
# Clinical case: Ageing

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# MARIA

64 years-old cisgender woman. Moves to our center from another city after her husband´s death, one year ago.

**She provides a clinical report with the following history:**

- ✓HIV+ A2 CDC. Acquired by sexual transmission and diagnosed in 1998.
- ✓ART since April 2002, no virological failure reported.
  Currently, on TAF/FTC RPV from 16/01/2019
- ✓Undetectable viral load (VL) from October 2002.
- ✓Latest blood test (11/2023): Hb 14,3 g/dl, leukocytes 4760, platelets 280000, total cholesterol 189, HDL 72, LDL 103, **CD4 749 (43%),** CD8 514 (29,6%), CD4/CD8 ratio 1,46
- ✓Serologies of HBV, HCV and syphilis: negative.

# More clinical data:

- ✓Toxic habits: tobacco smoker (10 packet-year).
- ✓Traumatic fracture of  left tibial maleolus in 2011.
- ✓Densitometry (2021): T score on hip -1,4, spine -2,6 and  L4 -3,4.
- ✓Right L5 sciatica, L4-L5 hernia, periodic epidural infiltrations for pain control.
- ✓Frequent accidental falls.
- ✓Gastroesophageal reflux

**Physical examination:**

- ✓Weigth: 69 Kg (BMI:26,95 kg/m2) Overweight
- ✓Height: 160 cm
- ✓Blood pressure 100/60 mmHg

# Evolution documented on her clinical report:

- From september 2022:
  - Significant general weakness and functional limitation with easy fatigue, and “sensation of limited capacity to do any activity”. No shortness of breath or signs of fluid overload.
- From 2023 (after husband´s death) she refers anxiety, sadness and hopeless.
- No weight loss during the last years
- Her relative (daughter) who has been living with her the last month, shows concern about her slow movements, frequent falls, and sleep disturbances : she used to have vivid nightmares with violent movements and screaming. She had a fall from bed last week  with a facial wound.
- Slow gait with low arms swinging was observed at examination.

# Question 1: ¿Do we need any additional clinical data or investigations?

1) Yes, we must check thyroid hormones, cortisol, muscle enzymes, rheumatic markers and Fried scale.
2) Yes, we need a brain magnetic resonance (MR)
3) Co-medication apart form ART must be checked
4) Answer 1 and 3 are correct.

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4) **Answer 1 and 3 are correct.**

# Additional test

- Thyroid hormones,cortisol, muscle enzymes and rheumatic markers: normal levels
- Renal function: Creatinine 1,2 mg/dl, Sodium, potassium, Calcium and D vitamin in normal range

Frailty Related phenotype

✓ Slow movement

✓ Weak handgrip

✓ Reduced level of activity

X Unintentionally lost of weight

✓ Feels exhausted

Phenotipic Frail

www.mdcalc.com/calc/2201/veterans-aging-cohort-study-vacs-1.0-index

# Medications:

- Clonazepam
- Sertraline
- Gabapentine
- Amitriptyline
- Acetamynophen
- Oxycodone/naloxone
- Diclofenac
- Alendronate
- Cholecalciferol and calcium supplements
- Metoclopramide

# 64 years-old HIV woman

**Previous conditions**

- Smoker
- Virologically supressed HIV infection with TAF/FTC/RPV
- Ostheoporosis and previous fracture
- Lumbar disc hernia
- Chronic pain

**Current evaluation**

- Functional limitation
- Weakness
- Frequent falls
- Deppresive mood
- Anxiety and sleep disturbances
- NO weight loss
- NO appetite loss
- Normal blood test

# Question 2: ¿Which is the most likely diagnosis?

1. Anxiety-depressive disorder
2. Neurocognitive disorder
3. Drug toxicity
4. Geriatric syndrome

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# Management

- Check drug interactions
- Comorbidities evaluation
- Interrupt unnecessary medication
- Evaluate other investigations

# Major interactions

- Clonazepam-oxicodone
- Amitriptyline-Sertraline
- Oxycodone-gabapentin
- Metoclopramide:
  D2R antagonism

**Interventions**

- Primary care doctor report
- Referred to Psychiatrics
- Referred to pain team to stop oxycodone
- Talk to her family (daughter)
- Stop smoking

**Amitryptiline: High anticholinergic effect (ACB score:3)**

# Six months later..

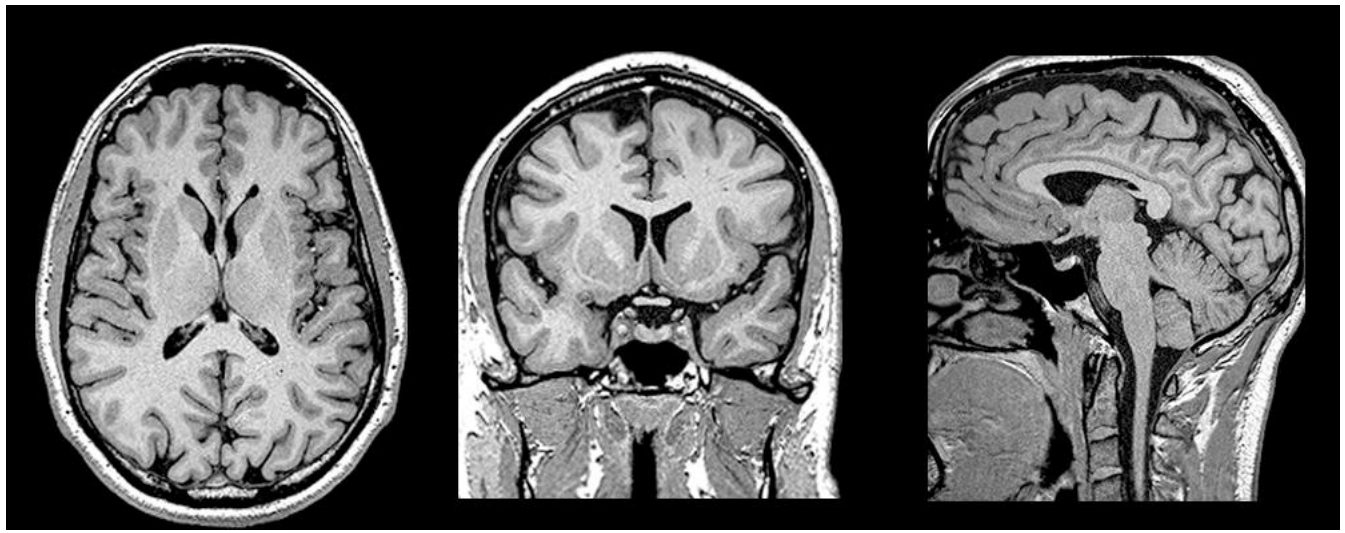
- Amitryptiline , oxycodone and metoclopramide were stopped
- She walks daily but mantaining a low gait speed. No falls
- Mild rest tremor in her right arm

BRADYKINESIA
REST TREMOR

# Question 3: ¿Which is the most likely diagnosis?

1. Anxiety-deppresive disorder
2. Neurodegenerative disease
3. Drug toxicity
4. Geriatric syndrome

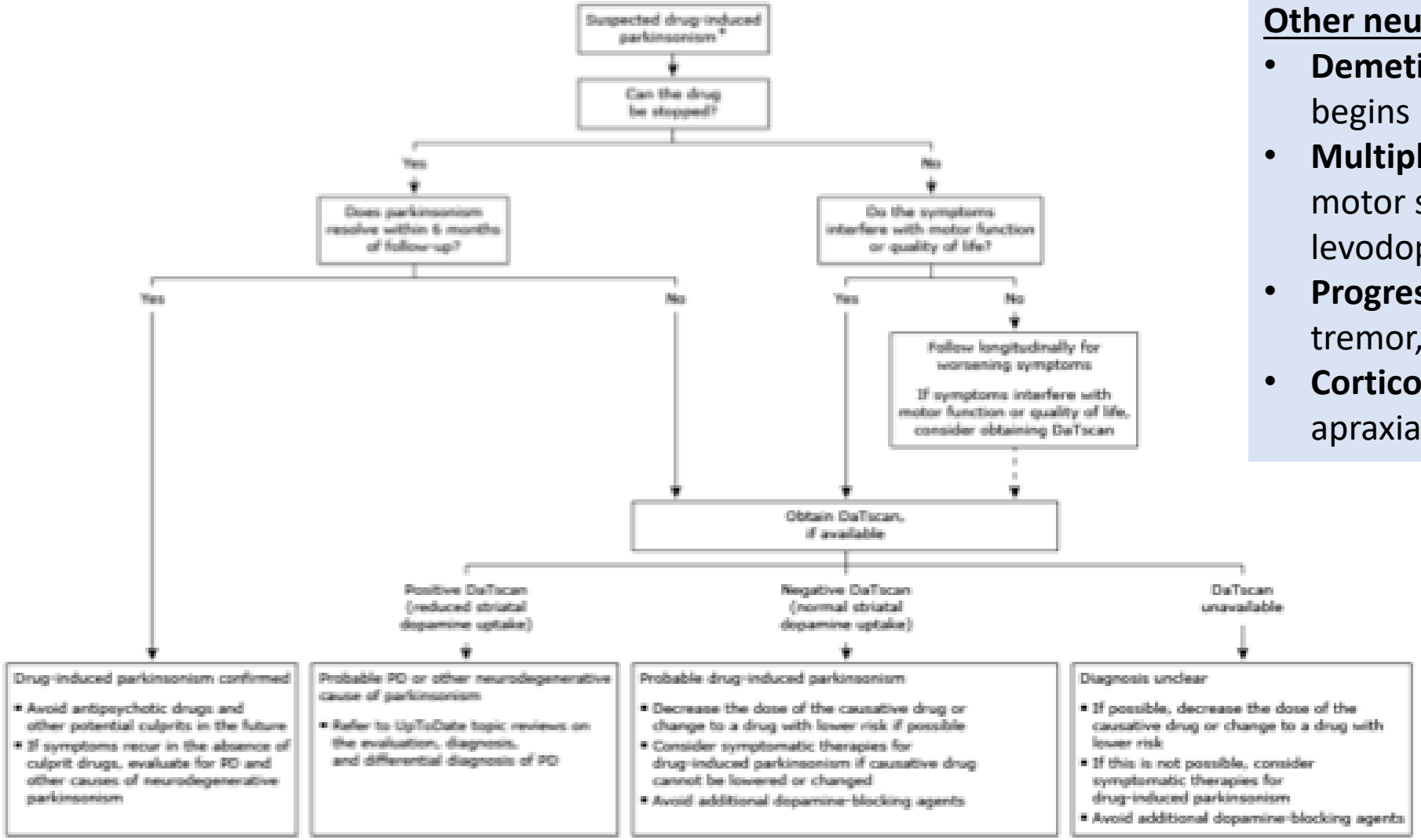
# Referred to Neurologist..



Normal brain MRI and LP

- DaTscan suggested Parkinson´s Disease (PD)
- Levodopa initiated
- Clear improvement of bradikynesia, rigidity and tremor
- No falls, six months after treatment

# PD *vs* Drug-induced parkinsonism




**<u>Other neurodegenerative disorders</u>**

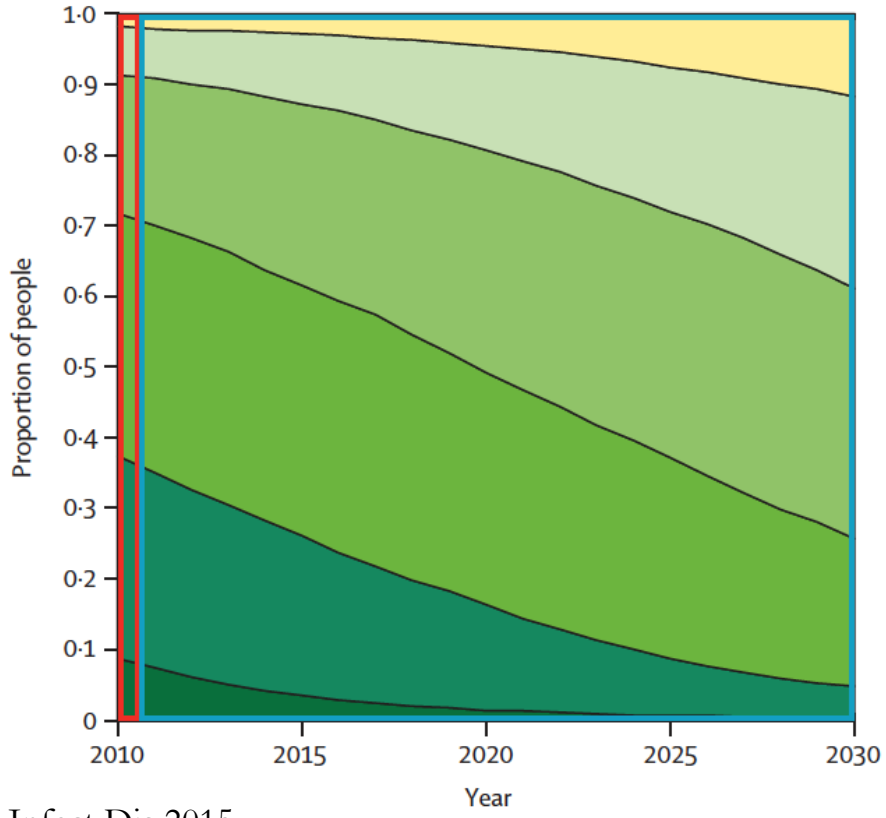
- **Demetia with Lewy bodies:** dementia begins before
- **Multiple system atrophy**: symmetric motor symptoms; Poor response to levodopa
- **Progressive supranuclear palsy**: no tremor, poor response to levodopa
- **Corticobasal degeneration**: aphasia, apraxia, poor response to levodopa

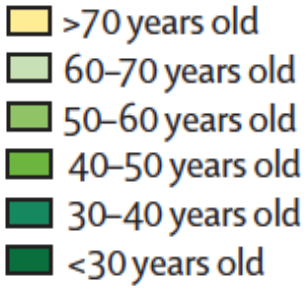
# PD *vs* Secondary Parkinsomism

| **Secondary parkinsonism** | **Causes** | **Examples** |
|---|---|---|
| | Drug-induced | Antipsychotic agents, metoclopramide, prochlorperazine, tetrabenazine, valproic acid |
| | Vascular | Vascular parkinsonism, vascular dementia |
| | Toxic | Carbon disulfide, carbon monoxide, cyanide, MPTP, manganese, organic solvents |
| | Metabolic | Hypoparathyroidism, pseudohypoparathyroidism, chronic liver failure, extrapontine myelinolysis, end-stage kidney disease with diabetes, type 2 diabetes |
| | Structural | Normal pressure hydrocephalus, chronic subdural hematoma, tumors involving striatonigral circuits, head trauma |
| | Infectious | Encephalitis lethargica, HIV/AIDS, neurosyphilis, prion disease, progressive multifocal leukoencephalopathy, toxoplasmosis |
| | Genetic | Wilson disease, neurodegeneration with brain iron accumulation, neuroacanthocytosis |

# Evolution of PLWH

**Parametric model, data of 10.278 patients from holand**
**ATHENA cohort (1996 - 2010) with projection to 2030**

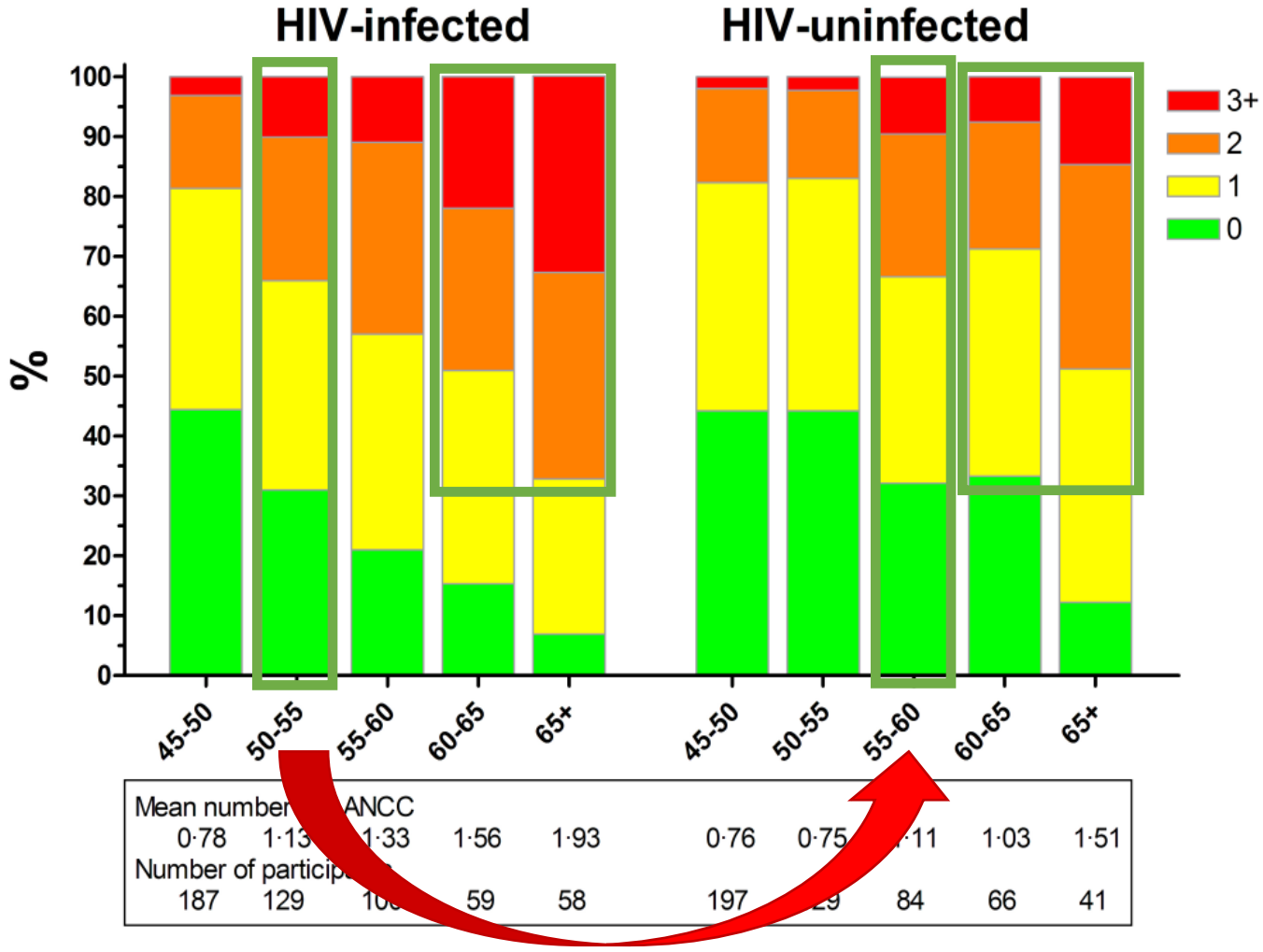



**Proportion of patients >60 yo will change from 8% in 2010 to 39% in 2030**

Smit M, et al. Lancet Infect Dis 2015

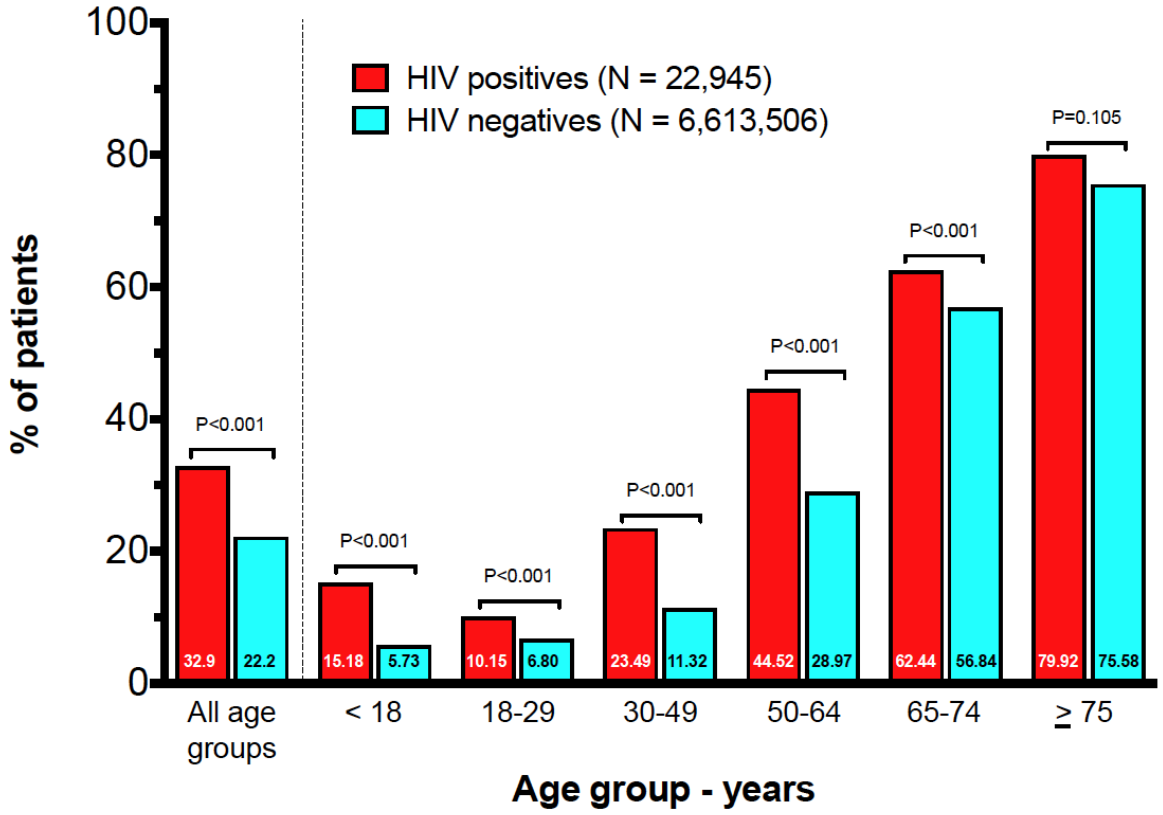
# Prevalence of comorbidities HIV and age related

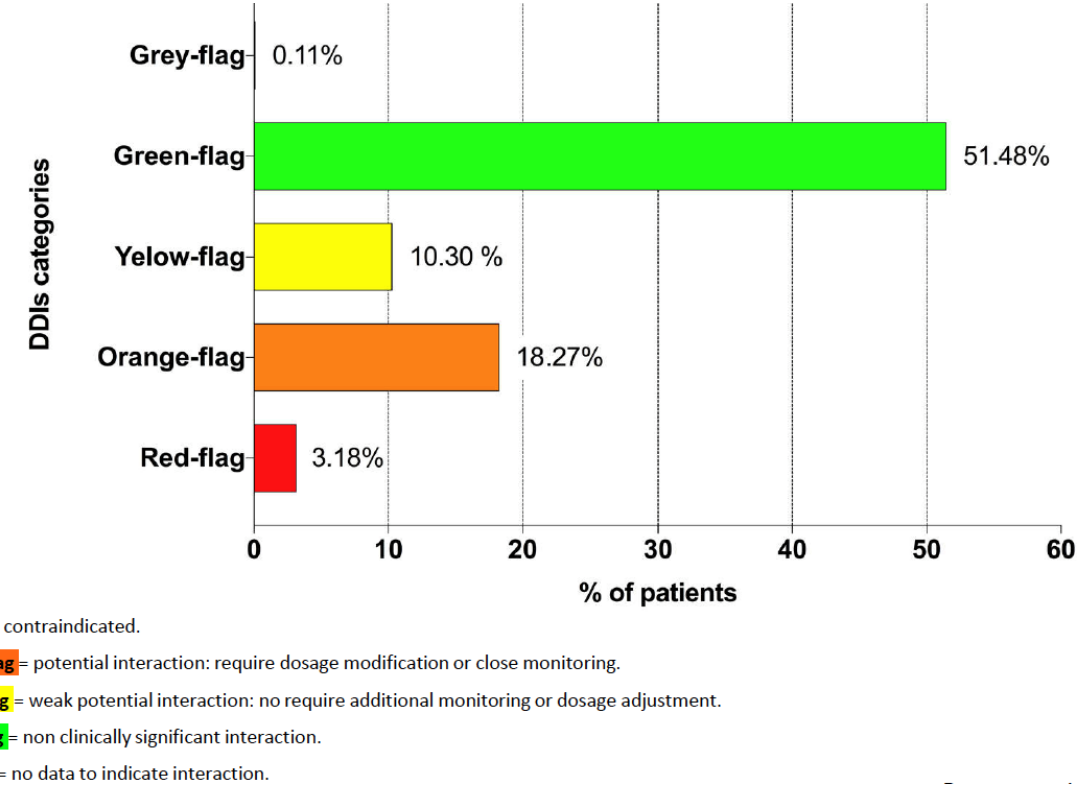



The older the patient the more frequent comorbities
More cardiovascular, metabolic and renal disease.

Schouten J, et al. Clin Infect Dis. 2014;59:1787–97

# Polypharmacy in PLWH

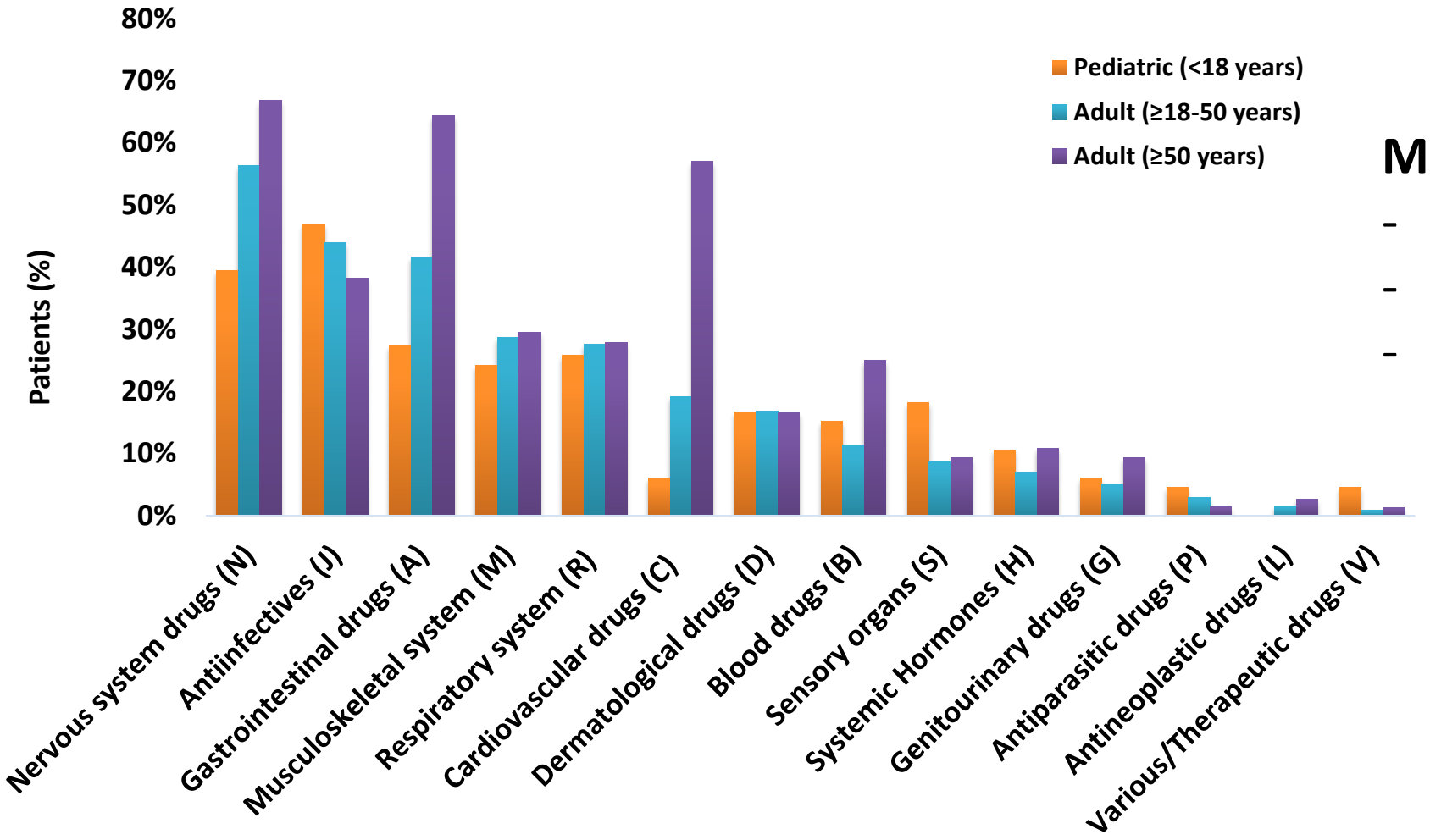



**More frequent DDI**

López-Centeno B,Polypharmacy and Drug-Drug Interactions in People Living With Human Immunodeficiency Virus in the Region of Madrid, Spain: A Population-Based Study. Clin Infect Dis. 2020 Jul 11;71(2):353-362.

# Co-meds in HIV-infected individuals according to ATC code



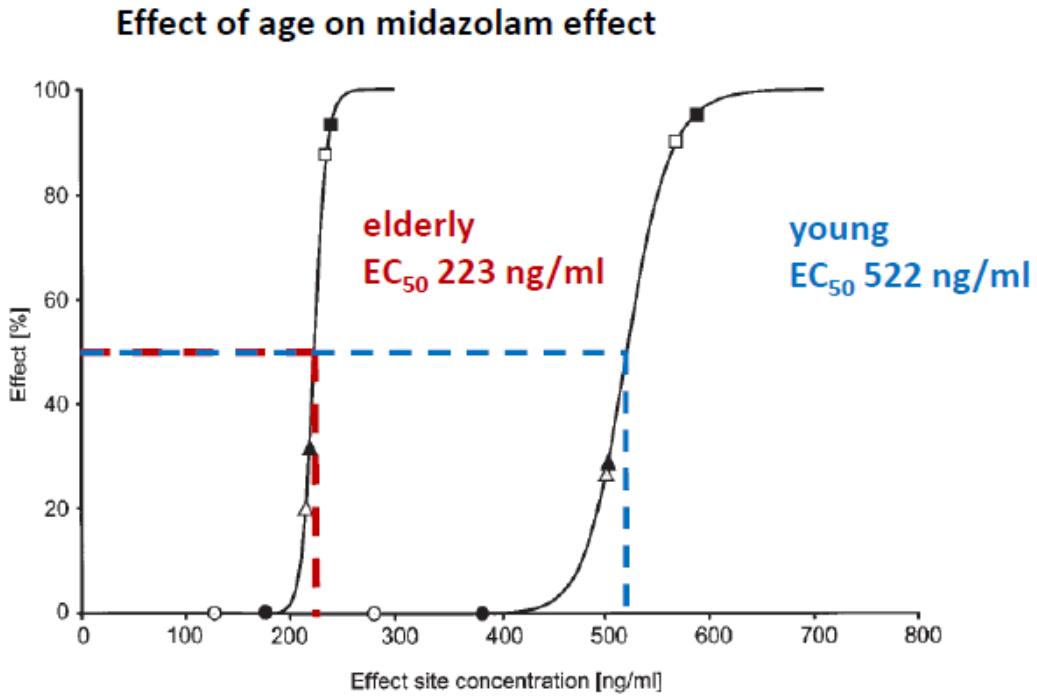

**More common drug groups:**

- **CNS / PSQ**
- **Gastrointestinal**
- **Cardiovascular /metabolic**

López-Centeno B,Polypharmacy and Drug-Drug Interactions in People Living With Human Immunodeficiency Virus in the Region of Madrid, Spain: A Population-Based Study. Clin Infect Dis. 2020 Jul 11;71(2):353-362.

# Age associated pharmacodynamics changes increase drugs sensitivity

**Age associated changes in pharmacodynamics:** ➔ increase sensitivity to certain drugs




- **Assessment of the concentration-hypnotic/sedative effect relationship of midazolam in young (24-28 y) and elderly (67-81 y)**
- **Total dose of midazolam needed to reach sedation in elderly is about half that needed in younger (age related changes in affinity of drugs to receptor sites or ↓nb receptors)**

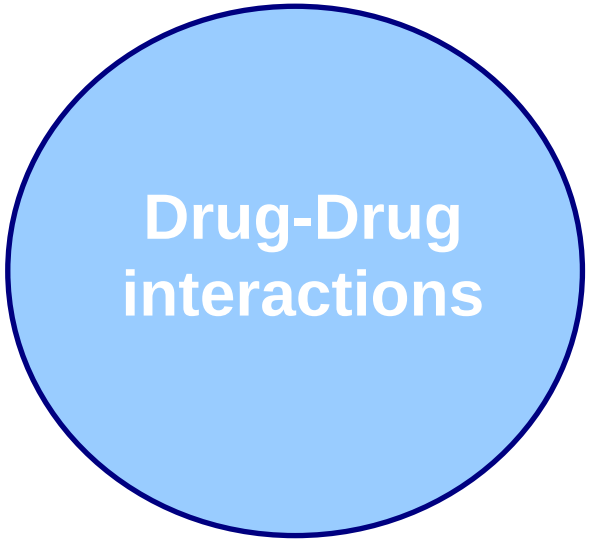
Albrecht S et al. Clin Pharmacol Ther 1999

# Negative consequences of polypharmacy


The half (52%) of old PLWH in US doesn´t take the drugs as they were prescribed


Treatment discontinuations because of adverse events increases with age.

It could be difficult to differentiate geriatric syndromes from AEs




Slide from MIAMI couse 2019

# Deprescribing and check DDI: electronic tools

**Interactions:**

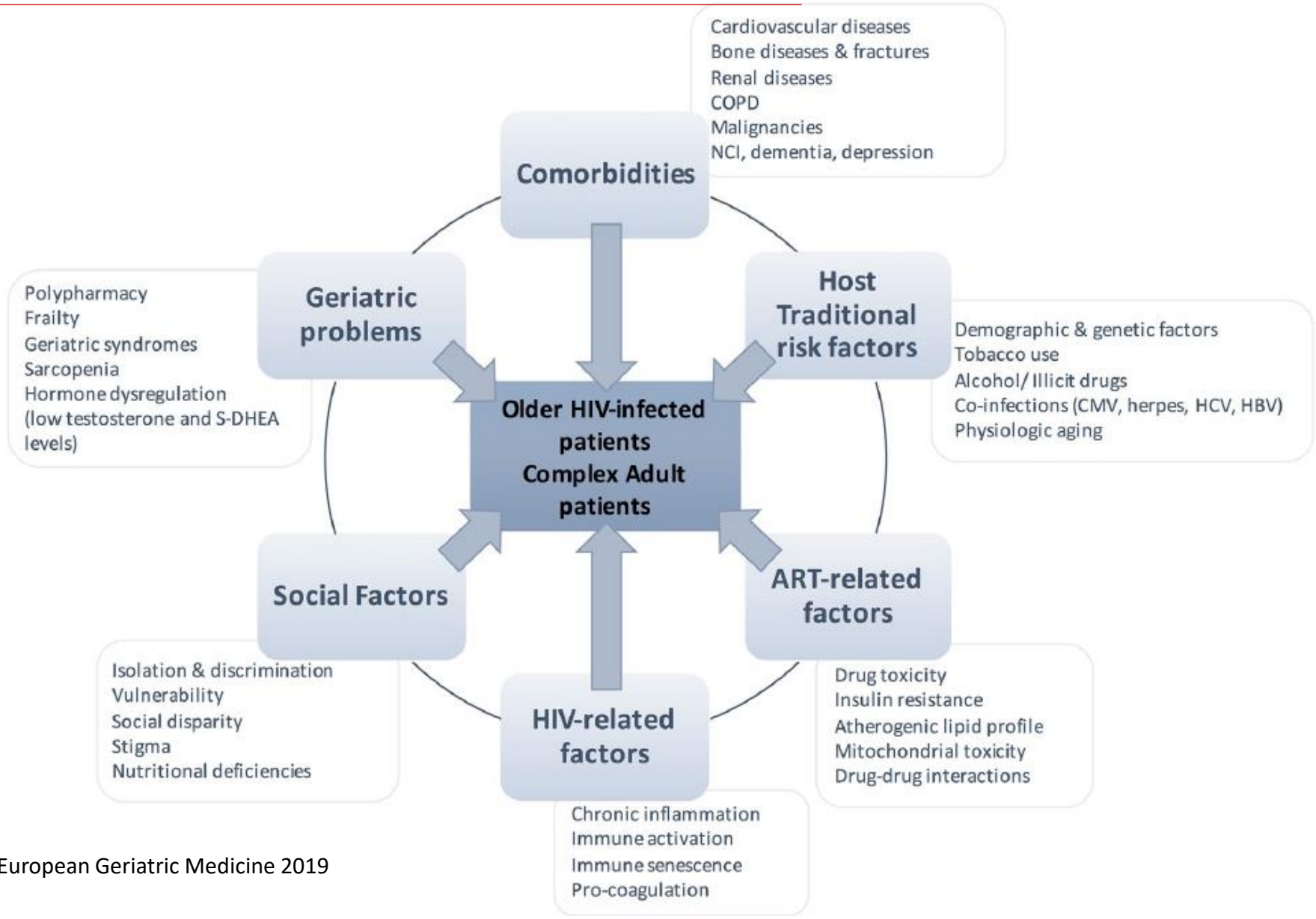
http://www.interaccionesvih.com/

**Deprescribing:** Medstopper.com

**Anticholinergic burden calculator**: www.acbcalc.com/


- AIDS Info. US Departament of Health and Human Service (DHHS). Se incluyen tablas con información sobre interacciones. En inglés).
- HIV Medication Guide (acceder a interactions) (No solo ofrece información de interacciones de antirretrovirales sino también de todo tipo de fármacos entre sí.)
- Liverpool HIV Pharmacology Group, University of Liverpool (Ofrece amplia información de interacciones de los antirretrovirales y otros aspectos relacionados. En inglés)
- Liverpool HIV Pharmacology Group, University of Liverpool. Interacciones de los fármacos empleados para el tratamiento del virus de la hepatitis C.
- Medscape multi-drug interaction checker. (No solo ofrece información de interacciones de antirretrovirales sino también de todo tipo de fármacos entre sí. En inglés).

# Factors associated to ageing and HIV

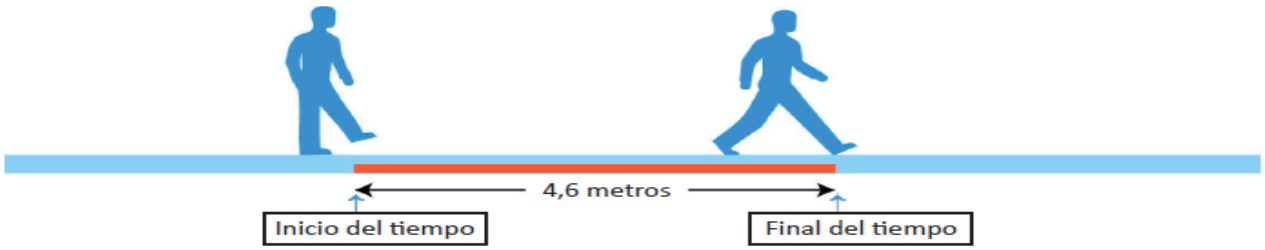



Montejano R, de Miguel R and Bernardino JI. European Geriatric Medicine 2019
https://doi.org/10.1007/s41999-018-0152-1

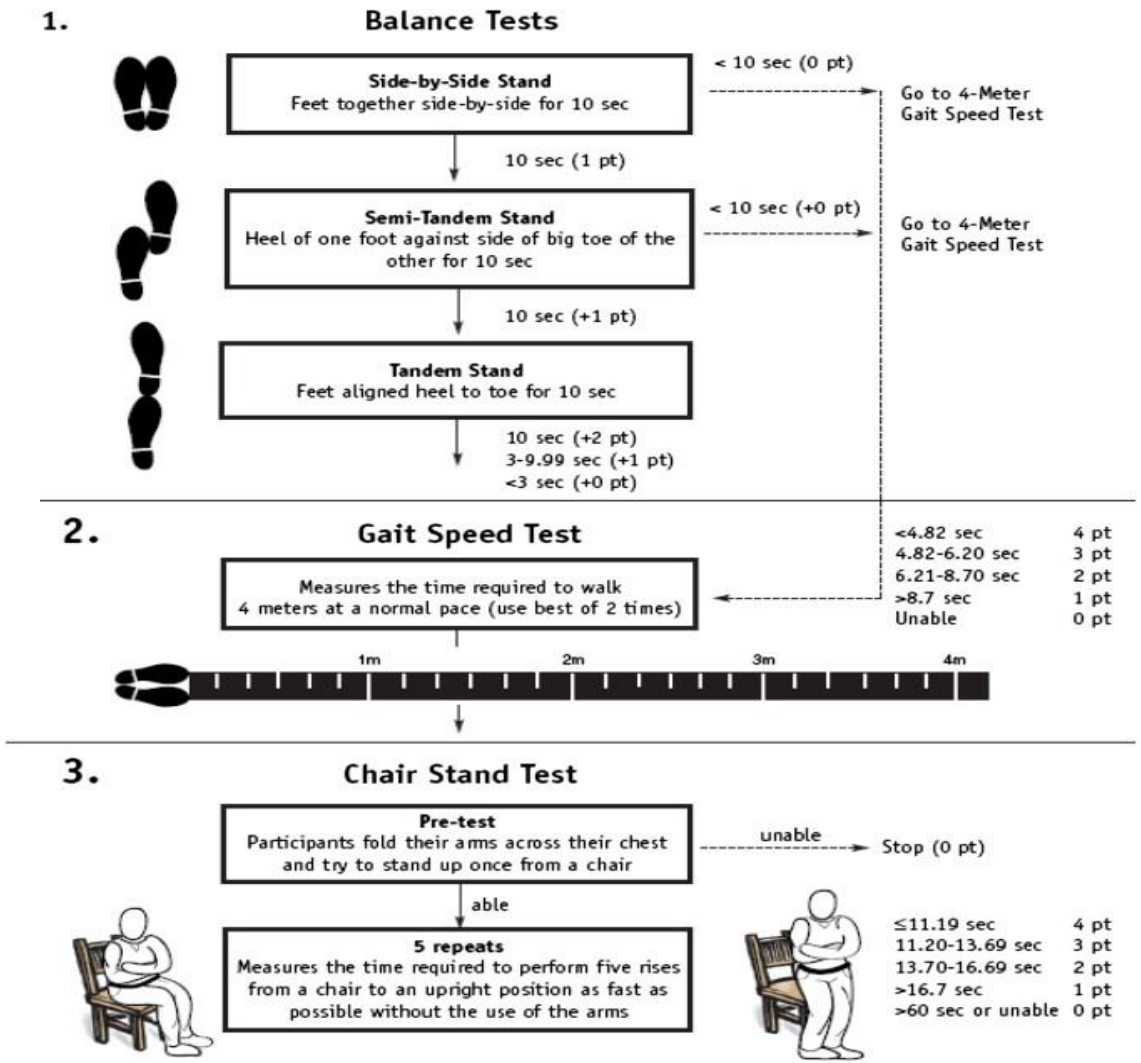
# Screening frailty

| Tool | Original reference | Time | Special team |
|---|---|---|---|
| Study of Osteoporostic Fractures Index (SOF) | Ensrud et al. Arch Intern Med 2008 | <5 min | No |
| Edmonton Frailty Scale | Rolfson et al. Age Ageing 2006 | <5 min | No |
| Fatigue, Resistance, Illness, Loss of Weight (FRAIL Index) | Morley et al. J Am Med Dir Assoc 2008 | <10 min | No |
| Clinical Frailty Scale | Roockwood et al. Can Med Assoc J 2005 | 5 min | No |
| Prisma-7 | Raiche et al. Arch Gerontol Geriatr 2007 | 5 min | No |
| Sharebrooke Postal Questionnaire | Hebert et al. Age Ageing 1996 | <5 min | No |
| Short Physical Performance Battery (SPPB) | Guralnik et al. J Gerontol 1994 | <10 min | No |
| Gait speed | Cesari M. | <5 min | No |

## Gait speed

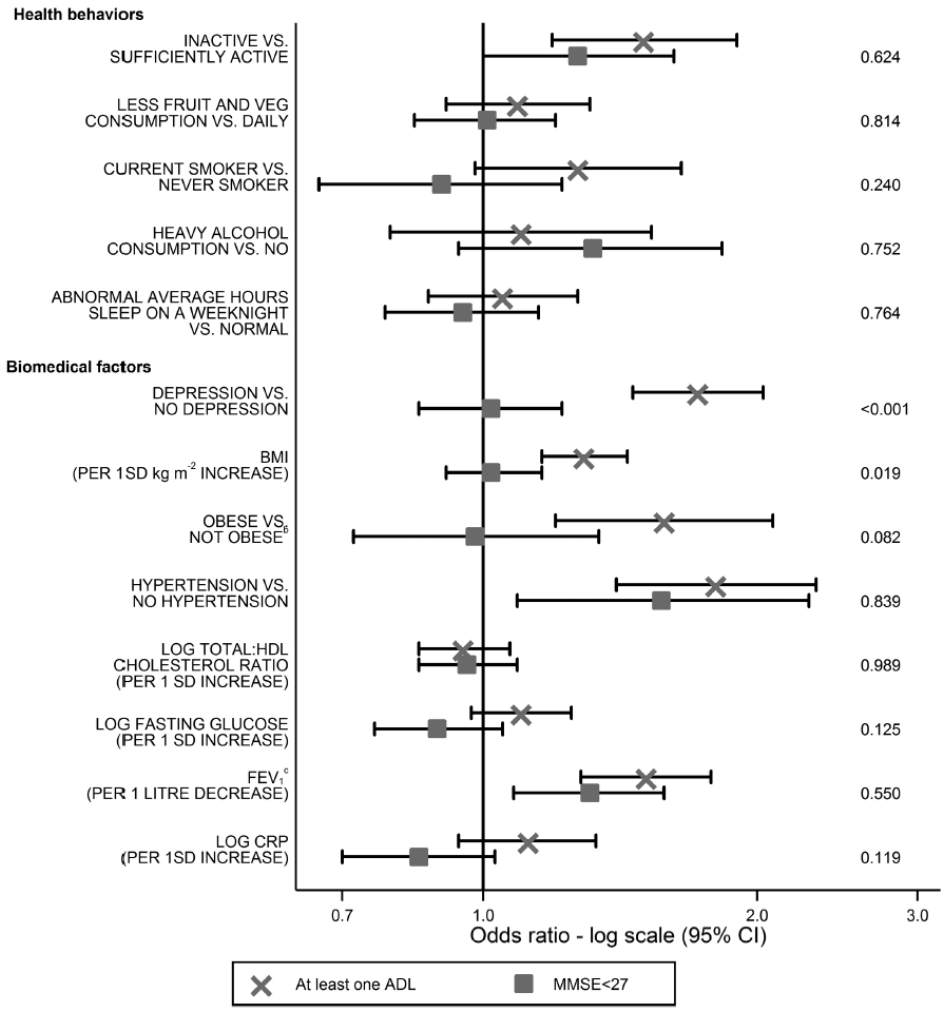



## SPPB




Guralnik et al. J Gerontol 1994

# In general population >50 years, modifiable risk factors predicts functional limitation and cognitive impairment after 20 years




Modifiable risk factors:

- ✓ Lack of physical activity
- ✓ Depression
- ✓ Obesity
- ✓ FEV1: Tobacco

Brunner E et al. Gerontol A Biol Sci Med Sci, 2017

# Frailty transition patterns (meta-analyses)

N=42775 old patients in 16 studies, mean follow up of 3,9 years (1-10)

**Frail patients:**

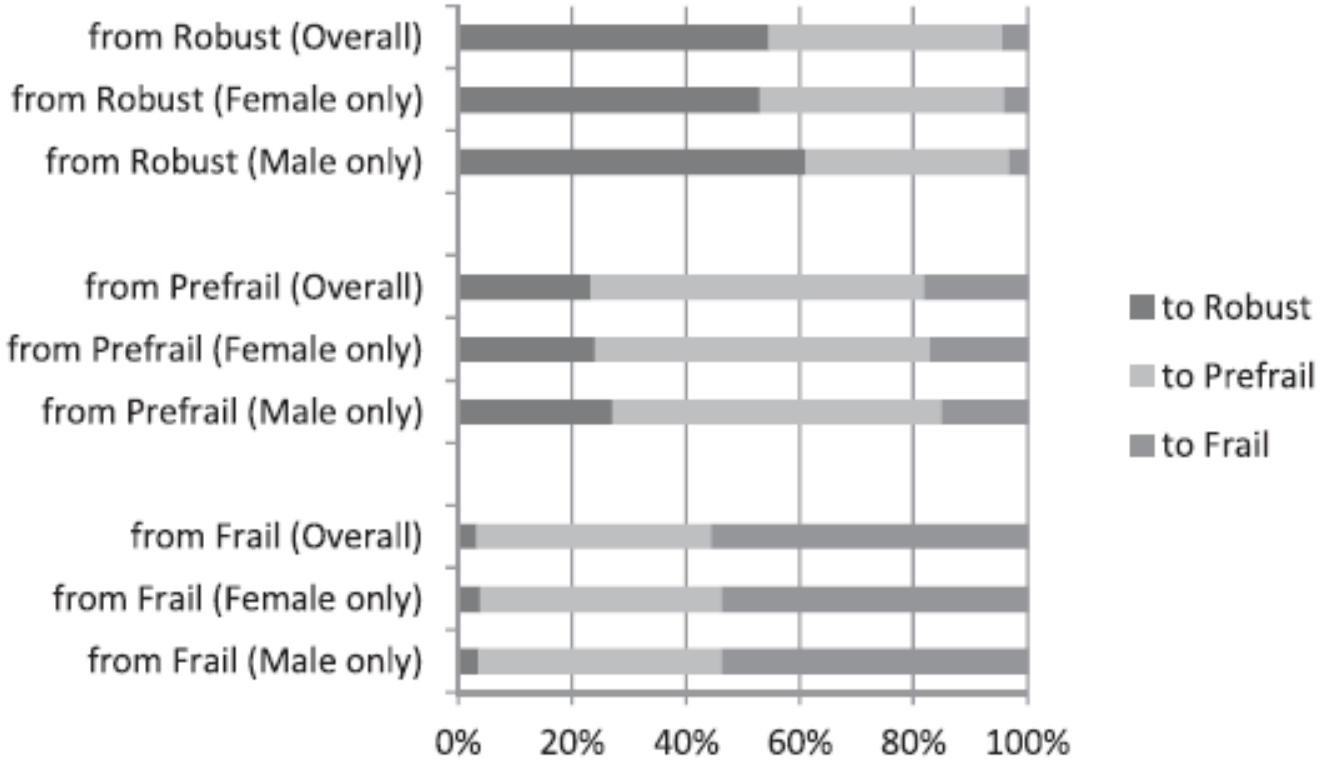
Improve: 13.7% (95%CI=11.7–15.8%)

Worse 29.1% (95%CI=25.9–32.5%)

**Pre-frail:**

**Improve: 23.1% (95%CI=18.8–27.6%),**

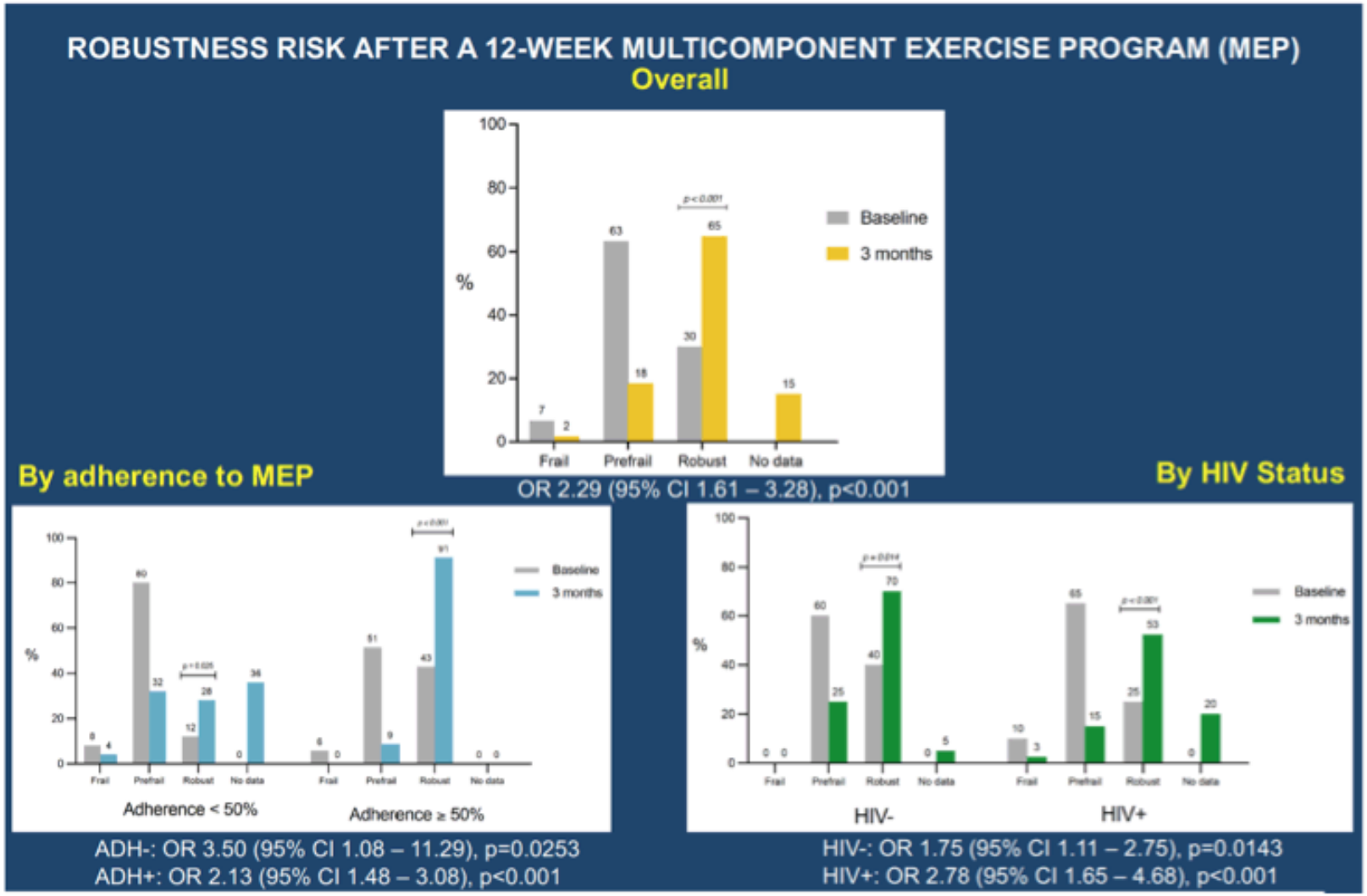
Worse: 18.2% (95%CI=14.9–21.7%)




Stratified and meta-regression analyses showed **age, gender and follow-up period** were associated with frailty transition patterns.

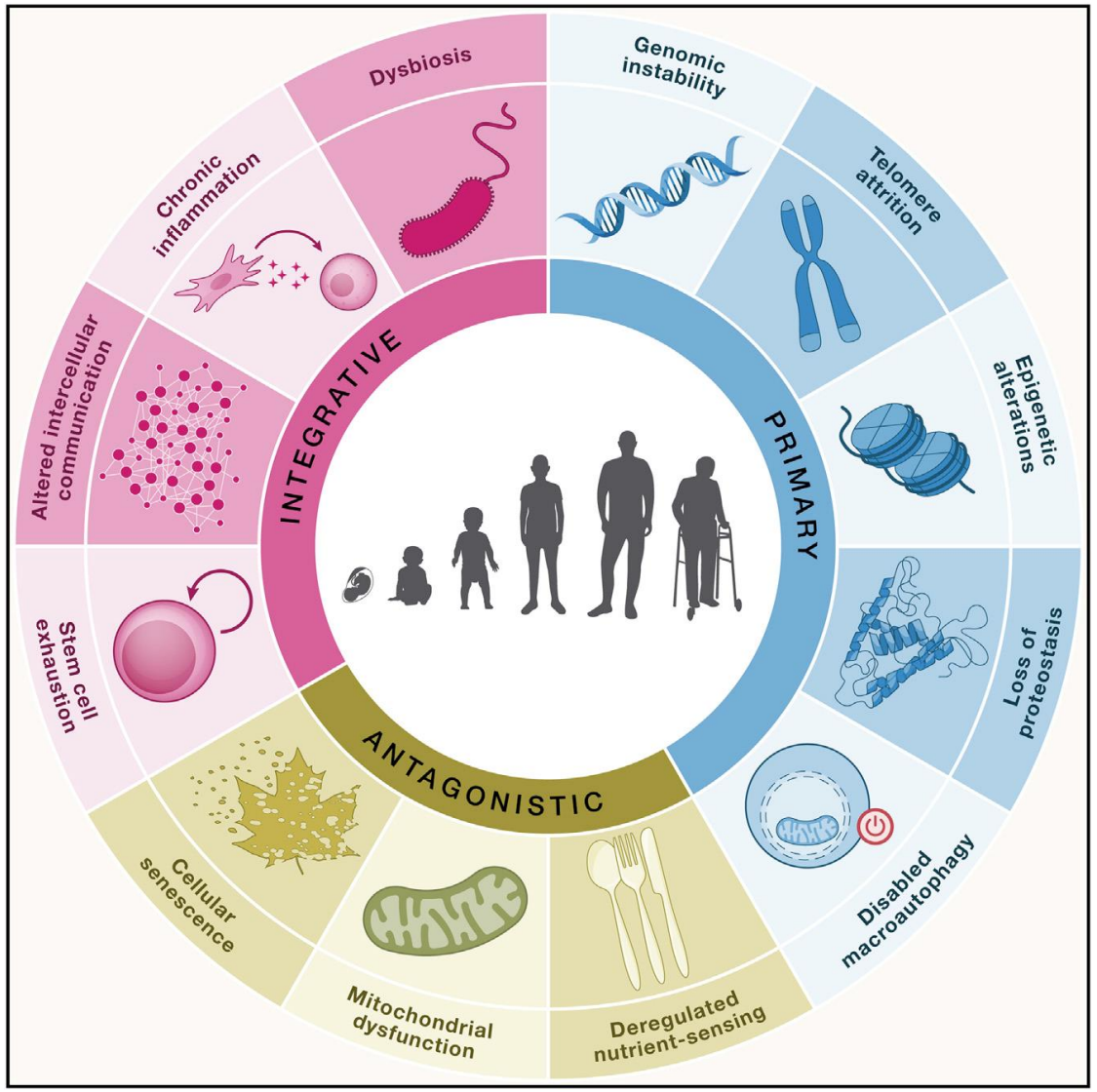
**Kojima G. Ageing Research Reviews 2019; 50: 81–88**

# A 12-week multicomponent exercise program reverse frailty in older adults living with HIV




CROI 2023.Brañas F. et al.P701

# Hallmarks of ageing




12 hallmarks of ageing interconnected among each other.

Also interconected with 8 hallmarks of health which include:

- Maintenance of homeostasis,
- Adequate responses to stress.

López-Otín et al.Cell 2023

# Holistic approach of ageing

1. Adapt therapeutic target to frailty state
2. Prescribe multicomponent and strength excercise
3. Nutrition
4. Reach a BMI between 20-25 kg/m2
5. Supplement vitamin D if deficiency
6. Deprescribing unnecessary medication and avoid polypharmacy (Beers, STOP-STAR criteria)
7. Technological resources to promote independence

# Conclusions

- ✓PLWH are getting older with important comorbidities
- ✓Identification of vulnerability is a priority
- ✓Vulnerable situations may be reversible with a preemptive intervention
- ✓Polypharmacy must be evaluated and unnecesary drugs stopped periodically
- ✓We must be proactive to promote a healthy ageing