Guideline-based global approach to the management of faints and falls in a dedicated outpatient facility

The Faint & Fall Study

Clinical Investigation Plan (CIP)

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1. Background.

Transient loss of consciousness (or its colloquial synonymous "faint") is a term that encompasses all disorders characterized by self-limited loss of consciousness, irrespective of the mechanism. Syncope is the most frequent cause of transient loss of consciousness. By including the mechanism of unconsciousness, i.e. transient global cerebral hypoperfusion, the current syncope definition of the European Society of Cardiology excludes other causes such as epileptic seizures and certain common syncope mimics, such as psychogenic pseudosyncope (1). Falls are very frequent in the older people. A variety of risk factors, i.e., abnormalities of gait, balance and lower limb joints, cognitive status, visual status, environmental hazard and drug interaction predispose patients to fall (2). If unwitnessed falls are not due to mechanical slips or trips (i.e. are unexplained or nonaccidental), it is likely that the patient experienced a syncopal event and displayed lack of awareness for loss of consciousness (1,2). Age-related memory impairment or more established forms of cognitive impairment are frequently associated with poor recall and therefore the lack of an accurate history of events (the so called “retrograde amnesia”). Management of falls in such circumstances is the same as that for syncope. In addition, it has been hypothesized that cardiovascular disorders are responsible for up to 77% of patients presenting with a fall related to unexplained loss of consciousness (3). Thus, the evaluation of faints and falls frequently overlap in older people. Owing to the heterogeneous etiology of faints and falls, their management is by necessity multidisciplinary, involving cardiologists, internists, geriatricians, neurologists, physiatrists, orthopedics, oculists, etc.

There is a gap between the best available scientific evidence provided by guidelines on syncope (1) and falls (2) and the need for the dissemination of these concepts into clinical practice. The multidisciplinary nature of faint and falls is the major barrier to the dissemination of guidelines and to a comprehensive management that covers all the aspects of faints and falls. The absence of a systematic global approach to faints and falls incurs higher health and social care costs, unnecessary hospitalizations and diagnostic procedures, prolongation of hospital stays, lower diagnostic rates, and higher rates of misdiagnoses and symptom recurrence.

2. Aims of the study.

To assess the effectiveness (adherence) of a patient flow pathway and cost of a guideline-based global approach to the management of faints and falls in patients referred to dedicated multidisciplinary outpatient facilities. We will considerer the following endpoints:

Primary-endpoint:

I. Point and interval prevalence estimation of patients with unexplained falls ( ), among those who underwent fall diagnostic assessment at initial presentation ( ), and then moved to faint pathway for prosecution of diagnostic assessment (Figure 1), and its determinants.

Secondary endpoints:

I. Point and interval estimate of the agree proportion between initial presentation and final diagnosis in patients initially assigned to faint and those with unexplained falls.
II. Descriptive comparison between patients initially assigned to faint and those with unexplained falls in terms of diagnostic assessment and adherence rate to the recommendations of the guidelines (see appendix).
III. Descriptive cost analysis of the faint and fall protocol (costs of investigations per patient).

Moreover, all previous analysis will be performed also for predefined age subgroups (≥75, 74-65 and 64-40 years).

3. Study design

Prospective observational study

Inclusion criteria

- Consecutive patients aged ≥40 years referred to the Faint & Fall Clinics for assessment of an episode of faint or fall. The possible hospitals to recruit patients are Istituto Auxologico Italiano and Ospedale di Careggi, University of Florence. The patients will be recruited from the second half of 2020 and the recruitment will continue until to the achievement of the sample size (defined below).

Exclusion criteria:

- Patients with age <40 years
- Patients with incidental fall
- Patients with an established diagnosis of syncope
- Patients in whom syncope and fall are secondary symptoms of severe underlying comorbidities (e.g: acute myocardial infarction, pulmonary embolism, acute haemorrage)

A screening log of excluded patients (Faint & Fall Registry) will be collected.

Patients' flow

Each included patient will undergo to the faint and fall protocol, to assess the effectiveness of a patients' flow pathways (shown in the figure 1) developed in accordance with the most recent guidelines on syncope of the European Society of cardiology (1) and of guidelines on falls of the American and British Geriatrics Societies (2). The detailed flow pathway is described in the Appendix.

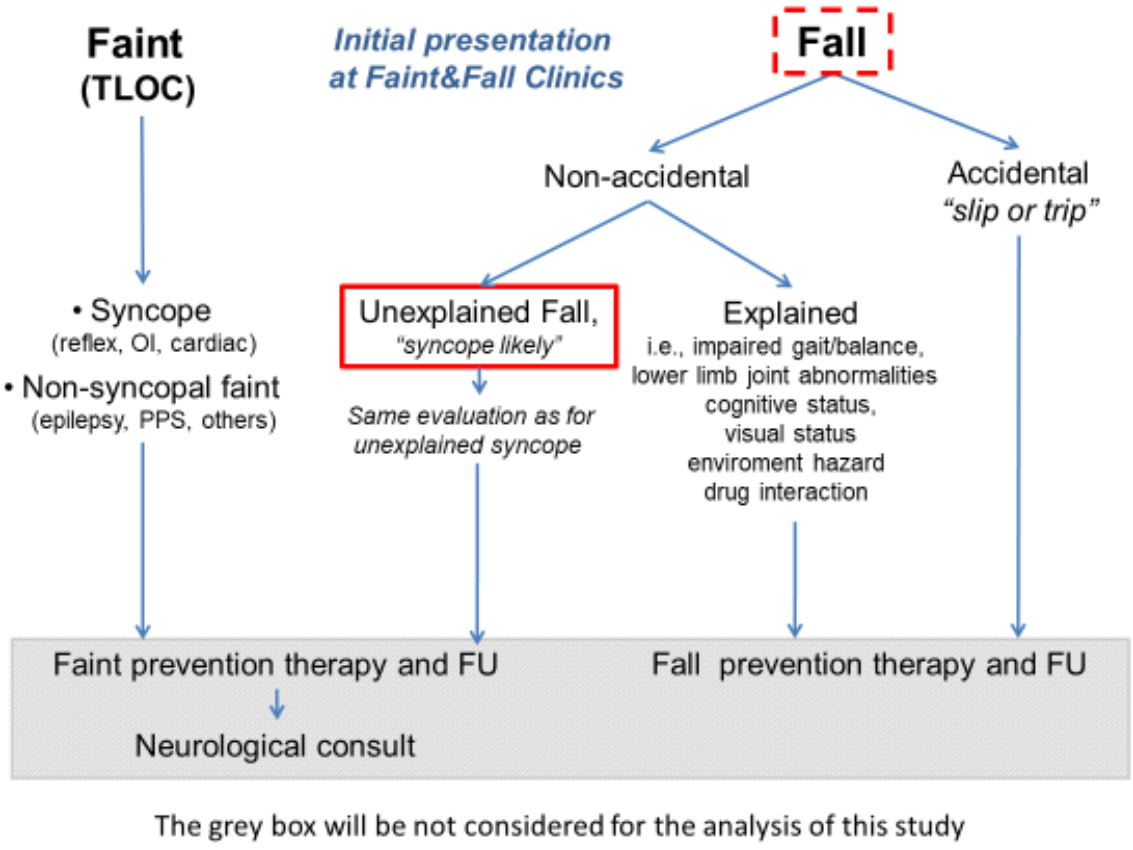


Figure 1. Schematic description of the patients' flow pathways in the Faint & Fall multidisciplinary outpatient clinics
Abbreviations: OI=orthostatic hypotension; PPS=psychogenic pseudosyncope

4 Sample size

A sample size of 340 produces a two-sided 95% confidence interval with a width equal to 10% when the prevalence of unexplained falls is 30% (sample size calculated with software PASS 14 Power Analysis and Sample Size Software (2015). NCSS, LLC. Kaysville, Utah, USA, ncss.com/software/pass.).
This sample size will allow to calculate an interval estimate of the agree proportion between initial presentation and final diagnosis in patients initially assigned to unexplained falls with a width varying from 0.12 to 0.19 assuming a prevalence of agree varying from 0.9 to 0.6. Analogously, a sample of 100 unexplained faint will guarantee the same coverage.

5 Statistical analysis

Continuous data will be summarized by means of mean value and standard deviation (SD) if the variable follows a Normal distribution or median and interquartile range in case of non Normal distribution. Categorical data will be summarized by means of absolute and relative frequencies.

For primary endpoint we will calculate the proportion of unexplained fall and its 95% interval confidence through normal approximation method. The same calculation will be carried out for the agree proportion between initial presentation and final diagnosis in patients initially assigned to faint and those with unexplained falls. Finally, to detect the determinants of unexplained falls at initial presentation we will apply a linear discriminant analysis [5].

6 References

1. Brignole M, Moya A, de Lange FJ, et al., ESC guidelines for the diagnosis and management of syncope, Eur Heart J. 2018; 39: 1883–1948.

2.Panel on Prevention of Falls in Older Persons. Summary of the updated American Geriatrics Society/British Geriatrics Society clinical practice guideline for prevention of falls in older persons. J Am Geriatr Soc 2011; 59:148–157.

3. Davies AJ, Kenny RA. Falls presenting to the accident and emergency department: types of presentation and risk factor profile. Age Ageing. 1996; 25: 362-366.

4. Daccarett M, Brignole M, Malasana G, Sherwood R, Jatter T, Hamdan M. Journal of Primary Care & Community Health 2011; 2: 173-180

5. George C. J. Fernandez. Discriminant Analysis, A Powerful Classification Technique in Data Mining. SUGI 27

7 Appendix

A) Fall assessment

A1. Definitions.

Incidental fall is defined as any fall related to high velocity action or sports, contact or high-risk activities, or a state of intoxication.

Accidental fall is defined as any fall due to slipping or tripping. Tripping included stumbling, catching feet on objects, stepping into curbs, twisting of ankle or knee joint, becoming tangled up in a walker, or falling because the walker or cane hit an object (ie, furniture, doorframe) or part of the person (ie, leg, foot, shoe).

Nonaccidental fall is defined as a fall occurring in the absence of the above criteria. A nonaccidental fall is further categorized as **explained or unexplained** depending on whether the physician concluded a clear cause-effect relationship between a risk factor or an inherent disease and the fall itself. In a patient presenting for fall who has a history of previous syncope/s is likely that that the fall was syncopal.
Remark. If a risk factor or disease is present but the cause-effect relationship with the fall is unlikely or uncertain, the fall is considered unexplained (i.e. "syncope likely") and the patient isfurtherly evaluated in the syncope pathway

A2. Multifactorial fall risk assessment

Potential risk factors are defined according to the recently published guidelines (2).
Risk factor for fall are assessed in all patients with accidental and non-accidental falls(primary end-point). A falls risk assessment is not considered necessary for older persons reporting only a single fall without reported or demonstrated difficulty or unsteadiness in walking or standing.

a) Gait, balance, and lower limb joint abnormalities are considered a risk factor if there was usage of an assistive device without physical therapy, abnormal muscle strength, diminished proprioception, and impaired cortical, cerebellar, or extrapyramidal function, or a known walking deviation.
Gait and balance assessment includes foot and footwear problems.
The test for gait or balance is the Short Physical Performance Battery (SPPB) (Figure 2). The short physical performance battery (SPPB) *[Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, Wallace RB. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. N Engl J Med.1995; 332: 556–61*] combines a balance test in three positions of increasing difficulty, 4-m gait speed and a repeated chair-standing test (Fig. 2). By comparing the timings recorded with those obtained in a reference population, the result of each test is converted into a score, which ranges from 0 (poor performance) to 4 (optimal performance), so that thefinal score of the battery ranges between 0 and 12.

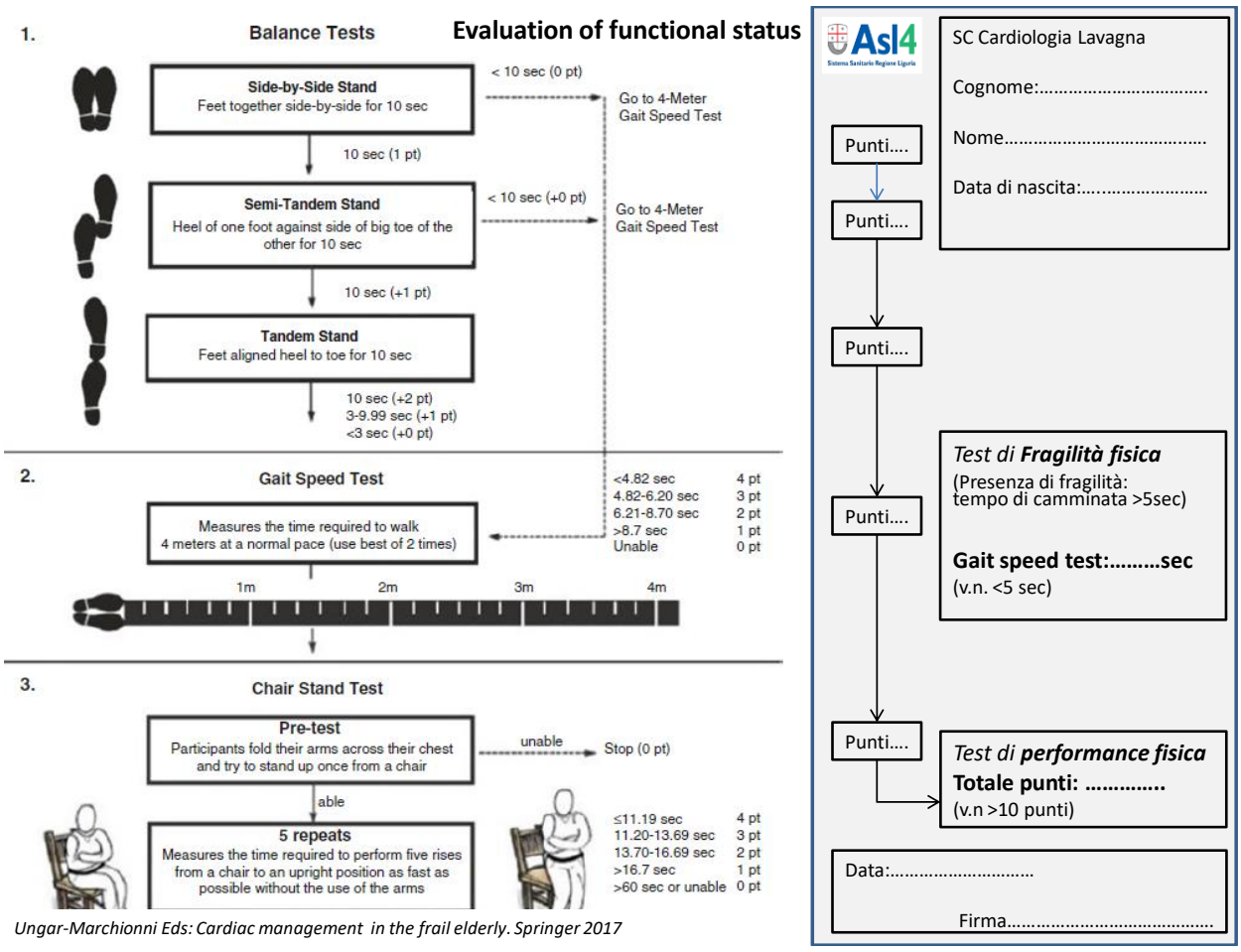
b) Drug interaction. The strongest risk associations occur with psychotropic medications, including serotonin reuptake inhibitors, and polypharmacy. Drug interaction is recognized as a risk factor if

the patient was taking 9 or more medications, 2 or more medications from the same class *(Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR,Beers MH. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensuspanel of experts. Arch Intern Med. 2003; 163: 2716-2724).*
The presence of orthostatic hypotension (spontaneous or drug-induced) requires full cardiovascular autonomic assessment (refer to syncope evaluation)

c) Cognitive status is considered to be abnormal if there was impairment in activities of daily living.

d) Visual status is considered a risk factor if bilateral visual acuity was less than20/40 with or without corrective lenses, development of cataracts, macular degeneration, glaucoma, and other conditions that would suggest an effect on risk of falling

e) Environmental hazards is considered a risk factor if there was inadequate lighting, rugs or loose carpets, inadequate bathroom safety equipment, stairs at home, bathroom on a different level of the living room, or lack of elevated toilet seat.



Ungar-Marchionni Eds: Cardiac management in the frail elderly. Springer 2017

Figure 2. Short Physical Performance Battery (SPPB) test

A3. Fall risk assessment in frail patients at risk of fall

- BRASS score
- HFRM score
- MORSE score

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Applicare etichetta identificativa
Cognome
Nome
Data di nascita

Scala BRASS (Blaylock Risk Assessment Screening Score)

ETA' *(una sola opzione)*	**Punteggio**
55 anni o meno	0
56 – 64 anni	1
65 – 79 anni	2
80 anni e più	3

CONDIZIONI DI VITA E SUPPORTO SOCIALE *(una sola opzione)*	**Punteggio**
Vive con il coniuge	0
Vive con la famiglia	1
Vive solo con il sostegno del familiare	2
Vive solo con il sostegno di amici/conoscenti	3
Vive solo senza alcun sostegno	4
Assistenza domiciliare/residenziale	5

STATO FUNZIONALE *(una sola opzione)*		**Punteggio**
Autonomo (indipendente in ADL e IADL)		0
Dipendente in	Alimentazione/nutrizione	1
	Igiene/abbigliamento	1
	Andare in bagno	1
	Spostamenti/mobilità	1
	Incontinenza intestinale	1
	Incontinenza urinaria	1
	Preparazione del cibo	1
	Responsabilità nell'uso di medicinali	1
	Capacità di gestire il denaro	1
	Fare acquisti	1
	Utilizzo di mezzi di trasporto	1

STATO COGNITIVO *(una sola opzione)*	**Punteggio**
Orientato	0
Disorientato in alcune sfere* qualche volta	1
Disorientato in alcune sfere* sempre	2
Disorientato in tutte le sfere* qualche volta	3
Disorientato in tutte le sfere* sempre	4
Comatoso	5

*Sfere: spazio, tempo, luogo e sé

MODELLO COMPORTAMENTALE *(una sola opzione)*	**Punteggio**
Appropriato	0
Wandering (CONFUSO)	1
Agitato	1
Confuso	1
Altro	1

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MOBILITA' *(una sola opzione)*	Punteggio
Deambula	0
Deambula con l'aiuto di ausili	1
Deambula con assistenza	2
Non deambula	3

DEFICIT SENSORIALI *(una sola opzione)*	Punteggio
Nessuno	0
Deficit visivi o uditivi	1
Deficit visivi e uditivi	2

NUMERO DI RICOVERI PREGRESSI/ACCESSI AL PRONTO SOCCORSO *(una sola opzione)*	Punteggio
Nessuno negli ultimi 3 mesi	0
Uno negli ultimi 3 mesi	1
Due negli ultimi 3 mesi	2
Più di due negli ultimi 3 mesi	3

NUMERO DI PROBLEMI CLINICI ATTIVI *(una sola opzione)*	Punteggio
Tre problemi clinici	0
Da tre a cinque problemi clinici	1
Più di cinque problemi	2

NUMERO DI FARMACI ASSUNTI *(una sola opzione)*	Punteggio
Meno di tre farmaci	0
Da tre a cinque farmaci	1
Più di cinque farmaci	1

Punteggio totale (somma dei punteggi)	

Punteggio totale – Indice di rischio

0 – 10 rischio basso	Soggetti a basso rischio di problemi dopo le dimissione: non richiedono particolare impegno per l'organizzazione della loro dimissione, la disabilità è molto limitata.
11 – 19 rischio medio	Soggetti a medio rischio di problemi legati a situazioni cliniche complesse che richiedono una pianificazione della dimissione, ma, probabilmente, senza rischio di istituzionalizzazione.
≥ 20 alto rischio	Soggetti ad alto rischio perché hanno problemi rilevanti e che richiedono una continuità di cure probabilmente in strutture riabilitative o istituzioni.

Data: _____ Firma infermiere:_____

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ETICHETTA
N° SDO

Hendrich II fall Risk Model (HFRM)

Item	Data ⇨ / Sigla ⇘ / Valore ⇩	Valutazioni		
Confusione / disorientamento	4			
Depressione [1]	2			
Disturbi della eliminazione (incontinenza, urgenza)	1			
Vertigine, capogiri (definizione soggettiva)	1			
Uomo	1			
Donna	0			
Farmaci antiepilettici [2]	2			
Uso di Benzodiazepine [3] Uso di neurolettici [4]	1			
Get up and go test "Alzarsi dalla sedia" (selezionare il punteggio)				
- Capace di alzarsi in un singolo movimento	0			
- Si spinge, riesce in un tentativo	1			
- Multipli tentativi, ma riesce	3			
- Incapace di alzarsi senza assistenza	4			
Cut off > 5 alto rischio	totale			

[1] Diagnosi clinica segnalata in anamnesi

[2] Esempi Farmaci Antiepilettici:

Dintoina - Aurantin	Fenitoina
Tegretol	Carbamazepina
Zarontin	Etosuccimide
Depakin	Ac. Valproico
Gardenale - Luminale	Fenobarbital
Topamax	Topiramato
Keppra	Levetiracetam
Rivotril	Clonazepam
Depamide	Valpromide
Tolep	Oxcarbazepina
Lamictal	Lamotrigina

[3] Esempi Benzodiazepine:

Valium - Ansiolin	Diazepam
Lexotan	Bromazepam
Tavor - Control - Lorans	Lorazepam
Frisium	Clobazam
EN	Clordemetildiazepam
Xanax	Alprazolam
Roipnol	Flunitrazepam
Minias	Lormetazepam
Flunox - Valdorm	Flurazepam

[4] Esempi farmaci neurolettici:

Talofen	Promazina
Largactil	Clorpromazina
Serenase - haldol	Aloperidolo
Entumin	Clotiapina
Modalina	Trifluperazina

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ETICHETTA
N° SDO

SCALA MORSE - VALUTAZIONE RISCHIO CADUTE

ITEM	Punteggio assegnato SIGLA INF →	Valutazione del	Valutazione del	Valutazione del
1. **Storia di caduta nei tre mesi precedenti**				
No	0			
Sì	25			
2. **Diagnosi secondarie** **Oltre alla diagnosi d'ingresso è documentata altra patologia a rischio (es. cerebrovascolari, cardiache, neurologiche, muscolo-scheletriche)**				
No	0			
Sì	25			
3. **Aiuti negli spostamenti:**				
Pz. allettato assistito a letto Pz. Cammina senza ausili	0			
Utilizzo di grucce, bastoni canadesi o deambulatori	15			
Il Pz. deambula appoggiandosi a mobili/arredi	30			
4. **Il Pz. è portatore di cateteri intravenosi o esegue terapie endovenose in continuo**				
No	0			
Sì	25			
5. **Passo/trasferimenti:**				
Passo normale	0			
Pz. allettato o immobilizzato	0			
Passo instabile e trasferimenti indecisi	10			
Passo e spostamenti deteriorati	20			
6. **Stato mentale:**				
Vigile orientato, riconosce le proprie abilità	0			
Dimentica le proprie limitazioni	15			
PUNTEGGIO OTTENUTO →				
[illegible]	Medio Rischio 25 - 50		Alto Rischio > 50	

A4. Multifactorial interventions

Education and information programs should be considered part of a multifactorial intervention. Only the adjusted subset of interventions that target the risk factors that have been identified through a fall risk factor assessment are prescribed (secondary end-point):

a) Reduction in medications, particularly psychoactive medications(strong evidence)
Psychoactive medications (e.g., sedative hypnotics, anxiolytics, antidepressants) and antipsychotics (e.g.,new antidepressants or antipsychotics) should be minimized or withdrawn, with appropriate tapering if indicated.
A reduction in the total number of medications or dose of individual medications should be pursued. All medications should be reviewed and minimized or withdrawn
The presence of orthostatic hypotension requires full cardiovascular autonomic assessment (refer to syncope pathway for diagnosis and treatment)

b) Adaptation or modification of home environment (strong evidence):Home environment assessment and intervention performed by a healthcare professional in order to mitigate identified hazards in the home: adequate lighting, rugs or loose carpets, adequate bathroom safety equipment, stairs at home, bathroom on a different level of the living room, or elevated toilet seat.

c) Exercise, particularly balance, strength, and gait training (strong evidence)prescribed by qualified health professionals or fitness instructors

d) Management of foot problems and footwear (weak evidence).Advise to walk with shoes of low heel height and high surface contact area

e) Management of visual deficits, especially cataract surgery(strong evidence). Advise not to wear multifocal lenses while walking, particularly on stairs (weak evidence). Insufficent evidence for other vision interventions

f) Vitamin D supplement of at least 800 IU per day in patients with proven vitamin D deficiency in order to reduce the fracture rate (high evidence)

g) Management of postural hypotension (spontaneous or drug-induced) (high evidence). Require full cardiovascular autonomic assessment (refer to syncope pathway for diagnosis and treatment)

Dementia. There is insufficient evidence to recommend for or against multifactorial or single interventions to prevent falls in older persons with known dementia

B) Faint assessment

Patients with unexplained fall perform the same evaluation as for faint

B1. Initial evaluation

To all:

- **history**
- **physical examination** (including standing BP)
- **standard ECG**
- **echocardiogram** (if SHD is suspected)

The initial evalution should be able to classify the patient in one of the following cathegories (primary end-point):

- Certain or highly likely diagnosis (if class I diagnostic criteria are met)
- Cardiac likely, to be confirmed by tests
- Cardiac unlikely, reflex or orthostatic hypotension likely to be confirmed by tests
- No diagnosis (unexplained syncope), to be investigated by tests
- Non-syncopal faint

B2. Early evaluation

In selected cases (when appropriate):

- **basic CV autonomic function tests** (if OH or NMS are suspected):
  - 3 min active standing test
    - Valsalva manoeuvre and deep breathing
    - carotid sinus massage (in pts >40 years)
    - tilt testing
    - ambulatory BP monitoring
- **prolonged ECG home monitoring** (if arrhythmia is suspected)
- **blood tests** (pO_2 & gas analysys, haematocrit & blood cells count, troponin, d-dimer)
- **exercise test** (if syncope had occurred during physical effort)

B3. Subsequent evalution

When indicated, in accordnce with the recommendations of ESC guidelines on syncope (secondary end-point):

- **Home evideo recording**
- **Implantable loop recorder**
- **Electrophysiological study**
- **Coronary angiography**

B4. Faint prevention therapy and follow-up

When indicated, in accordance with the recommendations of ESC guidelines on syncope (secondary end-point) (Figure 3):

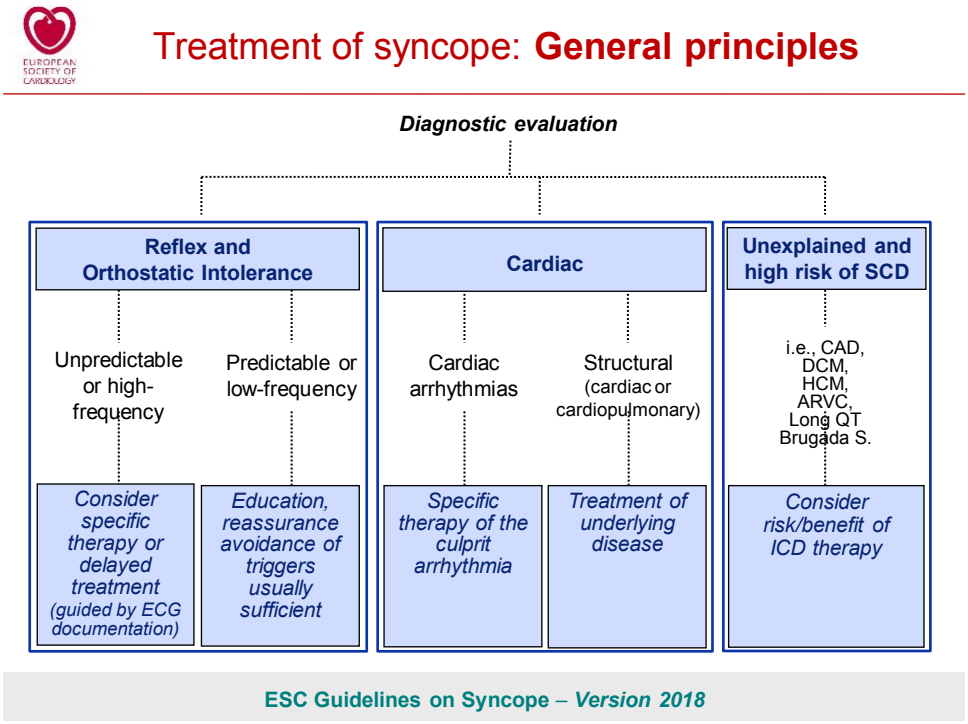
Treatment of syncope: General principles
Diagnostic evaluation
Reflex and Orthostatic Intolerance
Cardiac
Unexplained and high risk of SCD
Unpredictable or high-frequency
Predictable or low-frequency
Cardiac arrhythmias
Structural (cardiac or cardiopulmonary)
i.e., CAD, DCM, HCM, ARVC, Long QT Brugada S.
Consider specific therapy or delayed treatment (guided by ECG documentation)
Education, reassurance avoidance of triggers usually sufficient
Specific therapy of the culprit arrhythmia
Treatment of underlying disease
Consider risk/benefit of ICD therapy
ESC Guidelines on Syncope – Version 2018

Figure 3