HIV Neuropsychiatry

www.neuropsychiatry-hiv.com

Aging with HIV: focus on CNS

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DI MODENA E REGGIO EMILIA

Objective:

- to highlight the unmet needs of an ageing HIV population from a clinical and community perspective, and how service provision needs to change to address them
- To critically discuss the applicability of geriatric research tool in HIV research

Headings

- Epidemiological surveillance
- Prevention
- The ageing trajectories
- Multi-Component Interventions
- Health care provision

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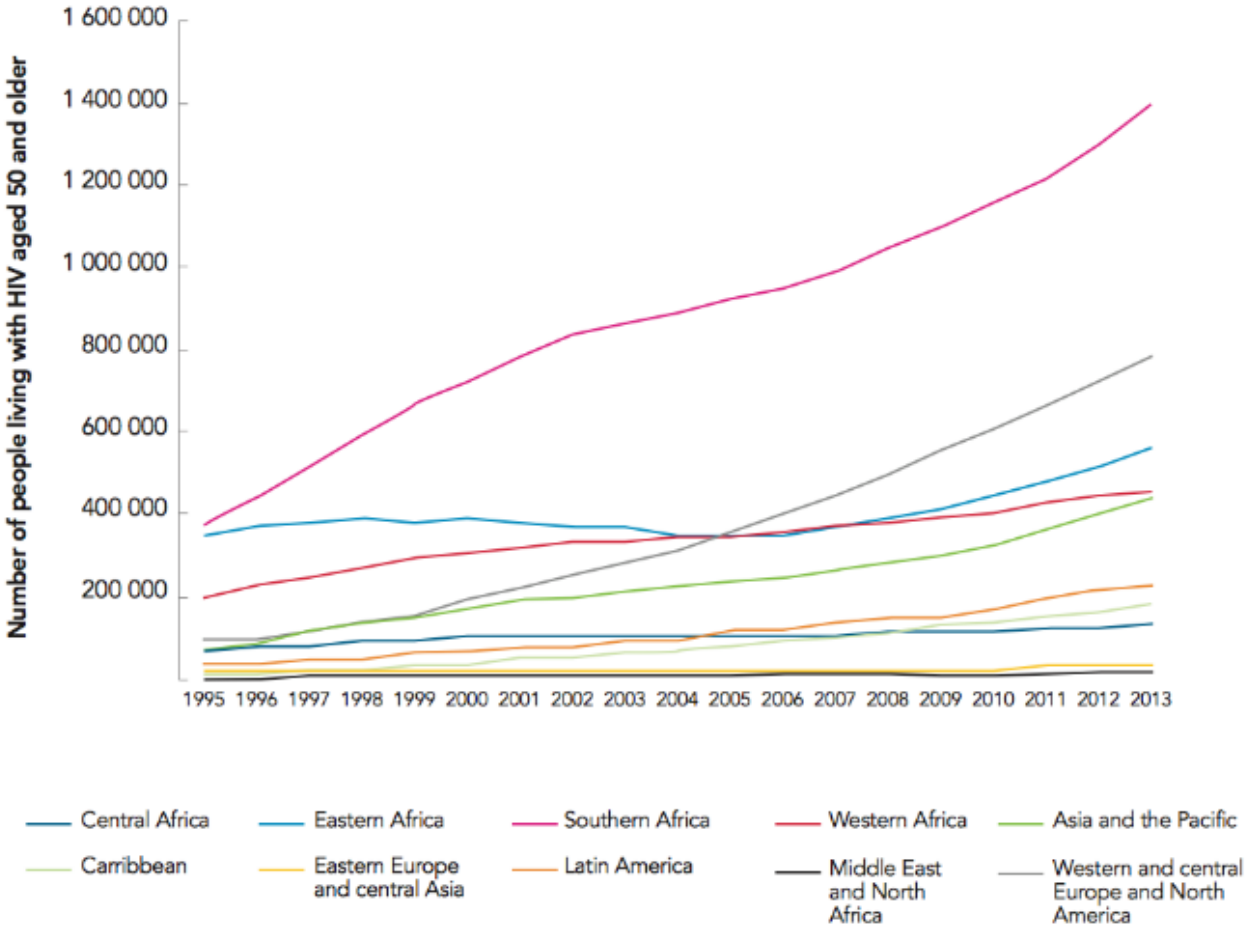
Life expectancy close to normal population Will this be true in a rapidly changing population?

- ✓ These projections assume that the risk of mortality in the relatively small proportion of older individuals in contemporary cohort studies will reflect the risk actually observed in the future population
- ✓ Survival bias: the current older population of HIV-infected individuals survived the pre-ART and early ART eras and may well be enriched for favourable host genetics and healthier lifestyles than the general population.

Hunt PW. Curr Opin HIV AIDS. 2014 Jul;9(4):302-8.

Estimated number of persons living with HIV aged ≥50 by region (1995-2013)



- ✓ There are approximately 4.2 million persons aged ≥50y living with HIV today.
- ✓ More than 2 million of which live in sub-Saharan Africa.

The Gap Report. Available at: http://www.unaids.org/sites/default/files/media_asset/UNAIDS_Gap_report_en.pdf. Accessed February 2015

Headings

- Epidemiological surveillance
- Prevention
- The pathway from disease to disability
- Multi-Component Interventions
- Health care provision

The Graying of AIDS

POSTS TAGGED 'AGE IS NOT A CONDOM'

Show Some Skin for a Great Cause!

Headings

- Epidemiological surveillance
- Prevention
- The ageing trajectories
- Multi-Component Interventions
- Health care provision

Male a

Robustness

Frailty

Disability

25 years

65 years

In the general population a 60 to 85% increase of fat mass, predominantly represented by visceral adiposity (VAT), is expected between 25 and 65 years of age; in the same period there is a 20% decline of skeletal muscle mass.

PATIENT AGEING TRAJECTORY

2000 — 2005 — 2010 — 2013 — 2015

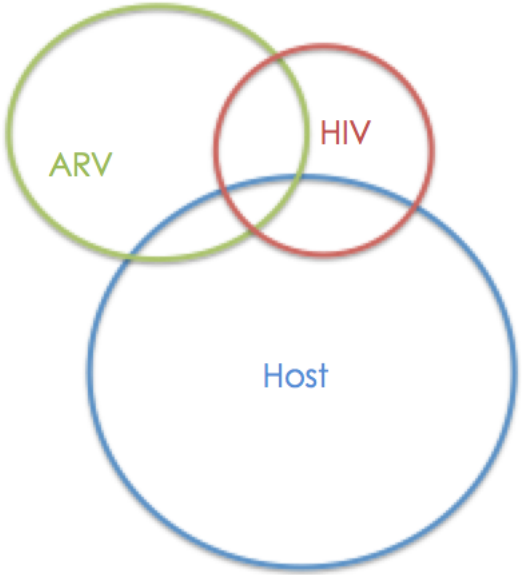
Drug toxicities — Co-morbidities — Multi-morbidities — Frailty — Disability

2002

2011

2015

Was my patient ever robust?



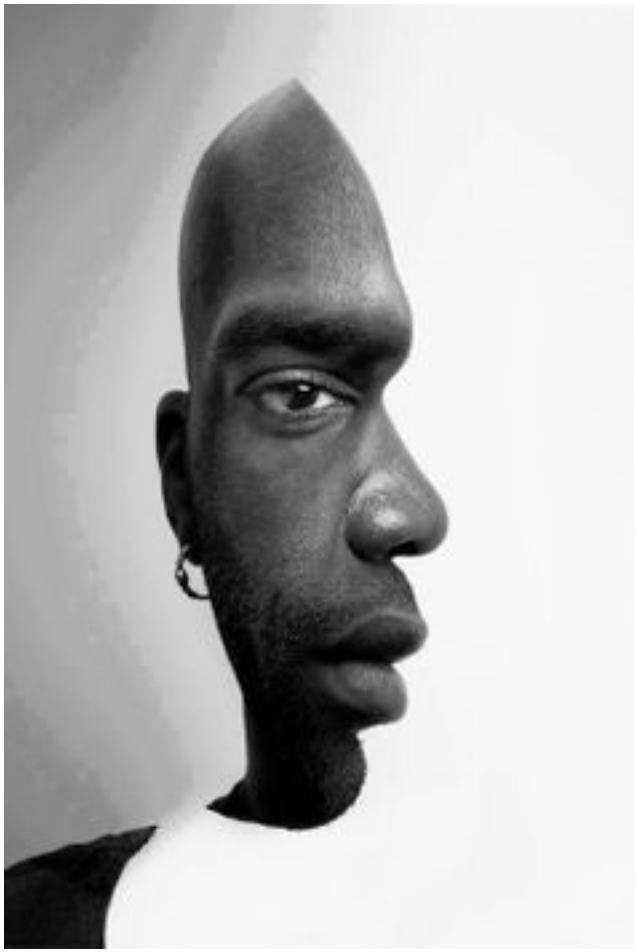
Was there a contribution of HIV and of drug toxicities?

Does HIV causes accelerated or accentuated risk of ….? A two sided perspective

1. To improve overall health and quality of life of a frail HIV individual:

- ✓ Screen
- ✓ Recognise
- ✓ Treat

HIV is associated with an increased risk of multimorbidity and mortality,
which is likely to take on increasing public health importance as the HIV epidemic gets older.



2. To identify target for intervention to prevent multimorbidity and frailty in HIV infection:

- ✓ Identify HIV specific mechanism

Although the clinical phenotype of HIV-associated multimorbidity shares many features with ageing-related frailty, its root causes may in fact be distinct, requiring different interventions for prevention.

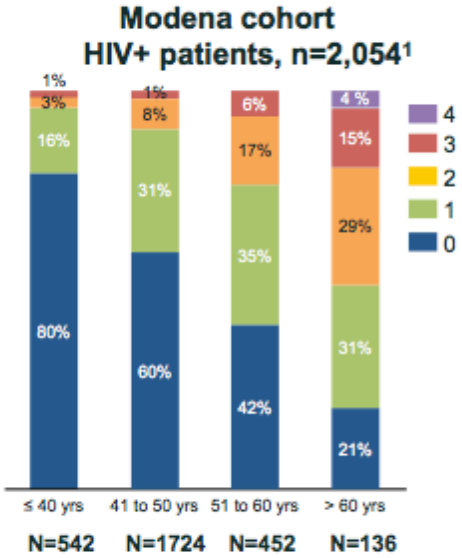
Hunt PW. Curr Opin HIV AIDS. 2014 Jul;9(4):302-8.

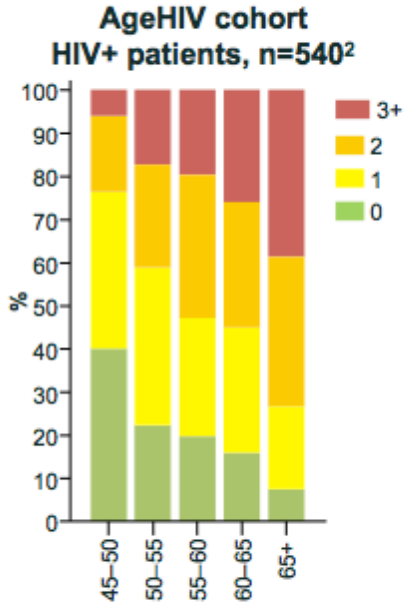
PATIENT AGEING TRAJECTORY

2000 2005 2010

Drug toxicities Co-morbidities Multi-morbidities

Prevalence of comorbidities and multimorbidity increases with age





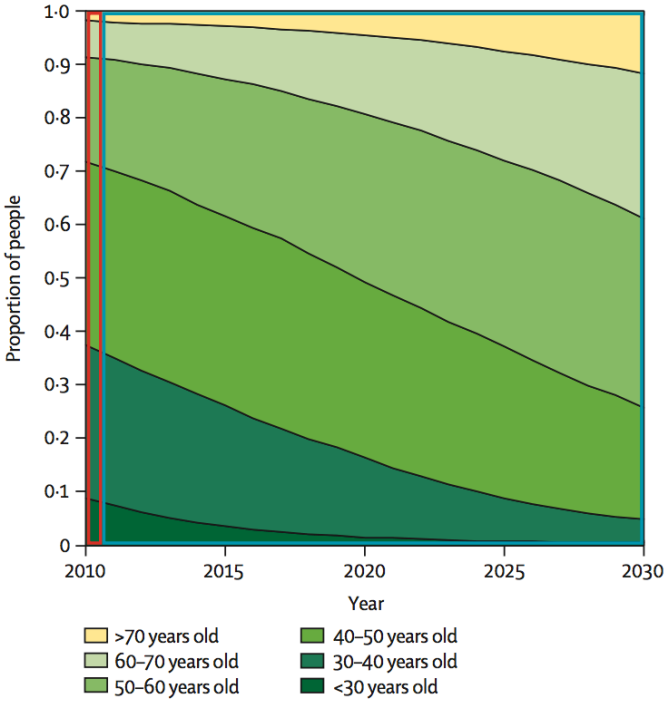
In the Modena cohort: Multimorbidity prevalence in those aged 51–60 years was 20%[1]
In the AgeHIV cohort: Multimorbidity prevalence was 40%[2]
Multimorbidity prevalence was higher in cases than controls in all age strata

1. Guaraldi G, et al. Clin Infect Dis. 2011;53:1120–6; 2. Schouten J et al. Clin Infect Dis. 2014; 59: 1787-1797

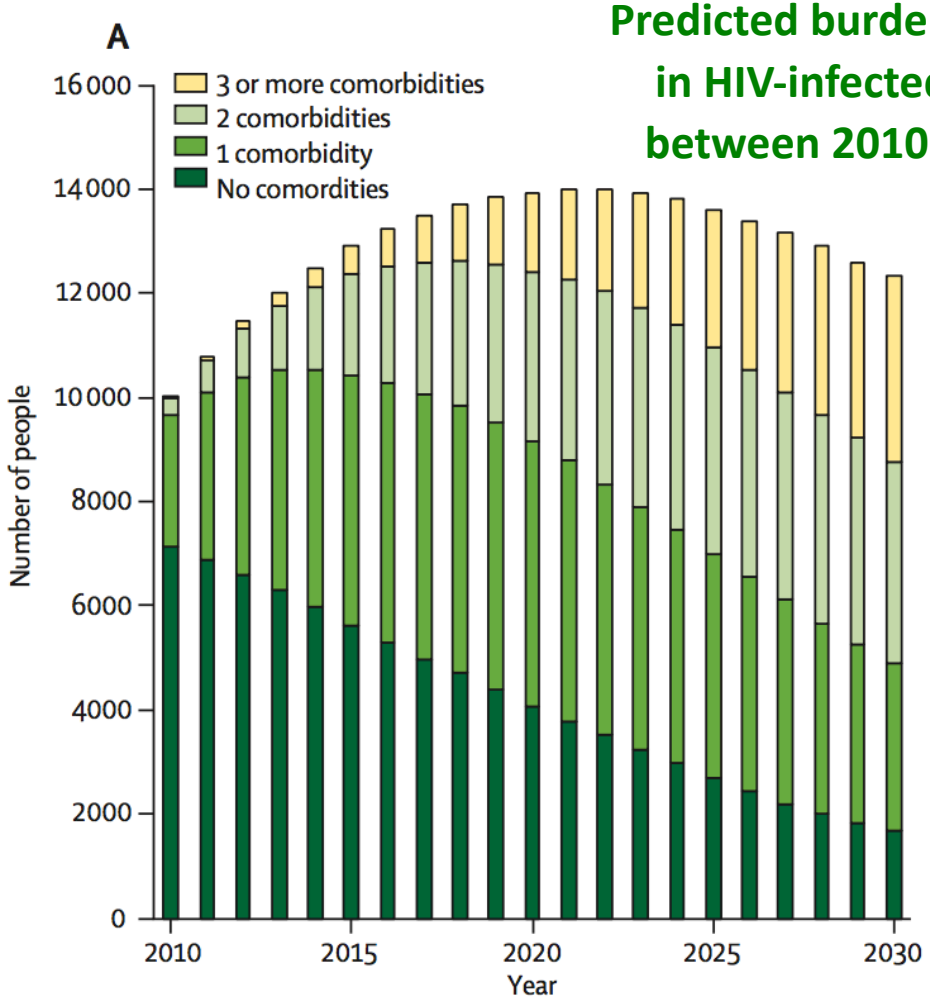
Future challenges for clinical care of an ageing population infected with HIV: a modelling study

Mikaela Smit, Kees Brinkman, Suzanne Geerlings, Colette Smit, Kalyani Thyagarajan, Ard van Sighem, Frank de Wolf, Timothy B Hallett, on behalf of the ATHENA observational cohort

Projected age distribution of HIV-infected patients



Predicted burden of NCDs in HIV-infected patients between 2010 and 2030



www.thelancet.com/infection **Published online June 10, 2015** **http://dx.doi.org/10.1016/S1473-3099(15)00056-0**

PATIENT AGEING TRAJECTORY

2000	2005	2010	2013
Drug toxicities	Co-morbidities	Multi-morbidities	Frailty

Frailty has been proposed as a measure of biological (opposed to chronological) aging

83 years old;
HTN, Hyperlipidemia, prior MI

83 years old;
HTN, Hyperlipidemia, prior MI

This variable vulnerability among people of the same chronological age is known as **frailty**

JAMDA 14 (2013) 392–397

JAMDA

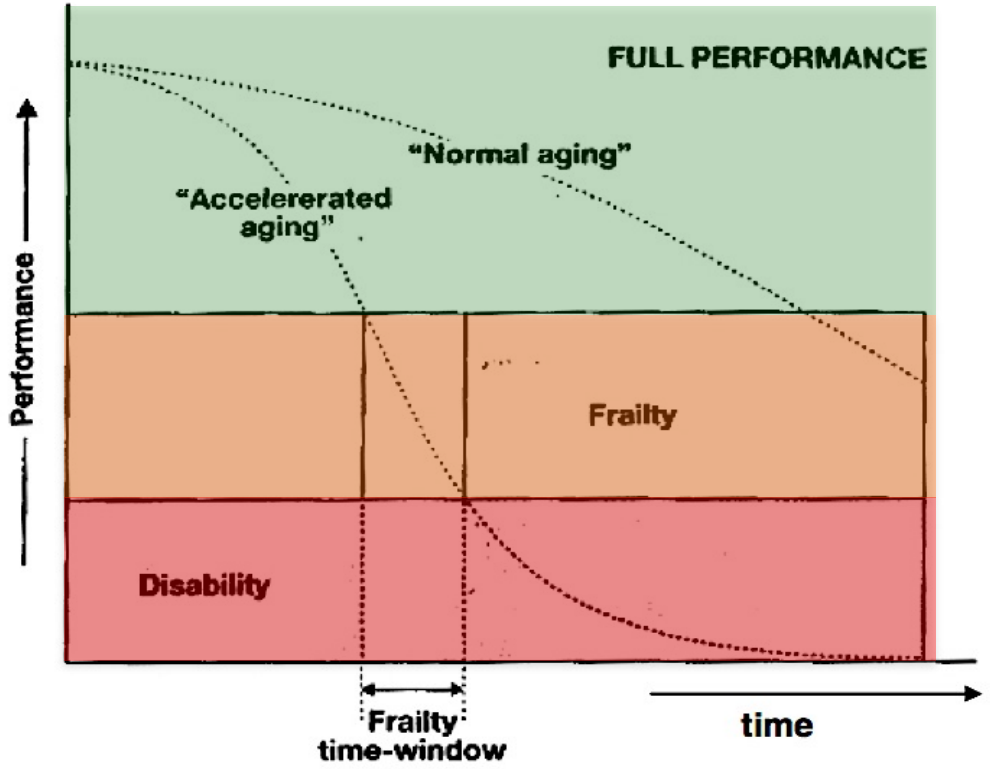
journal homepage: www.jamda.com

Special Article

Frailty Consensus: A Call to Action

John E. Morley MB, BCh [a,*], Bruno Vellas MD [b,c], G. Abellan van Kan MD [b,c], Stefan D. Anker MD, PhD [d,e], Juergen M. Bauer MD, PhD [f], Roberto Bernabei MD [g], Matteo Cesari MD, PhD [b,c], W.C. Chumlea PhD [h], Wolfram Doehner MD, PhD [d,i], Jonathan Evans MD [j], Linda P. Fried MD, MPH [k], Jack M. Guralnik MD, PhD [l], Paul R. Katz MD, CMD [m], Theodore K. Malmstrom PhD [a,n], Roger J. McCarter PhD [o], Luis M. Gutierrez Robledo MD, PhD [p], Ken Rockwood MD [q], Stephan von Haehling MD, PhD [r], Maurits F. Vandewoude MD, PhD [s], Jeremy Walston MD [t]

"…A medical syndrome with multiple causes and contributor that is characterized by diminished strength, endurance and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death…"

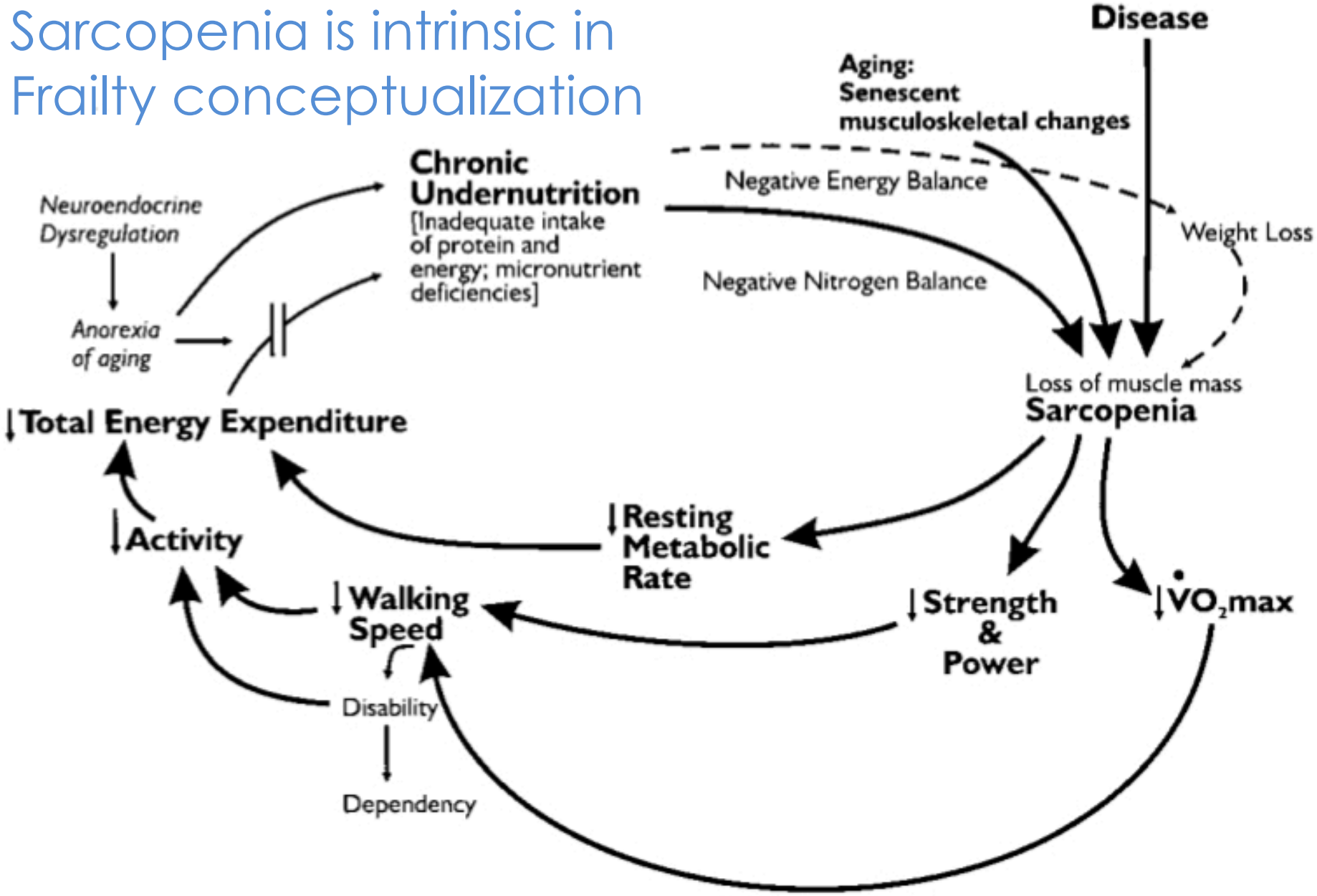


Frailty implication for clinical practice

Risk prediction

Trajectories of changes in the health status (Health transitions)

Sarcopenia is intrinsic in Frailty conceptualization



Fried LP, Walston J. Failure to thrieve.
In: Hazzard WR et al, eds. *Principles of Geriatric Medicine and Gerontology*. McGraw-Hill, 1998

Frailty recognition in clinical practice

Frailty Related Phenotype

A person can be said to be frail if they have any 3 of the following features:

1. They move slowly.
2. They have a weak handgrip.
3. They have reduced their level of activity.
4. They have (unintentionally) lost weight.
5. They feel exhausted.

✓ "pre-frail" is used when only one or two of these deficits is present.

✓ Clinically recognizable and not otherwise definable as being disabled or as having multiple co-morbid illnesses

Fried et al., *J Gerontol Med Sc* 2001

Frailty recognition in clinical practice

Fried et al., *J Gerontol Med Sc* 2001

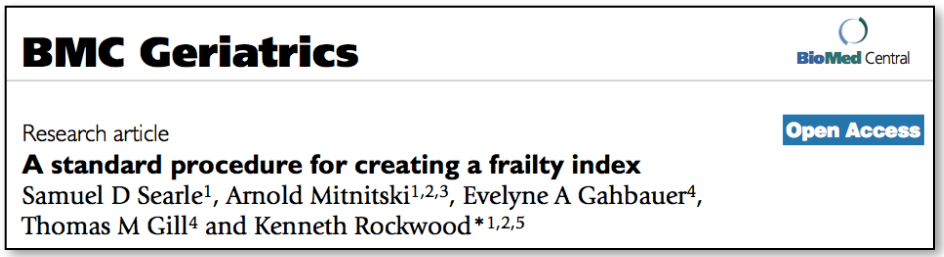
Frailty as a deficit accumulation

Frailty can be operationalized as deficit accumulation and can be expressed in a frailty index

A frailty index derived from routinely collected clinical data can offer insights into the biology of aging using mathematics of complex systems

Can be summarised as a scale from robust to terminally Ill

Rockwood et al. Lancet 1999;353:205-6



BMC Geriatrics

BioMed Central

Research article

Open Access

A standard procedure for creating a frailty index

Samuel D Searle[1], Arnold Mitnitski[1,2,3], Evelyne A Gahbauer[4], Thomas M Gill[4] and Kenneth Rockwood*[1,2,5]

BRIEF METHODOLOGICAL REPORTS

Relative Fitness and Frailty of Elderly Men and Women in Developed Countries and Their Relationship with Mortality

Arnold Mitnitski, PhD,[§] Xiaowei Song, PhD, Ingmar Skoog, PhD, MD,[‖] GA Broe, MBBS,[¶] Jafna L. Cox, MD,[†] Eva Grunfeld, MD,[‡] and Kenneth Rockwood, MD**

Variables can be included in a frailty index if they are deficits:

Can include measures of any health problems ("deficits") as long as:

- ✓ Related to age
- ✓ Related to poor health
- ✓ As a group, include multiple physiological systems
- ✓ As a group, should number at least around 30

The frailty index approach is robust across different settings, in different populations, using different numbers and types of health variables, consistently related to age and to adverse outcomes.

BMC Geriatrics 2008, 8:24

J Am Geriatr Soc 53:2184–2189, 2005.

The frailty phenotype and the frailty index: different instruments for different purposes

Matteo Cesari[1,2], Giovanni Gambassi[3], Gabor Abellan van Kan[1,2], Bruno Vellas[1,2]

Main characteristics of the frailty phenotype and the Frailty Index

Frailty phenotype	Frailty Index
Signs, symptoms	Diseases, activities of daily living, results of a clinical evaluation
Possible before a clinical assessment	Doable only after a comprehensive clinical assessment
Categorical variable	Continuous variable
Pre-defined set of criteria	Unspecified set of criteria
Frailty as a pre-disability syndrome	Frailty as an accumulation of deficits
Meaningful results potentially restricted to non-disabled older persons	Meaningful results in every individual, independently of functional status or age

Key points:

- ✓ The frailty phenotype may be more suitable for an immedi- ate identification of non- disabled elders at risk of negative events.
- ✓ The Frailty Index may summarise the results of a compre- hensive geriatric assessment providing a marker of deficits accumulation.
- ✓ The two instruments have different purposes and are to be considered complementary in the evaluation of the older person.

Age and Ageing 2013; 0: 1–3

Gérontopôle Frailty Screening Tool (GFST)

Patients aged 65 years and older without both functional disability (Activities of Daily Living score ≥5/6) and current acute disease.

	YES	*NO*	*Do not know*
Does your patient live alone?	☐	☐	☐
Has your patient involuntarily lost weight in the last 3 months?	☐	☐	☐
Has your patient been more fatigued in the last 3 months?	☐	☐	☐
Has your patient experienced increased mobility difficulties in the last 3 months?	☐	☐	☐
Has your patient complained of memory problems?	☐	☐	☐
Does your patient present slow gait speed (i.e., >4 seconds to walk 4 meters)?	☐	☐	☐

If you have answered YES to one or more of these questions:

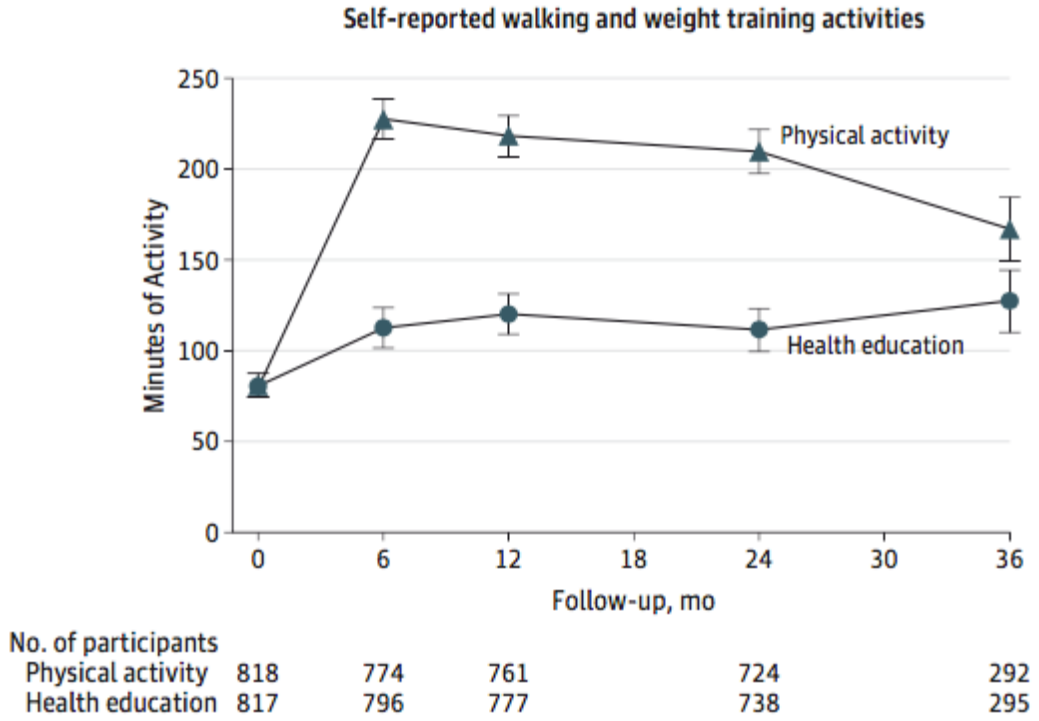
Do you think your patient is frail? ***YES*** ☐ ***NO*** ☐

If ***YES***, is your patient willing to be assessed for his/her frailty status at the Frailty Clinic? ***YES*** ☐ ***NO*** ☐

Original Investigation

Effect of Structured Physical Activity on Prevention of Major Mobility Disability in Older Adults

The LIFE Study Randomized Clinical Trial



CONCLUSIONS AND RELEVANCE

A structured, moderate-intensity physicalactivity program compared with a health education program reduced major mobility disability over 2.6 years among older adults at risk for disability.

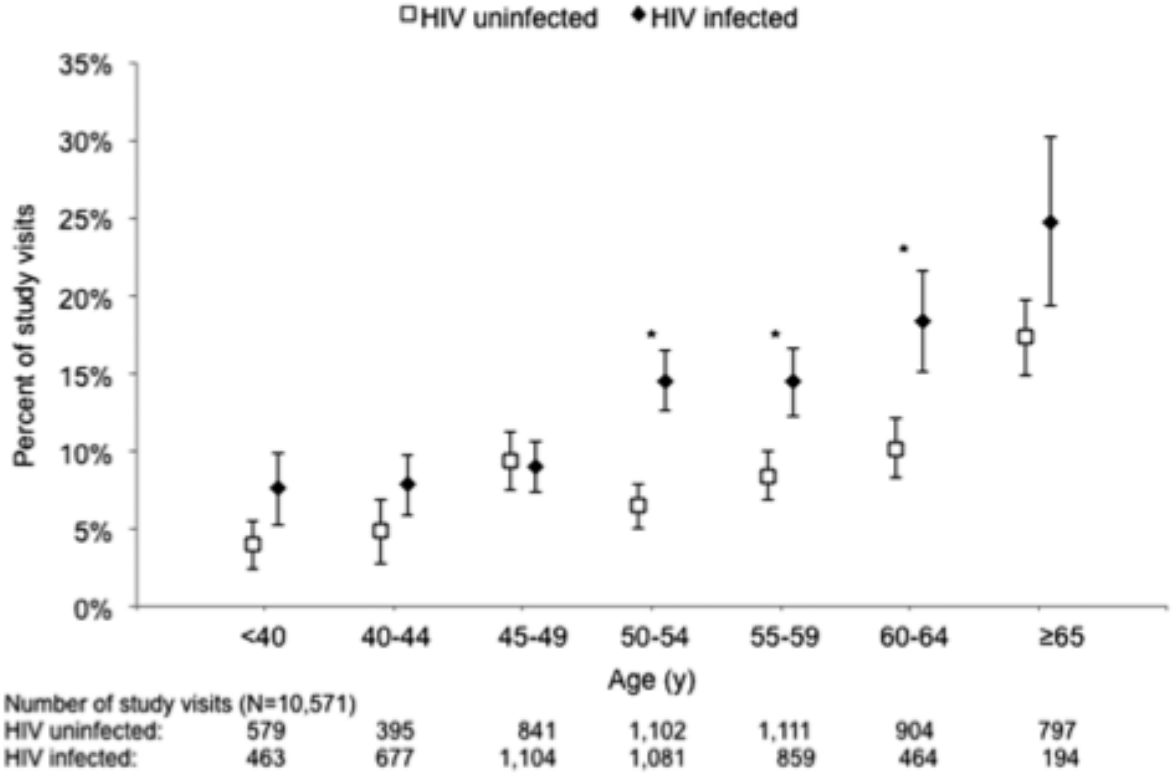
These findings suggest mobility benefit from such a program in vulnerable older adults

JAMA. 2014;311(23):2387-2396. doi:10.1001/jama.2014.5616

Journals of Gerontology: MEDICAL SCIENCES
Cite journal as: J Gerontol A Biol Sci Med Sci
doi:10.1093/gerona/glt148

Age, Comorbidities, and AIDS Predict a Frailty Phenotype in Men Who Have Sex With Men

Keri N. Althoff,[1] Lisa P. Jacobson,[1] Ross D. Cranston,[2] Roger Detels,[3] John P. Phair,[4] Xiuhong Li,[1] and Joseph B. Margolick[5]; for the Multicenter AIDS Cohort Study (MACS)



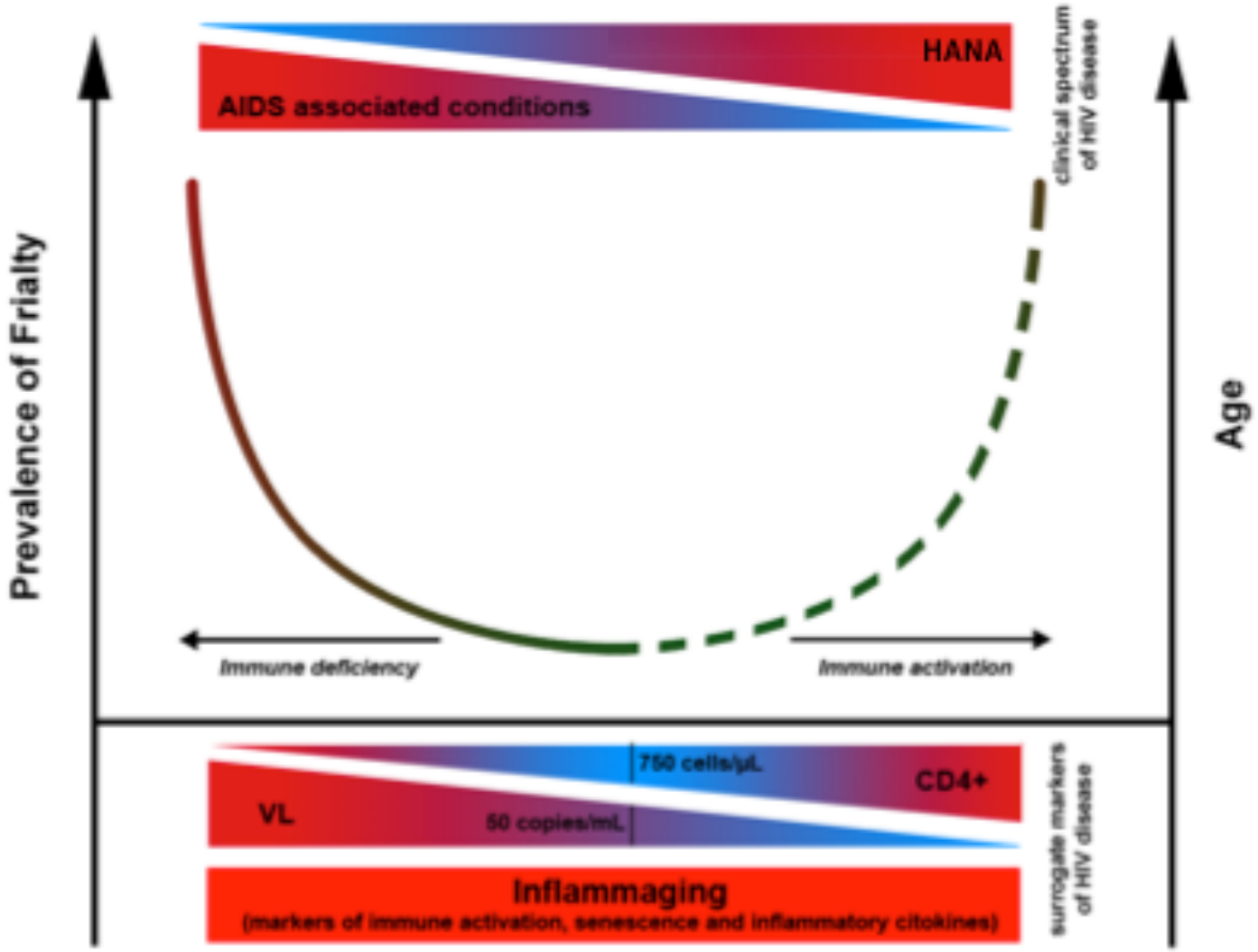
Factors associated with frailty-related phenotype (FRP) to predict MORTALITY in HIV-positive individuals on HAART

- **HIV-related measures**
  - Longer time since diagnosis (Aging!)
  - **AIDS diagnosis**
  - Lower current CD4 count
  - Lower nadir CD4 count
  - Low CD4/CD8 ratio
  - Detectable viral load
  - Protease inhibitor-containing HAART regimen
- **Social factors**
  - Smoke
  - Current unemployment
  - Low income in past year
  - **College degree**
- **Age**

- **Comorbidities**
  - Hepatitis C coinfection
  - Low BMI
  - High BMI
  - Lipodystrophy
  - **Depressive symptoms**
  - **T2DM**
  - **CKD**
  - Cognitive impairment
  - Inflammation
  - Weak upper and lower extremities

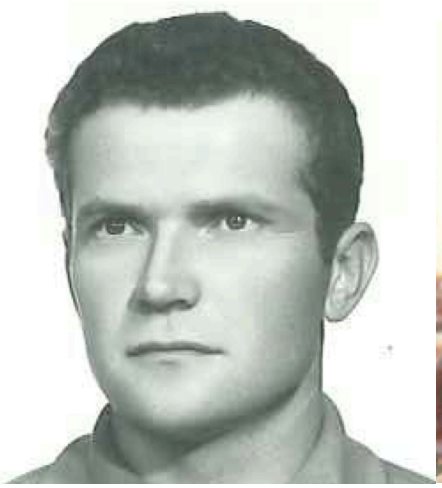
Terzian AS, J Womens Health (Larchmt), 2009;18(12):1965-1974. **Onen** NF. J Infect, 2009;59(5):346-352. **Piggott** DA. PloS One, 2013;8(1):e54910. **Ianas** V. J Int Assoc Provid AIDS Care, 2013;12(1):62-66. **Pathai** S, JAIDS 2013;62(1):43-51. **Erlandson** KM. HIV Clin Trials, 2012;13(6):324-334. **Shah** K. J Am Geriatr Soc, 2012; Mar;60(3):545-549. **Justice** AC, JAIDS, 2013;62(2):149-163. **Adeyemi** O, JAIDS 2013;63(2):e78-e81.

Hypothetical association between frailty, HANA and immune activation / inflammation



Mr. X case study

To what extent Pt Age changes our clinical practice?

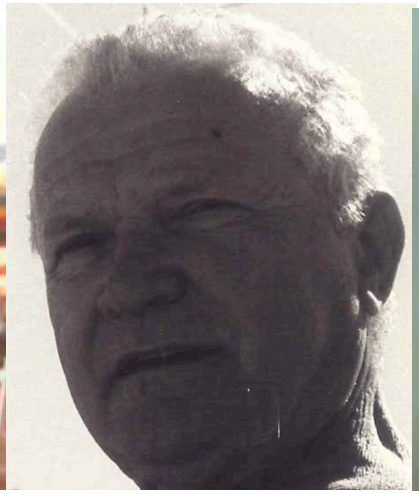


25 yrs
CD4=250µL
VL=73000/mL

Naive

45 yrs
CD4=650µL
VL<40/mL

Experienced



65 yrs
CD4=250µL
VL=73000/mL

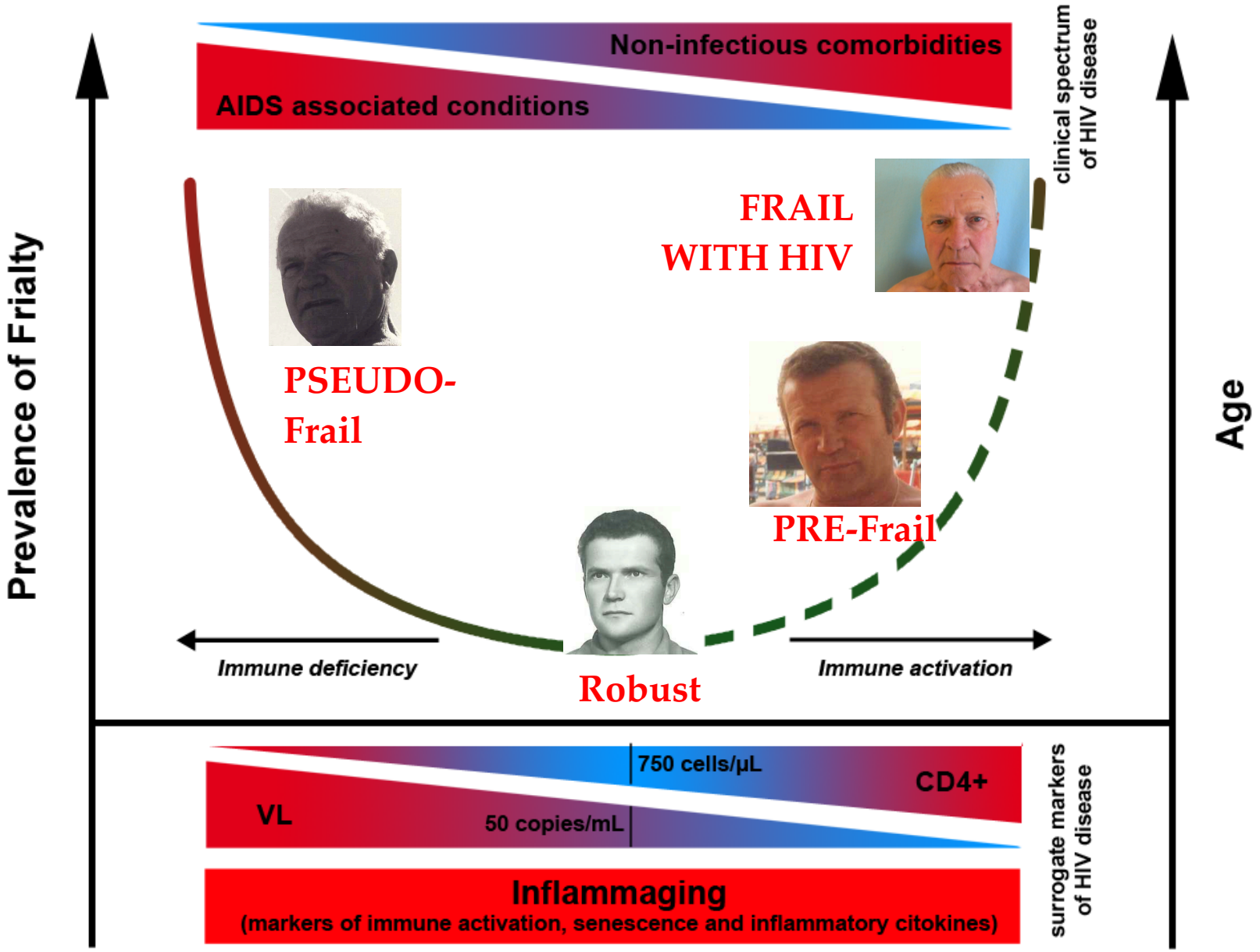
Naive

75 yrs
CD4=650µL
VL<40/mL

Experienced

The patient and his family provided consent to show these

Hypothetical association between frailty, HANA and immune activation / inflammation



Frailty Index at MHMC

We constructed a Frailty Index (FI) from health variables collected as part of routine assessments in an HIV clinic

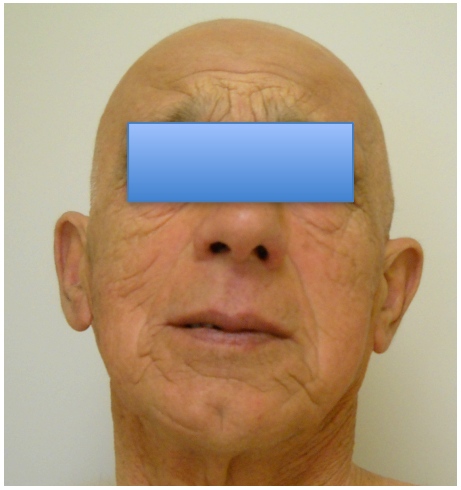
No.	Variable
1	Lipoatrophy
2	Lipohypertrophy
3	Non-alcoholic fatty liver disease
4	Menopause or male hypogonadism
5	High or low body mass index
6	High waist circumference
7	High visceral adipose tissue
8	Sarcopenia or presarcopenia
9	Insulin resistance
10	High total cholesterol
11	High low density lipoprotein
12	Low high density lipoprotein
13	High triglycerides
14	High homocysteine
15	Abnormal white blood cell counts
16	Anemia
17	Hepatitis C co-infection
18	Hepatitis B co-infection
19	Vitamin D insufficiency
20	Polypharmacy
21	Abnormal parathyroid hormone
22	Elevated D-dimer
23	Elevated C-reactive protein
24	Sedentary lifestyle
25	Atherosclerosis
26	Hyponatremia
27	Proteinuria or albuminuria
28	Elevated aspartate transaminase (AST)
29	Elevated alanine transaminase (ALT)
30	Abnormal alkaline phosphatase
31	Elevated gamma-glutamyl transphosphatase (GGT)
32	Low platelets
33	Abnormal potassium
34	Abnormal phosphorus
35	Abnormal thyroid stimulating hormone
36	Elevated total bilirubin
37	Unemployment

Guaraldi G, 16th International Workshop on Co-morbidities and Adverse Drug Reactions in HIV AIDS 2015 in press

Frailty Index use at Modena HIV Metabolic Clinic

Male
80 years
CD4=701
HIV VL<40 c/ mL

IMA,
HTN
T2DM
OO
Cirrhosis



Male
83 years
CD4=661
HIV VL<40 c/mL

IMA
OO

Visita [redacted] GIUSEPPE 07/04/1935 Anagrafica

Data Es:	HIVFI (>.4):	HIVMMFI (>.4):	FI (>.39):	MMFI (>.37):	Deficit:
20/05/2014	0,4693878	0,4418605	0,4883721	0,4594595	23
11/12/2012	0,4705882	0,4444444	0,5116279	0,4864865	24
13/12/2011	0,509804	0,4666667	0,5581396	0,5135135	26
13/12/2010	0,3921569	0,3555556	0,3953488	0,3513514	20
15/03/2010	0,3877551	0,3636364	0,4146341	0,3888889	19

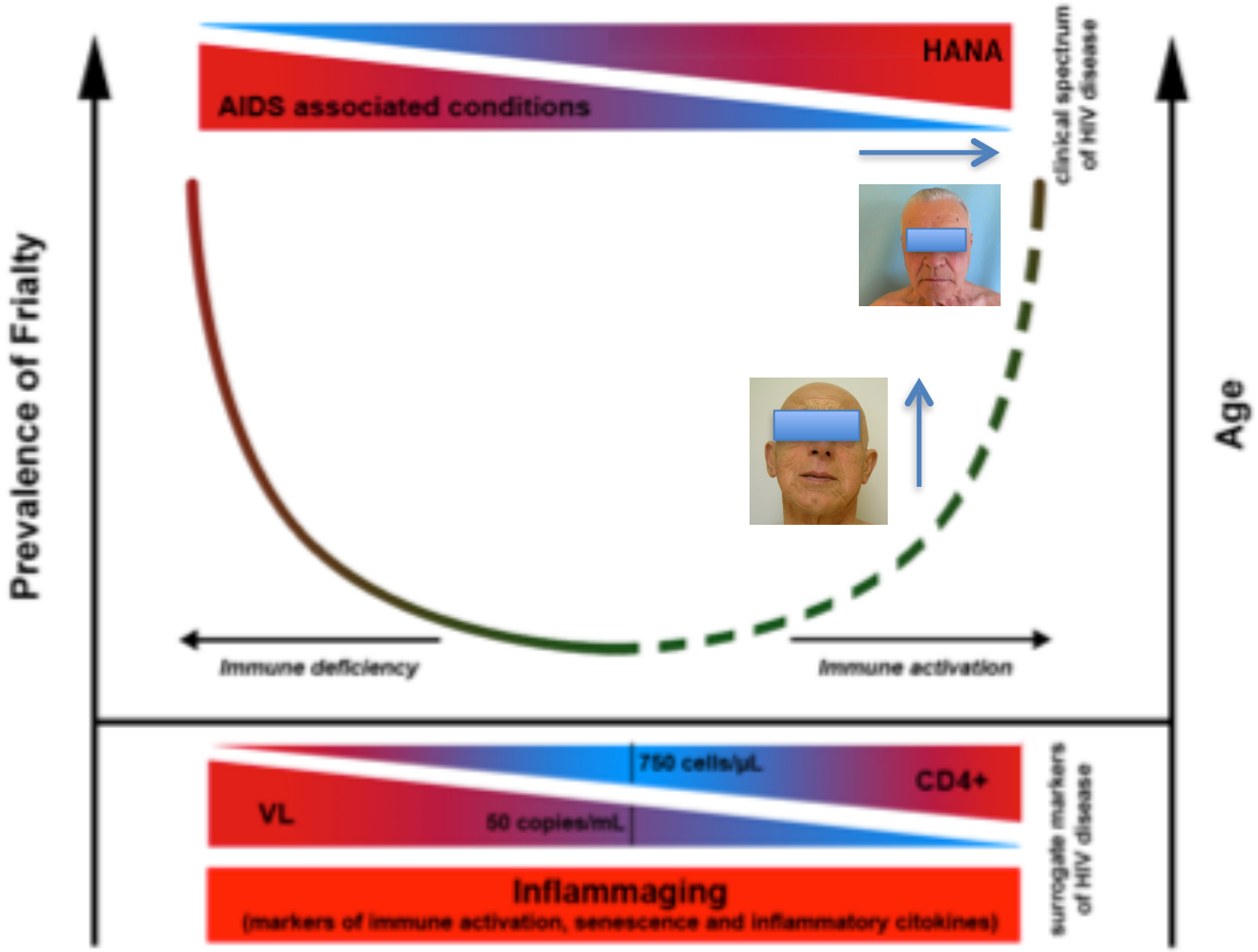
Visita [redacted] CARLO 29/09/1932 Anagrafica

Data Es:	HIVFI (>.4):	HIVMMFI (>.4):	FI (>.39):	MMFI (>.37):	Deficit:
11/11/2013	0,2708333	0,2380952	0,3023256	0,2702703	13
24/09/2012	0,2857143	0,255814	0,3333333	0,3055556	14
20/09/2011	0,22	0,1818182	0,255814	0,2162162	11
07/09/2010	0,24	0,2045455	0,2790698	0,2432432	12
04/06/2010					9

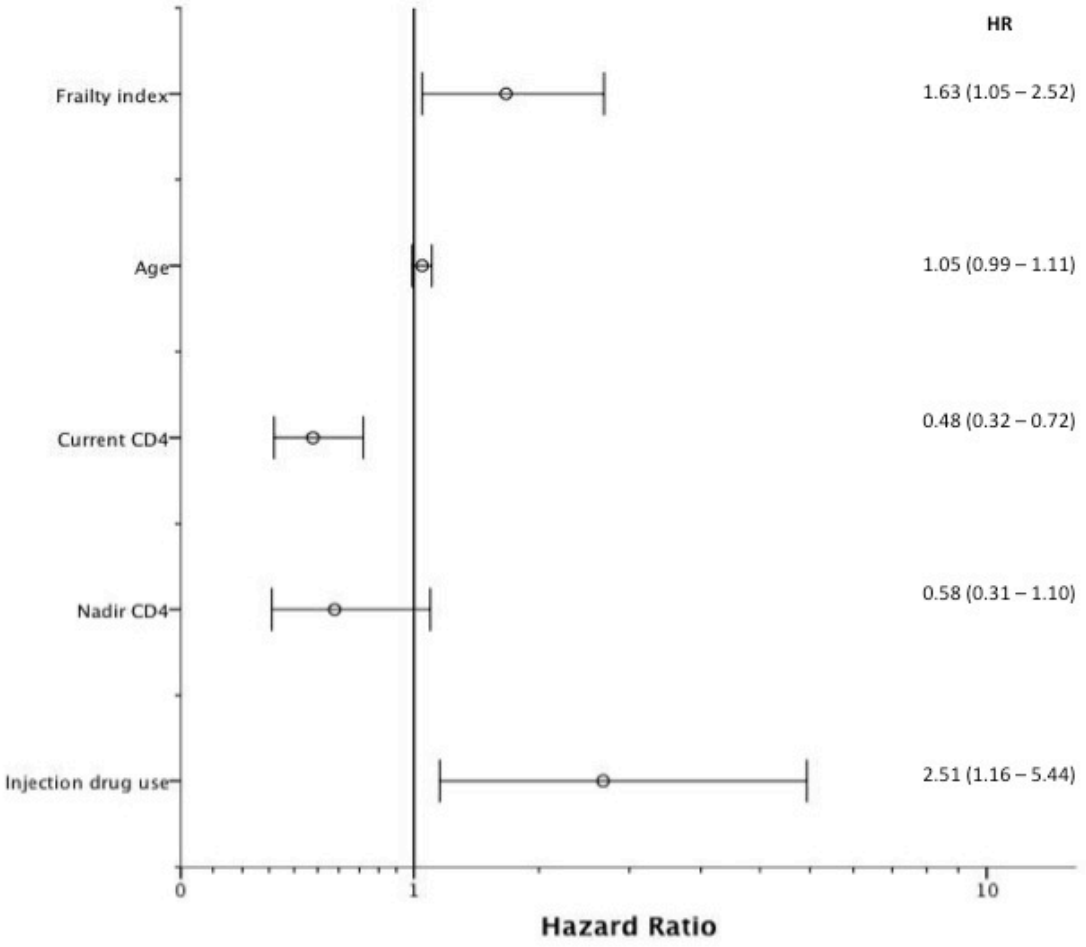
Frailty Index in routine clinical management:

- ✓ Comprehensive evaluation of clinical visit
- ✓ Evaluation of health transition
- ✓ Time interval of Follow Up visits
- ✓ Home base health care provision

Hypothetical association between frailty, HANA and immune activation / inflammation



Frailty index predicts survival independently from markers of HIV disease severity among people ageing with HIV

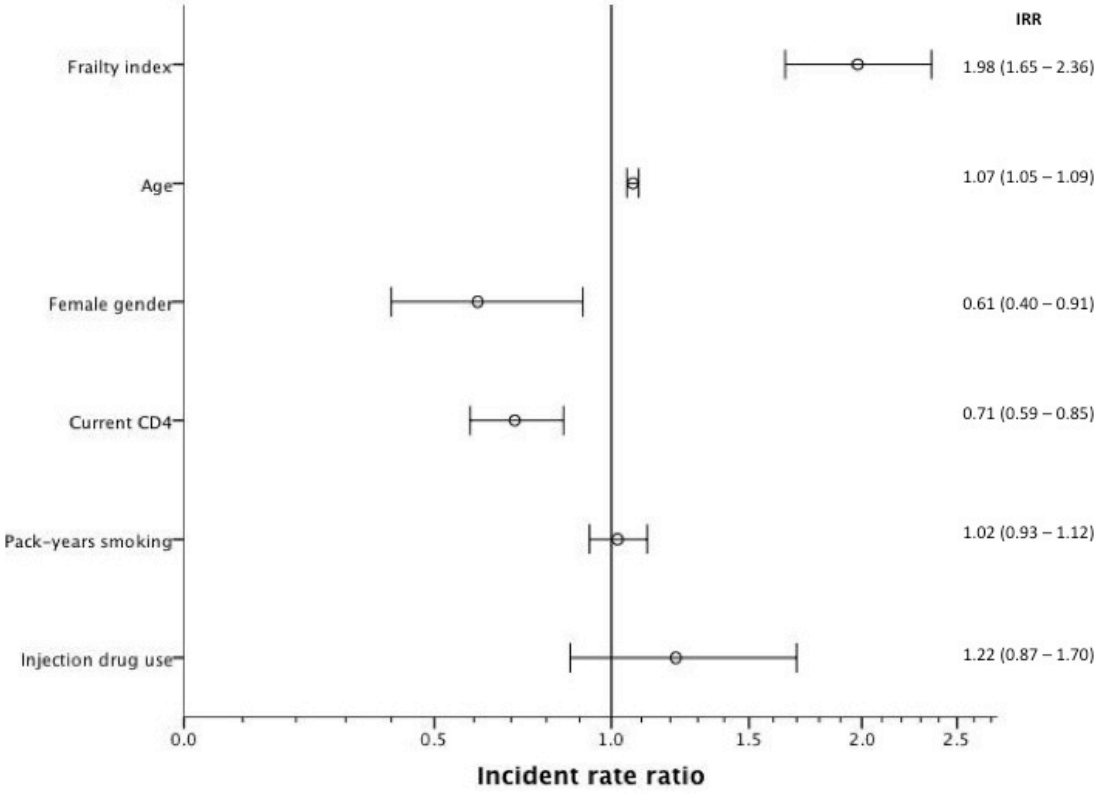


33 deaths over 8150 person-years follow-up (mortality rate; 0.40/100 PYFU)

Guaraldi G, 16th International Workshop on Co-morbidities and Adverse Drug Reactions in HIV
AIDS 2015 in press

Frailty index predicts incident multimorbidity independently from markers of HIV disease severity among people ageing with HIV

Poisson analyses to predict Mm



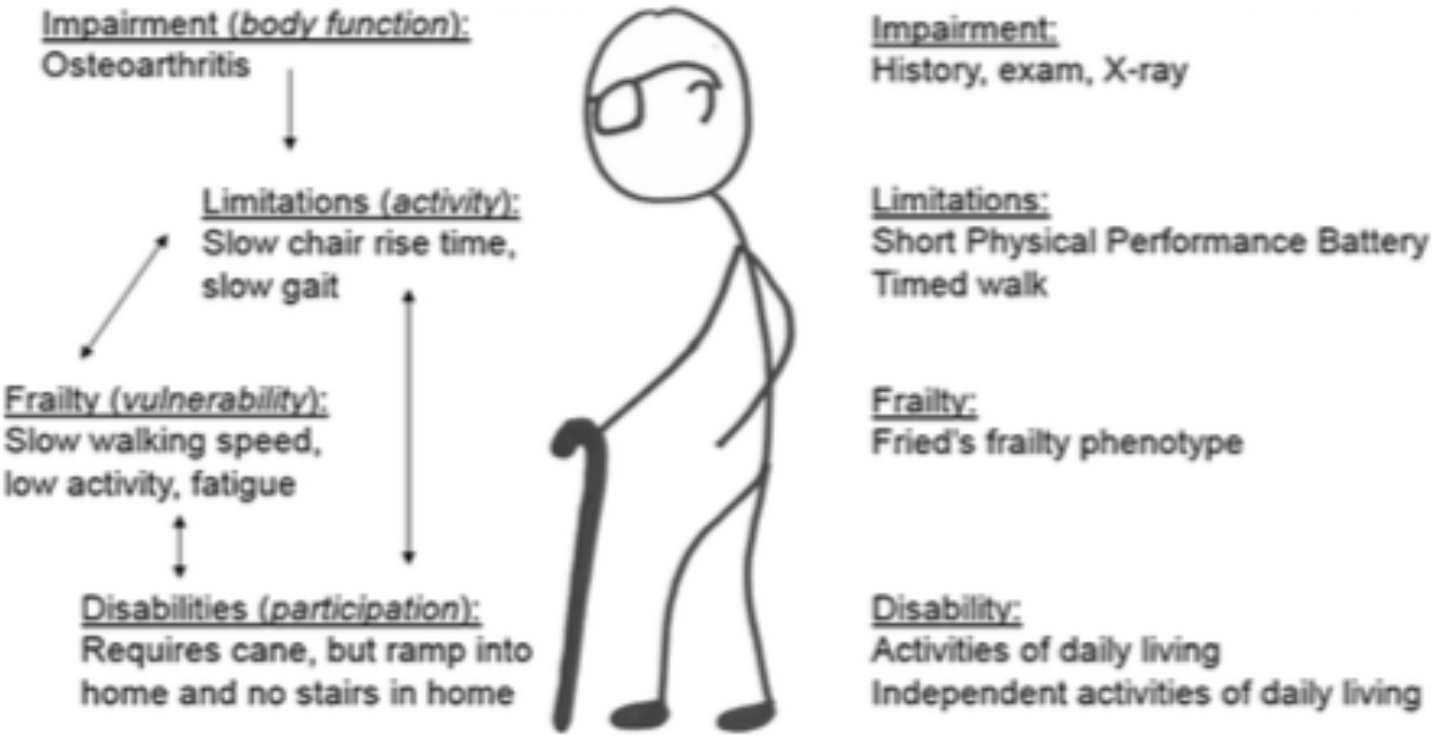
228 (9.4%) new MM over 6925 person-years follow-up (incident rate 3.29/100 PYFU)

Guaraldi G, 16th International Workshop on Co-morbidities and Adverse Drug Reactions in HIV. AIDS 2015 in press
Erlandson, K. M.,et al. Current HIV/AIDS Reports, 11(3), 279–290.

PATIENT AGEING TRAJECTORY

2000 | 2005 | 2010 | 2013 | 2015

Drug toxicities | Co-morbidities | Multi-morbidities | Frailty | Disability



Erlandson, K. M.,et al. Current HIV/AIDS Reports, 11(3), 279–290.

MAJOR ARTICLE

Association of Functional Impairment with Inflammation and Immune Activation in HIV Type 1–Infected Adults Receiving Effective Antiretroviral Therapy

Kristine M. Erlandson,[1,2] Amanda A. Allshouse,[3] Catherine M. Jankowski,[2] Eric J. Lee,[1] Kevin M. Rufner,[4] Brent E. Palmer,[5] Cara C. Wilson,[1] Samantha MaWhinney,[3] Wendy M. Kohrt,[2] and Thomas B. Campbell[1]

AIDS RESEARCH AND HUMAN RETROVIRUSES
Volume 29, Number 00, 2013

DOI: 10.1089/aid.2013.0020

Lipodystrophy and Inflammation Predict Later Grip Strength in HIV-Infected Men: The MACS Body Composition Substudy

Keith W. Crawford,[1,2] Xiuhong Li,[1,*] Xiaoqiang Xu,[1] Alison G. Abraham,[1,*] Adrian S. Dobs,[1] Joseph B. Margolick,[1] Frank J. Palella,[3] Lawrence A. Kingsley,[4] Mallory D. Witt,[5] and Todd T. Brown[1]

Headings

- Epidemiological surveillance
- Comorbidities
- Prevention
- The ageing trajectories
- Multi-Component Interventions
- Health care provision

EMPOWERMENT: Wellness checklist

Daily

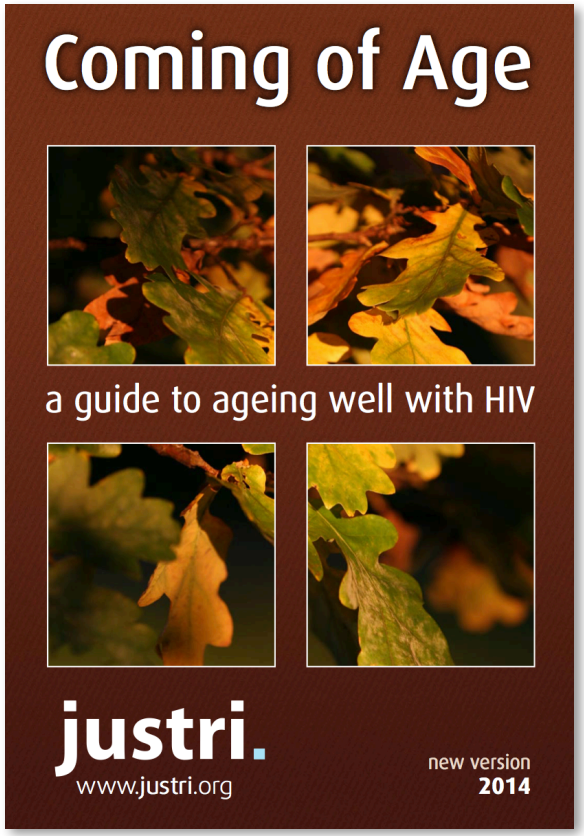
1. Could I exercize more today?
2. Have I bought the right food?
3. Should I drink less alcohol today?
4. Am I doing the right thing to help me sleep properly?
5. Am I doing something new today?
6. Am I keeping my brain active?

Weekly

1. Am I doing something nice with a friend this week?
2. What is my weight and is it changing?
3. Have I planned an active weekend?
4. Am I eating healthy?

Every three to four months

1. Do I feel well or unwell?
2. Have I had my checkup at the clinic?
3. What are my blood results?
4. Have I stopped smoking?
5. Are my finances in order?
6. How has my mood been recently?
7. What are my plans for the next few months?

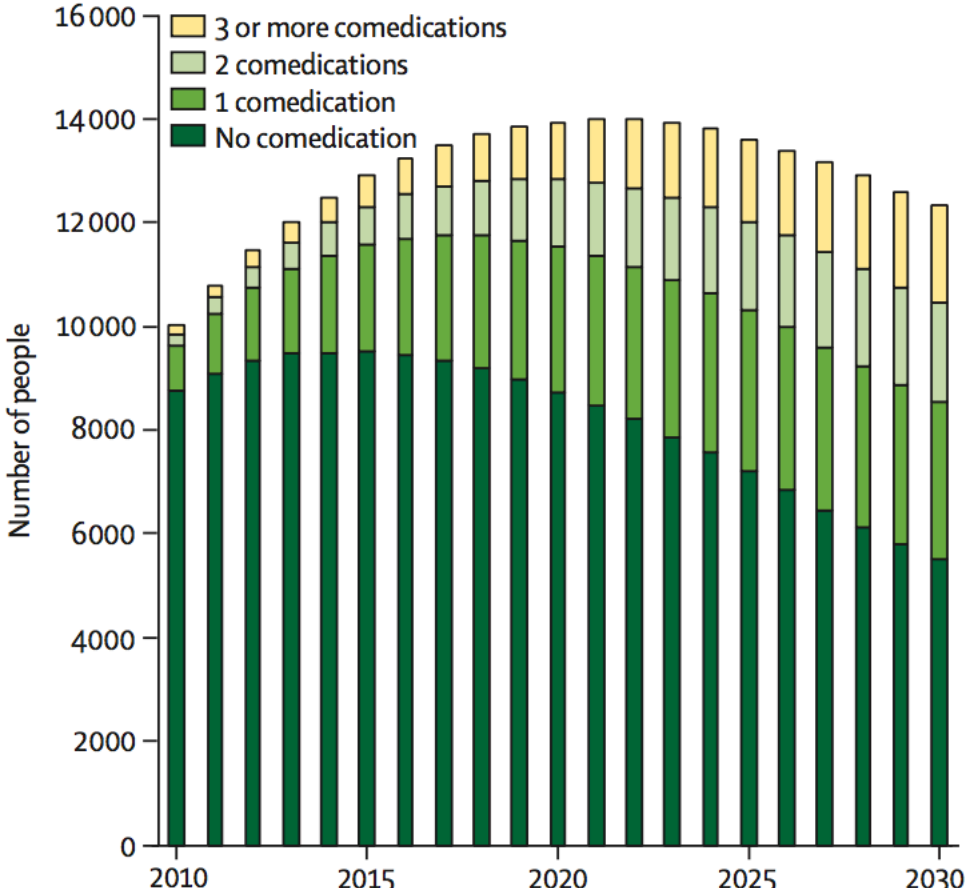


Coming of age. www.justry.org

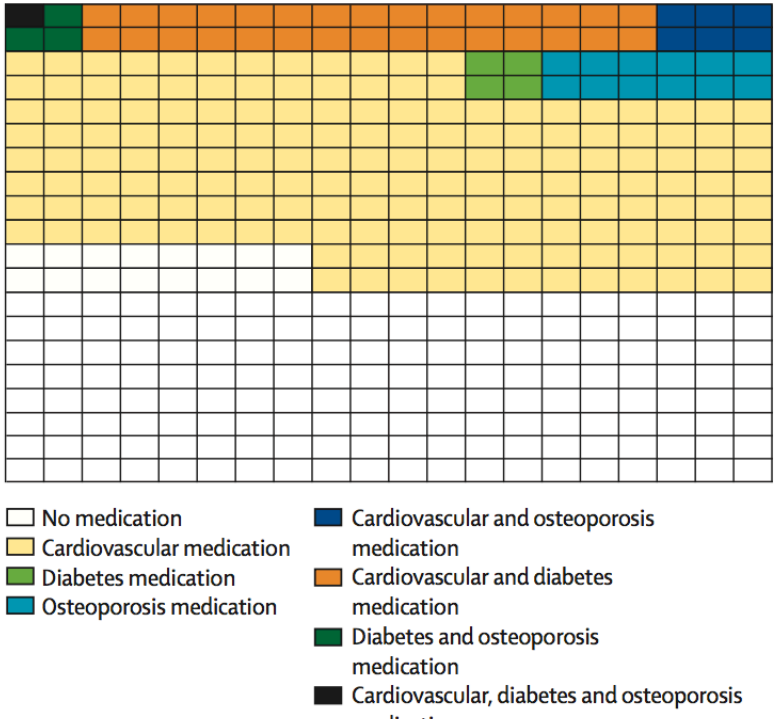
Future challenges for clinical care of an ageing population infected with HIV: a modelling study

Mikaela Smit, Kees Brinkman, Suzanne Geerlings, Colette Smit, Kalyani Thyagarajan, Ard van Sighem, Frank de Wolf, Timothy B Hallett, on behalf of the ATHENA observational cohort

Predicted burden of co-medications in HIV-infected patients between 2010 and 2030.



Predicted prevalence of comedication in 2030 as cross-section of number of patients on the different types of co-medications, based on a representative 400 patients (each square represents a patient). NCD=non-communicable disease.



www.thelancet.com/infection **Published online June 10, 2015 http://dx.doi.org/10.1016/S1473-3099(15)00056-0**

Novel concept in handling of HIV+ persons on stable ART at HIV clinics

- Comprehensive care of HIV+ persons involves:
  - Handling HIV-specific issues
  - General medicine – due to age related co-morbidities
  - Multidisciplinary approach
- Diversification of type of visits
  - Traditional f2f visit with responsible physician
  - Triage with experienced nurse
  - Community clinic
  - Telemedicine (for most stable patients)
- Enhancing self management
- Focus areas
  - Ensure retainment in care
  - Shared access to electronic systems (lab, medicine) to allow for proactive alert and prompts

HIV specialist physicians have to continue to lead the way to ensure optimization of quality of care for HIV+ persons

Lundgren J. Glasgow 2014

Take home message

- FI is applicable in clinical practice to describe health transition and suitable to depict the impact of ARV strategies in ageing trajectories
- Frailty is a significant **mediator & moderator** of the relationship between MM and Disability
- Both cognitive impairment and Depression are predictors of Frailty but the Depression moderate the impact of Cognitive impairment on Frailty
- Life style intervention and ARV strategies need to be integrated in the management of Senior HIV patients

Clinical suggestion:

- Diagnosis and treatment of depression is likely to be the most effective intervention to reduce the burden of Frailty and Disability

Thank you….
…and stay fit!