work Ability Index. Results are expressed as mean ± standard error. \*  $p < 0.01$  POTS vs. controls. Note that the subset of participants had several diseases, and total numbers of participants when adding for each disease does not match with the total numbers of coexisting diseases.

**Work Ability Index** questionnaire provided the Total WAI score (7-49) by including the 7 domains (Tuomi et al. 1991; Ilmarinen , 2019)

**Table 2.** The seven items explored by the Work Ability Index (WAI) and the total WAI score in POTS patients and controls.

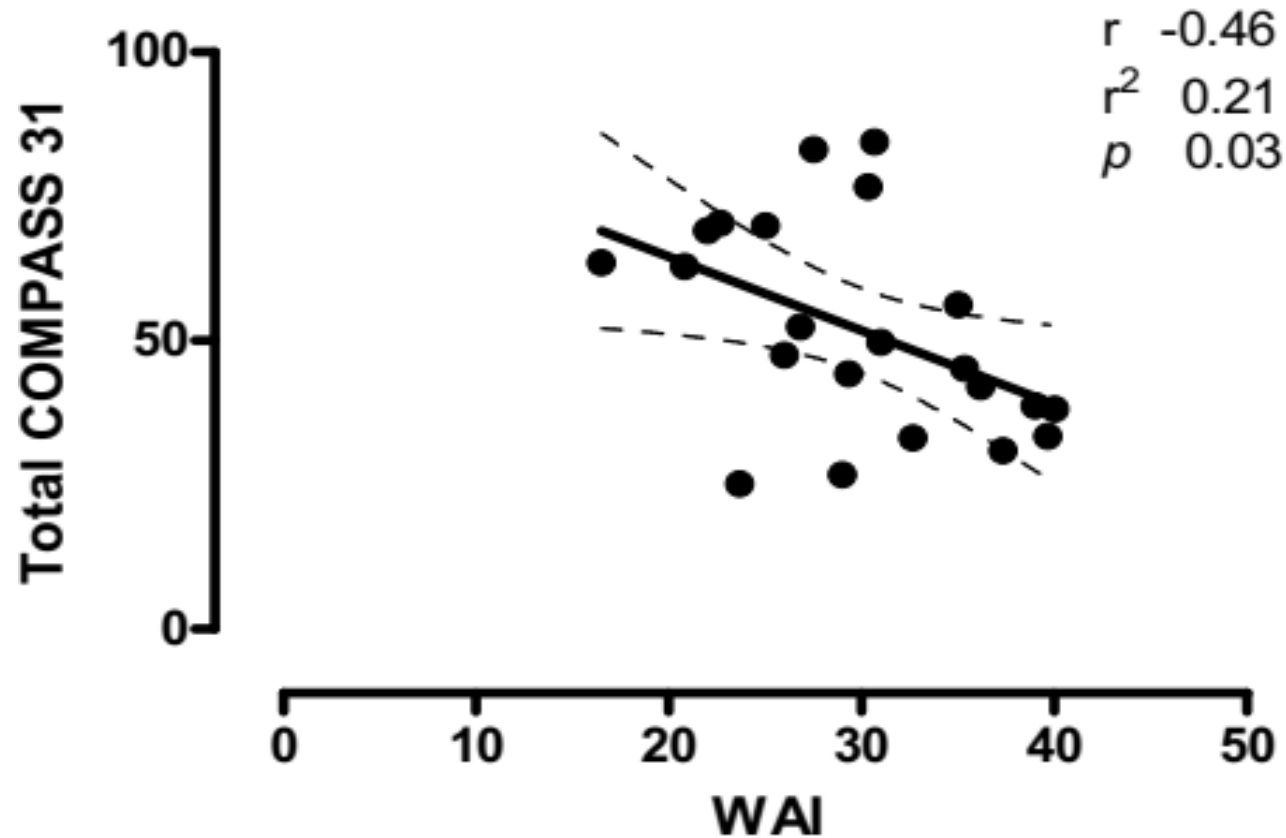
Work Ability Domains	POTS Patients (n = 22)	Controls (n = 18)	p Value
Current work ability compared to the lifetime best (0–10)	5.68 ± 0.39	9.06 ± 0.22	<i>p</i> < 0.01
Work ability in relation to the job demands (2–10)	6.73 ± 0.32	9.44 ± 0.22	<i>p</i> < 0.01
Current diseases diagnosed (1–7)	2.68 ± 0.31	6.50 ± 0.17	<i>p</i> < 0.01
Estimated work impairment (1–6)	3.50 ± 0.22	5.89 ± 0.08	<i>p</i> < 0.01
Sick leave in the last year due to the diseases (1–5)	2.98 ± 0.24	4.28 ± 0.11	<i>p</i> < 0.01
Own prognosis of work ability two years from now (1,4,7)	5.91 ± 0.37	7.00 ± 0.00	<i>p</i> = 0.01
Mental resources (1–4)	2.36 ± 0.18	3.46 ± 0.10	<i>p</i> < 0.01
Total WAI score	29.84 ± 1.40	45.63 ± 0.53	<i>p</i> < 0.01

Results are expressed as mean ± standard error.

<https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/33114659/>

## Autonomic disorders and work ability: POTS

Dysautonomia symptoms were evaluated using **COMPASS31** questionnaire:  
*6 autonomic domains, 0-100 (Sletten et al., 2012).*



# CONCLUSIONS

The WAI showed a reduced work ability in POTS compared to controls and identified several comorbidities that may promote frailty at work.

The higher the burden of autonomic symptom (COMPASS31), the lower the WAI.

A holistic approach of the patients, that should include an adequate treatment with physical exercise and the assessment of work impairment, may promote ergonomic and organizational intervention in work place aimed at keeping these patients active.

# Outline

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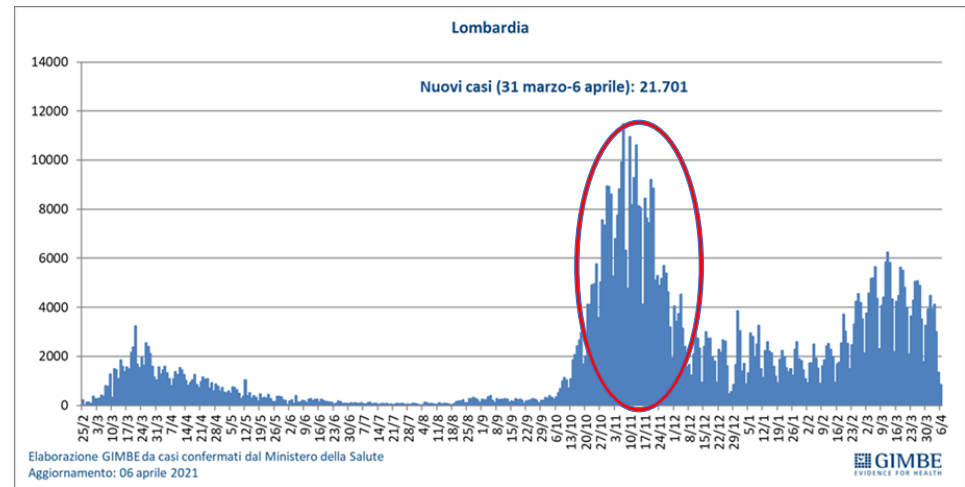
# AIMS

- To evaluate the time course of ANS dysfunction symptoms and work ability in patients admitted to the hospital for COVID19 in a 6 month follow-up.
- To assess the incidence of post-COVID19 autonomic syndrome in working age patients and their work ability.
- To evaluate the relationship between autonomic symptoms intensity and work ability at 6 months from hospital discharge.



## METHODS: Study population

We conducted a prospective study by consecutively enrolling **working age** (mean age  $53.6 \pm 8.4$ ) patients (**N=45**) that were hospitalized for COVID19 at Humanitas Research Hospital from December 2020 to March 2021.



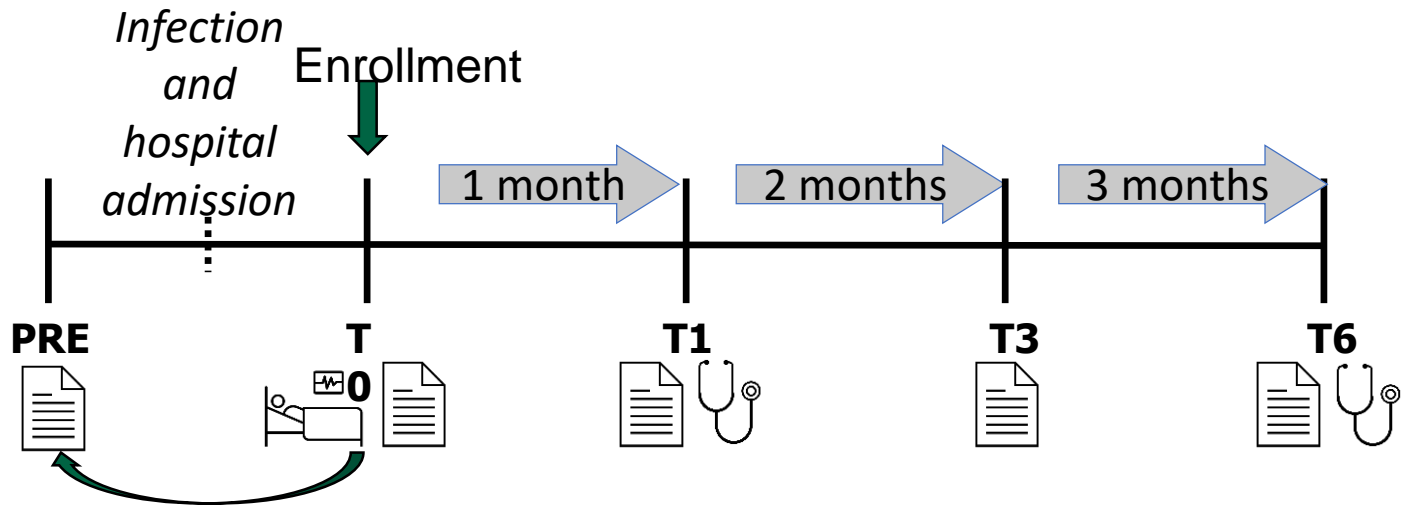
### Inclusion criteria

- Age between 18 and 67 years
- Both genders
- Active working status
- Possibility to complete the scheduled follow ups
- Possibility to maintain the standing position

### Exclusion criteria

- Patients diagnosed with: established autonomic syndromes, dementia, severe cognitive disturbances, chronic atrial fibrillation and epilepsy.

## METHODS: Protocol



Hospitalization.



Questionnaires: COMPASS-31, WAI, SF-36, modified VAS.

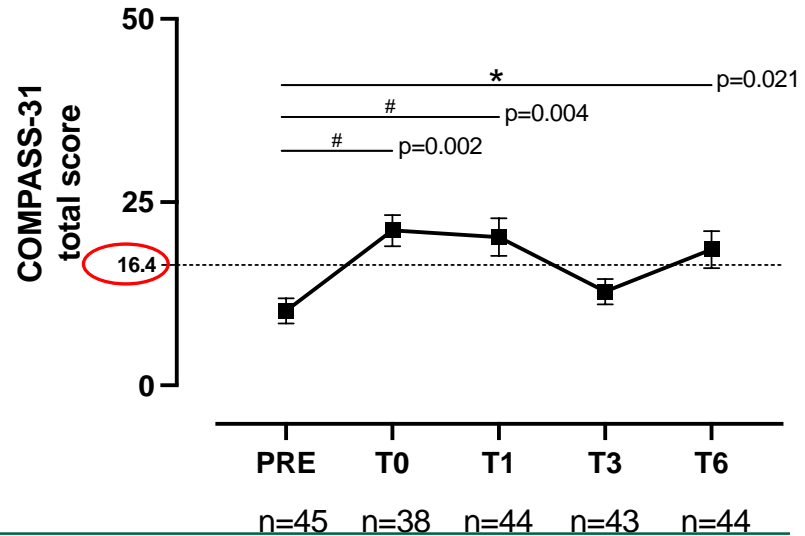


Ambulatory visit:

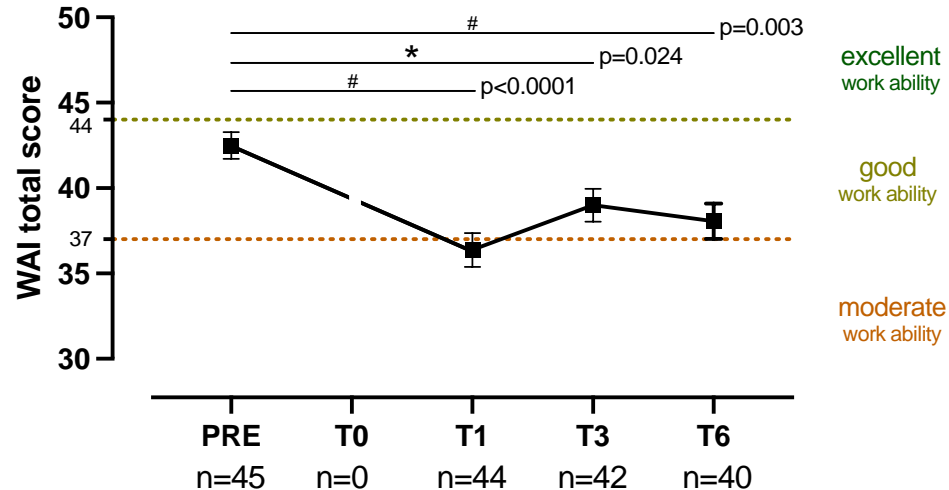
- History taking and physical examination.
- Active standing test, vitals measurements (HR, RR, BP, SpO<sub>2</sub>), 2-lead ECG and the VOSS.
- Blood sampling for inflammatory profiling (PTX3, IL-6, TNF).

# RESULTS: Autonomic symptoms and work ability in the entire cohort

- We can appreciate that at T0 and T1 autonomic symptoms were worse compared to PRE.
- At T6 the autonomic dysfunction symptoms still did not return to how they were before COVID19.

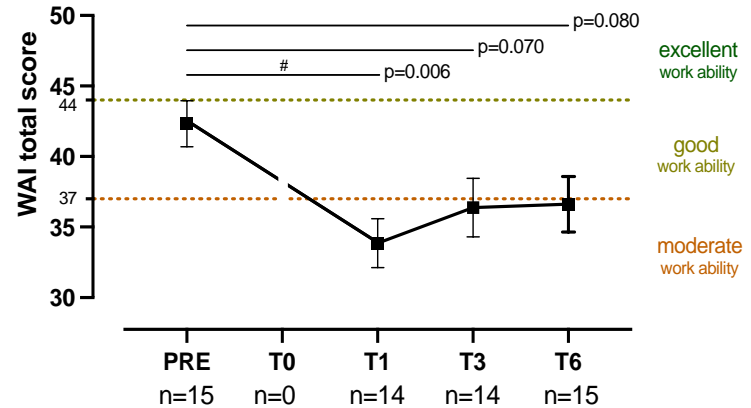
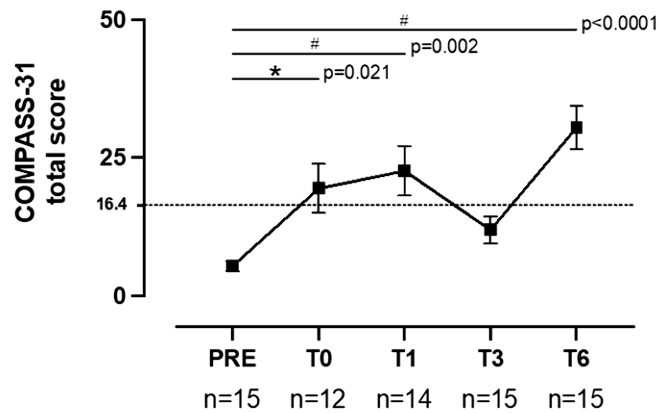


- The work ability of our cohort diminished after COVID19 resolution, and at T6 it still remains reduced.

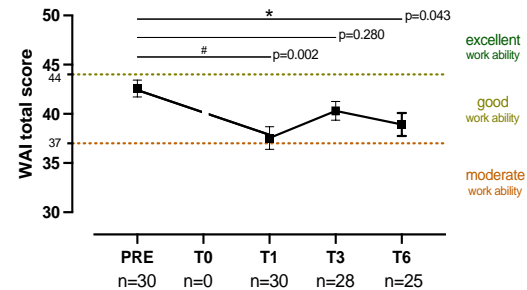
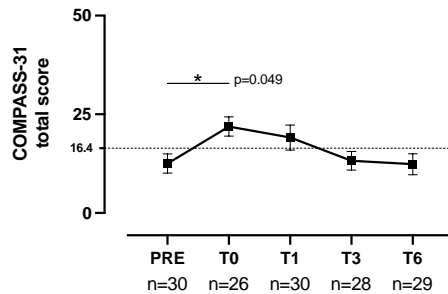


# Compass-31 and work ability index in sub-group A and B

- Sub-group **A** (N=15) accounted for **30%** of the study population.

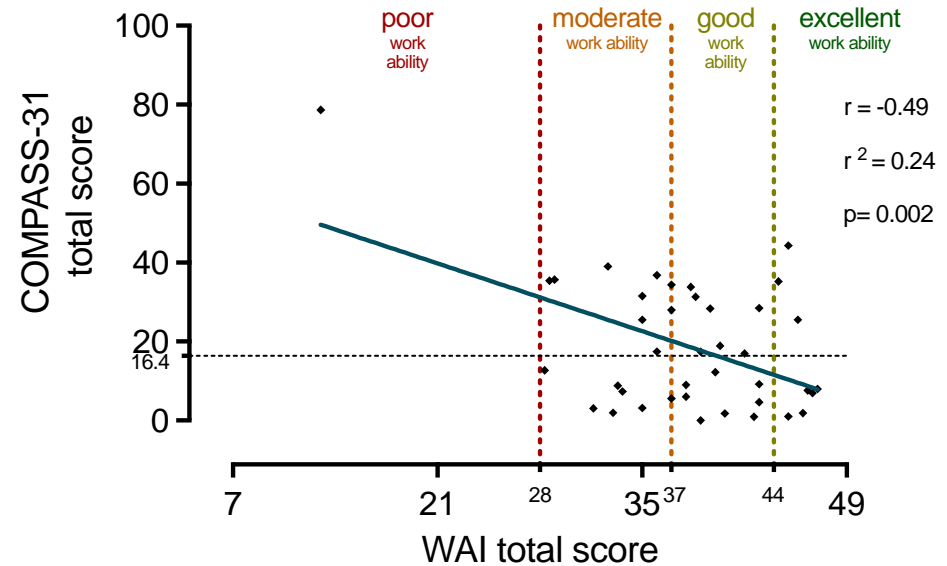


- Sub-group **B** (N=30).

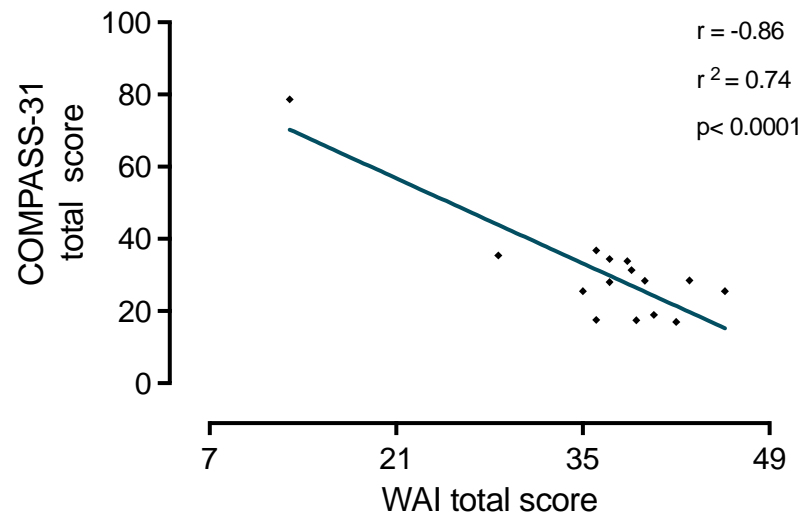


# Relationship between autonomic symptoms and work ability at 6 months

- An inverse relationship between COMPASS-31 score and WAI was seen in the entire cohort.



- In sub-group **A**, the inverse relationship was even more marked.



# CONCLUSIONS

- The presence of autonomic manifestations at 6-month after acute COVID19 and a reduced work ability (in the entire cohort) compared to the period before the disease occurrence (PRE).
- The incidence of post-COVID19 autonomic syndrome in our population, represented by the sub-group A, is 30%. These patients were also characterized by a significantly compromised work ability.
- At 6-months from acute COVID19 we found an inverse relationship between the intensity of the autonomic symptoms and work ability.

# TAKE HOME MESSAGES

- Il paziente con sincope/presincope necessita di una valutazione anche da parte del Medico del Lavoro che deve essere in grado di integrare la stratificazione del rischio clinico con quello occupazionale.
- Identificare l'ipotensione ortostatica, anche iatrogena, in età lavorativa può ridurre il rischio di incidenti dovuti a sincopi e presincopi.
- L'identificazione di sintomi e segni a carico del Sistema Nervoso Autonomo può consentire l'individuazione di ipersuscettibilità individuale a sincopi, presincopi e giustificare alcune condizioni di ridotta capacità lavorativa.
- Il corretto inquadramento clinico del paziente e gli interventi nel luogo di lavoro aiutano a gestire la ripresa del lavoro del paziente con sincope e/o disautonomia cardiovascolare.
- Le Syncope Units e i centri per l'inquadramento delle disautonomie possono supportare il Medico del Lavoro nella gestione di questi pazienti



**Syncope Unit**

**Internal Medicine**  
Tilt Test + autonomic nervous system evaluation  
24 hour long lasting BP monitoring  
External Cardio Event Recorder

**Cardiology**  
**Electrophysiology**  
PM, ICD, LRI, EP Lab

**Interventional Cardiology**

**Cardiology**  
24 hour ECG monitoring  
Cardiac stress test  
Echocardiography  
**Coronary Intensive Care Unit**

**Stroke Unit**  
EEG

**Neurology**  
EMG

- Internal Medicine
- Cardiology
- Neurology
- Stroke Unit

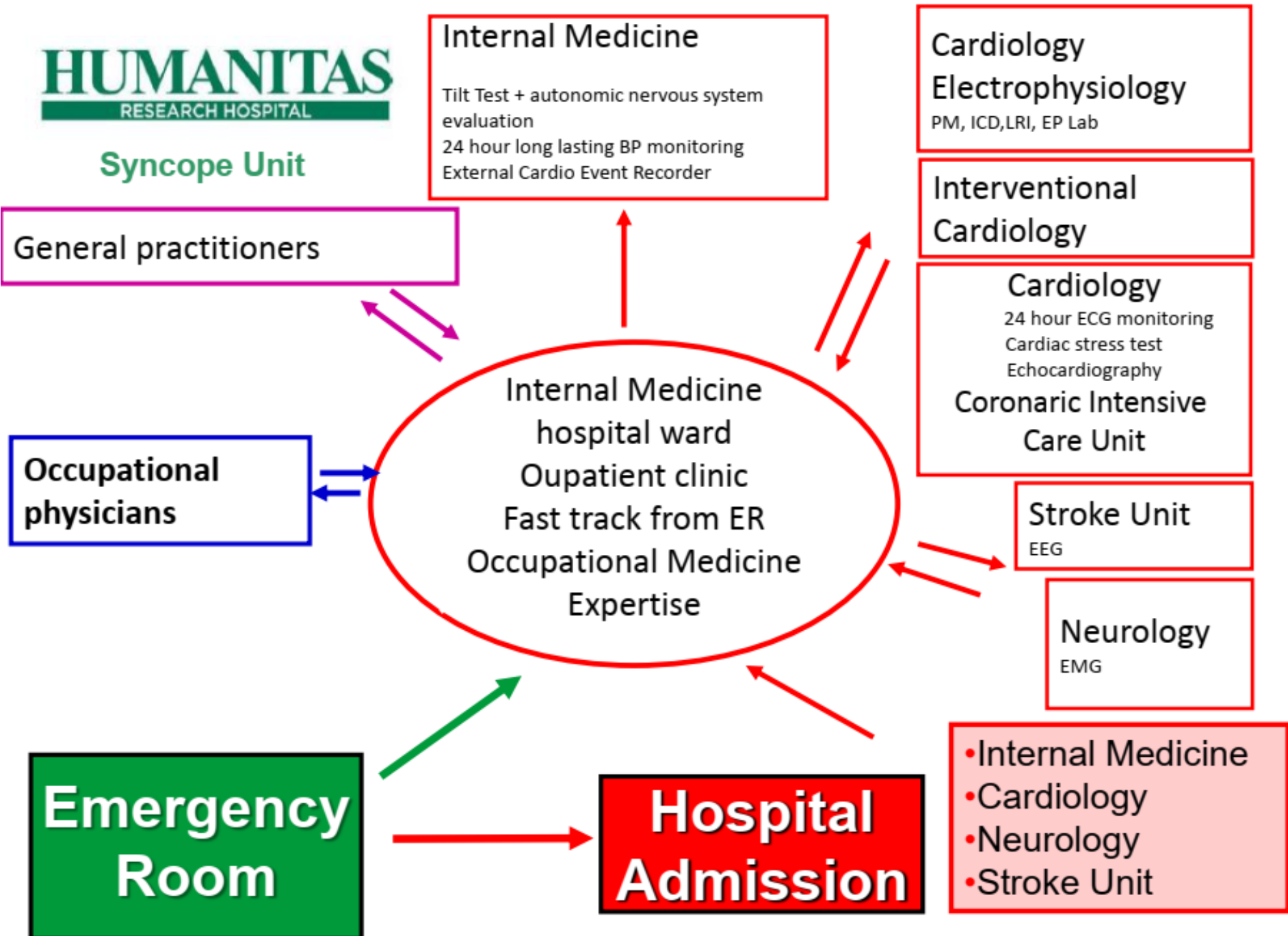
**General practitioners**

**Occupational physicians**

**Internal Medicine**  
hospital ward  
Outpatient clinic  
Fast track from ER  
Occupational Medicine  
Expertise

**Emergency Room**

**Hospital Admission**





## *2.1. Study Population*

All 754 workers consecutively enrolled for their periodic medical examination from July to December 2020 were asked to fill in an anamnestic questionnaire regarding the occurrence of syncope, presyncope, and falls (including those without any apparent cause) during their working life. The workers came from 10 companies and belonged to the health sector (57%), social and educational services (18%), industry (2%), and commerce (23%).

**Table 2.** Comparison of mean values of stress, sleep quality, and mental health in workers with or without syncope, presyncope and falls of unknown origin. (Mann–Whitney U test).

Type of Problem	Stress (ERI)	Sleep Quality (PSQI)	Mental Health (GHQ-12)
Syncope	1.05 ± 0.46 vs. 0.90 ± 0.43 ***	6.62 ± 4.32 vs. 4.81 ± 3.23 ***	2.48 ± 3.32 vs. 1.33 ± 2.32 ***
Recurrent syncope	1.15 ± 0.51 vs. 0.91 ± 0.42 ***	7.72 ± 4.54 vs. 4.87 ± 3.28 ***	3.34 ± 3.89 vs. 1.36 ± 2.33 ***
Recent syncope	1.17 ± 0.47 vs. 0.92 ± 0.43 *	7.56 ± 5.01 vs. 5.00 ± 3.39 *	2.67 ± 2.97 vs. 1.46 ± 2.49 ***
Presyncope	1.06 ± 0.46 vs. 0.88 ± 0.41 ***	6.88 ± 3.97 vs. 4.39 ± 2.98 ***	2.40 ± 3.21 vs. 1.16 ± 2.10 ***
Fall of unknown cause	0.97 ± 0.46 vs. 0.92 ± 0.43	6.22 ± 4.28 vs. 4.93 ± 3.33 **	2.33 ± 3.57 vs. 1.40 ± 2.34

**Notes.** \*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$ .

**Web Table 3 Advice for driving**

**Disorder causing syncope**

**Cardiac arrhythmias**

Untreated arrhythmias

Cardiac arrhythmia, not life-threatening, medical treatment

Cardiac arrhythmia, life-threatening (e.g. inheritable disorders), medical treatment

Pacemaker implant

Catheter ablation

Implantable cardioverter defibrillator implant

**Structural cardiac/cardiopulmonary**

**Orthostatic hypotension (neurogenic)**

Syncope while sitting

**Reflex syncope**

Single/mild

Recurrent and severe

**Unexplained syncope**

**Group 2 (professional drivers)**

Unfit to drive

After successful treatment is established

Permanent restriction

After appropriate function is established (first post-implant visit)

After successful treatment is established

Permanent restriction

After appropriate function is established

After successful treatment is established

No restriction unless it occurred during driving or without prodromes

After successful treatment is established.

Particular caution if it occurred during driving or without prodromes

After diagnosis and appropriate therapy is established

The main cause of syncope while driving was neurally mediated (37,3%)

*Sorajja et al, Circulation 2009*

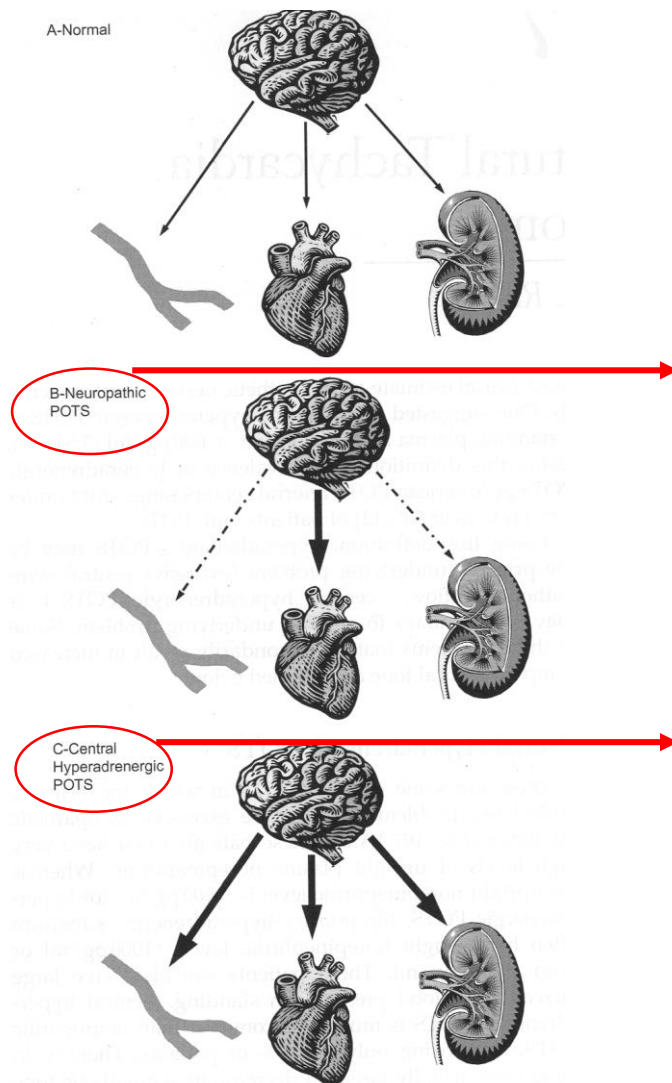
Patients with POTS are sometimes clinically diagnosed as having *anxiety disorders* such as panic disorder, and *memory problems*.

**Anxiety and hypervigilance**—Anxiety and somatic vigilance are significantly higher in patients with POTS, which raises the issue of the role of somatic hypervigilance in the source of the symptoms.<sup>36,37</sup> Masuki et al<sup>36</sup> attempted to dissect the psychological and physiologic contributions to tachycardia. Detailed physiologic and psychometric studies showed that although anxiety is commonly present in POTS, the heart rate response to orthostatic stress is not caused by anxiety but is instead a response to an underlying physiologic abnormality.

Sheldon et al  
*Heart Rhythm*. 2015 June ; 12(6): e41–e63. doi:10.1016/j.hrthm.2015.03.029.

Masuki et al  
*J Appl Physiol*. 2007; 102:896–903.

# Phenotypes



## Neuropathic

- Impairment of sympathetic innervation to the lower limbs (less norepinephrine spillover = less sympathetic activation in their lower extremities).

*Jacob G et al. N Engl J Med. 2000;343:1008–14*

- Ganglionic  $\alpha 3$ -acetylcholine receptor antibody found in 14% of patients adds further support for functional sympathetic denervation.

*Thieben M et al. Mayo Clin Proc 2007;82:308-13*

## Hyperadrenergic

Elevated levels of plasma norepinephrine (> 600 pg/mL). Central sympathetic overactivity (“Autonomic storm”)

*Figuroa JJ et al. Clin Auton Res 2010;20:305*

# Other mechanisms

- **POTS associated with poor conditioning:**

previously health patients who undergo a period of bedrest associated with some illness or life-long orthostatic intolerance.

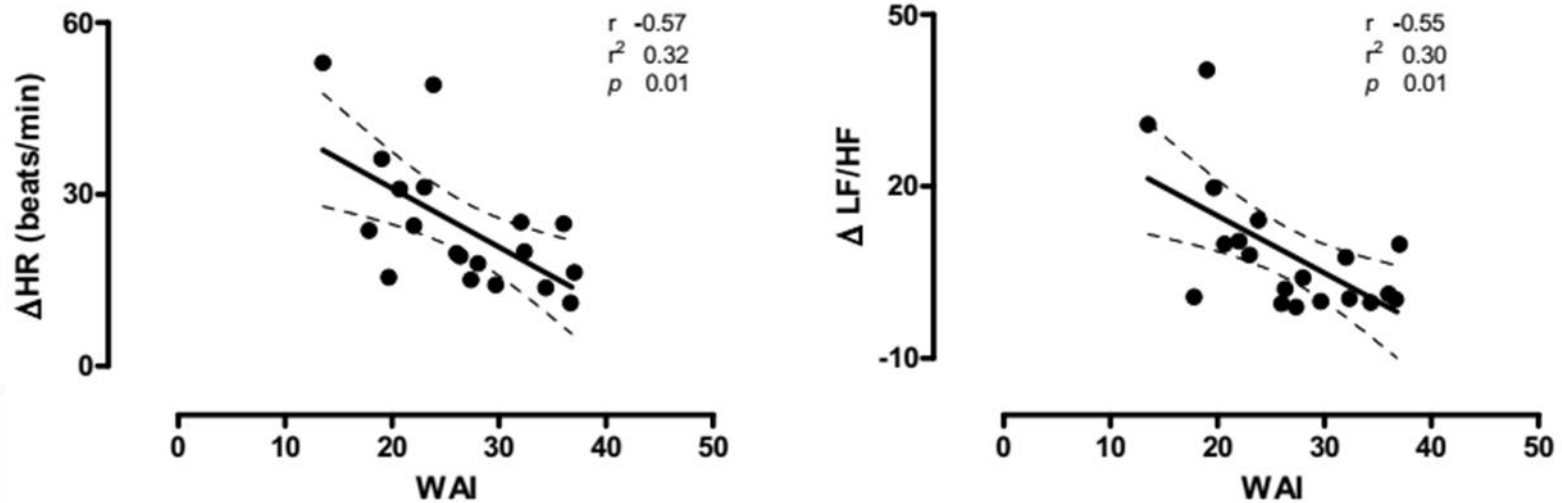
- **Hypovolemia and blood volume regulation:**

some patients with POTS have low blood volumes. They have also inappropriately low levels of standing plasma renin activity and aldosterone compared with normovolemic subjects. This paradox remains unexplained.

Jacob G. et al Am J Med 1997; 103:128-33  
Raj S. et al Circulation 2005; 111: 1574-82



## Autonomic disorders and work ability: POTS



**Figure 3.** Relationships between the individual changes induced by 75° head-up tilt of heart rate (HR), the marker of cardiac sympatho-vagal modulation (LF/HF) and the Work Ability Index (WAI) in POTS patients.

1.The higher the burden of autonomic symptom (COMPASS31), the lower the WAI.

2.The higher the HR and LF/HF increase during standing, the lower the WAI. The cardiac sympathetic overactivity while standing seems to play a negative role on work capability and performance.

## METHODS: Identifying patients affected by post-COVID19 autonomic syndrome

- Through the COMPASS-31 total score and a previously established cut-off of 16.4 (D'Amato, 2020), we were able to identify two sub-groups:

- **Sub-group A:** comprehended those patients that developed «post-COVID19 autonomic syndrome». These patients had no autonomic symptoms before COVID19 and they started having them after the infection resolution.

- **Sub-group B:** comprehended the remaining population.

## Orthostatic intolerance in sub-group A

- In sub-group **A**, on COMPASS-31, the most altered autonomic domain was **orthostatic intolerance** (score range: 0-40).

PRE  $\rightarrow$  T6  
1.07  $\pm$  4.13  $\rightarrow$  17.07  $\pm$  9.38

