Evoluzione dei modelli
di gestione dell'infezione da HIV
Bologna . 30 maggio 2019

Anche i pazienti con malattia da HIV invecchiano: necessità di nuovi modelli di cura

VANNI BORGHI

AOU MODENA

The "Lisbon patient"

Miguel from Lisbon
He lives alone, prepares his own meals, and autonomously takes care of his medication.

Miguel was born on May 11, 1919
He is he first person living with HIV entering his 100th year of life.

https://beta.ctvnews.ca/national/features/the-lisbon-patient--meet-the-man-who-is-living-with-hiv-at-100.html

The "Lisbon patient"

HIV history

- ✓ Diagnosed HIV at the age of 84
- ✓ Presumably infected at the age of 75 YRS
- ✓ Nadir CD4 was <100 cells/μL and was AIDS presenter.
- ✓ Current CD4=560cells/μL (34%) with CD4/CD8=0.97.
- ✓ HIV RNA below limit of detection

Enviorment

- ✓ He lives in a healthy environment
- ✓ He never had financial difficulties
- ✓ His daughter lives next door (75 years old)

- ✓ He walks 30 min every day

https://beta.ctvnews.ca/national/features/the-lisbon-patient--meet-the-man-who-is-living-with-hiv-at-100.html

Piano Nazionale della Cronicità (PNC)

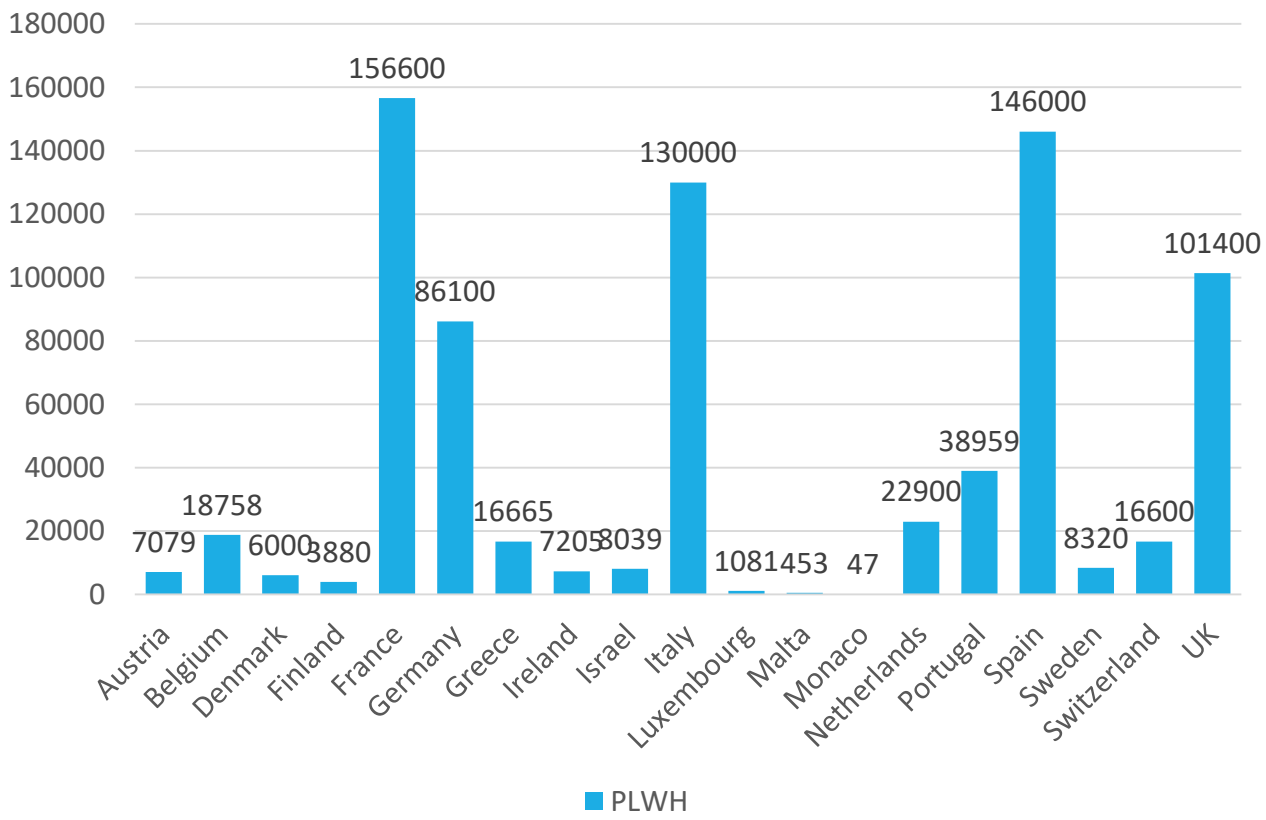
1. **Stratificazione popolazione**
2. Promozione salute, prevenzione, diagnosi precoce
3. **Presa incarico e gestione paziente**
4. **Erogazione interventi personalizzati**
5. Valutazione qualità cure

Obiettivi:

-Responsabilizzare tutti gli attori coinvolti

-Integrare le Cure Primarie e le Cure Specialistiche

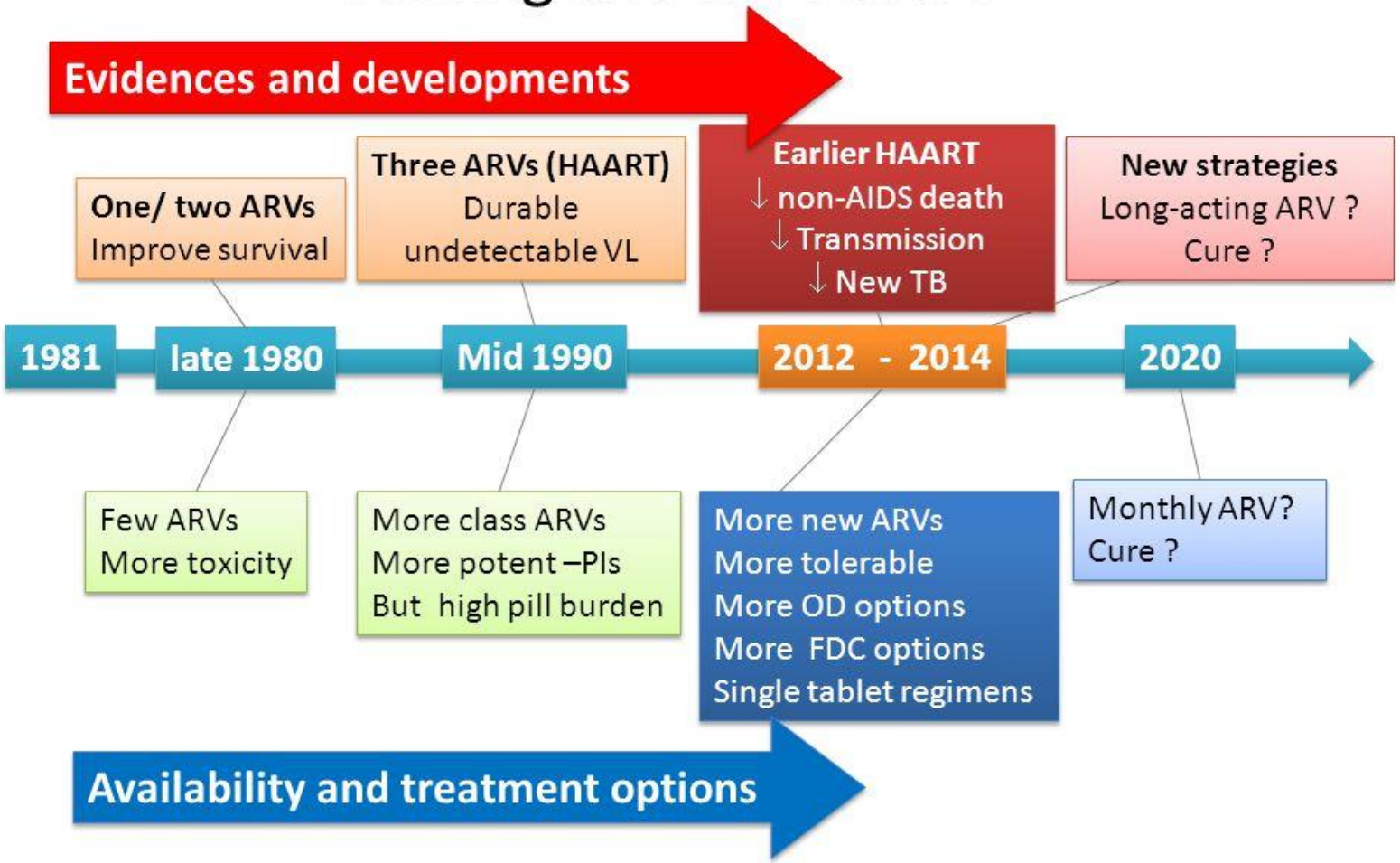
Estimated number of people living with HIV: countries in the West WHO subregions, reported in 2018



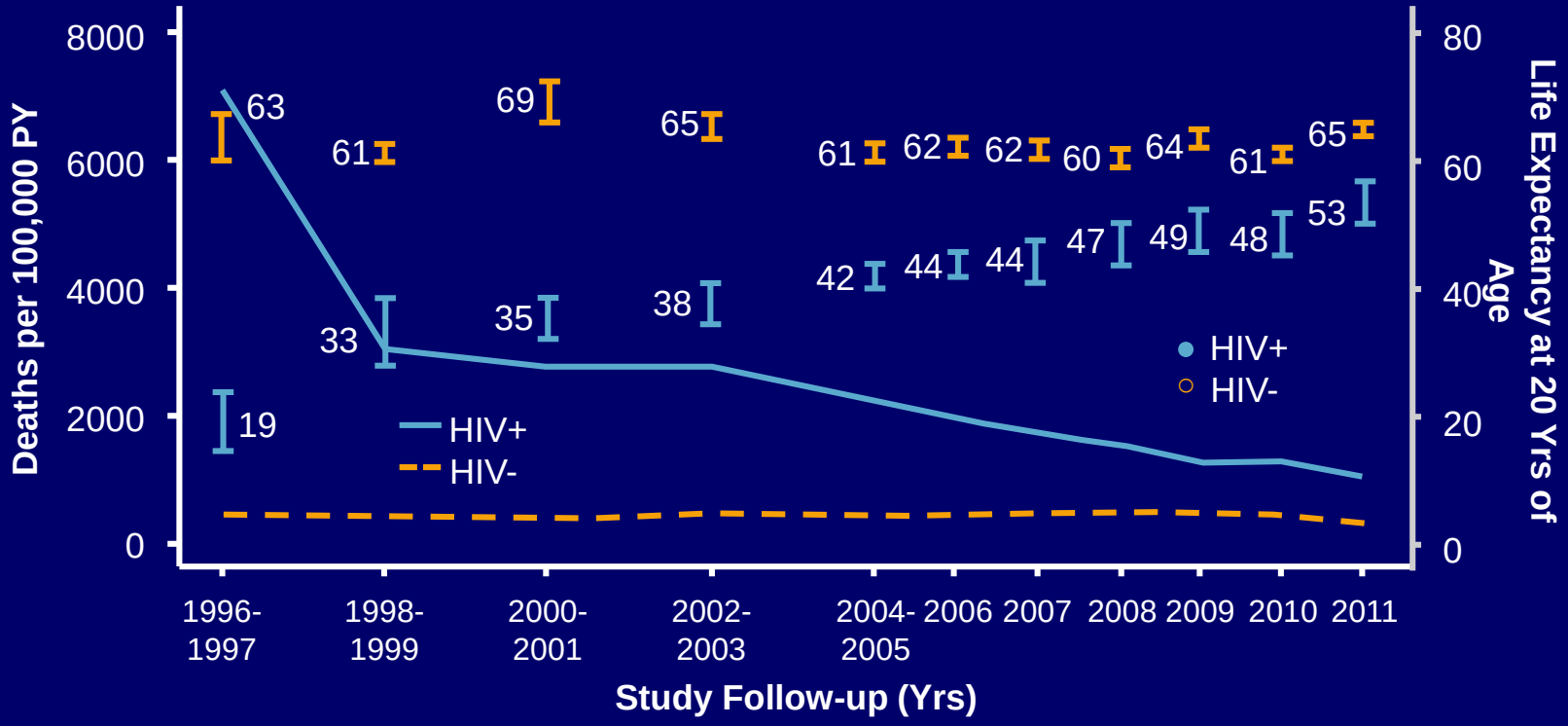
ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Three Decades of HIV/AIDS

Learning and the Future



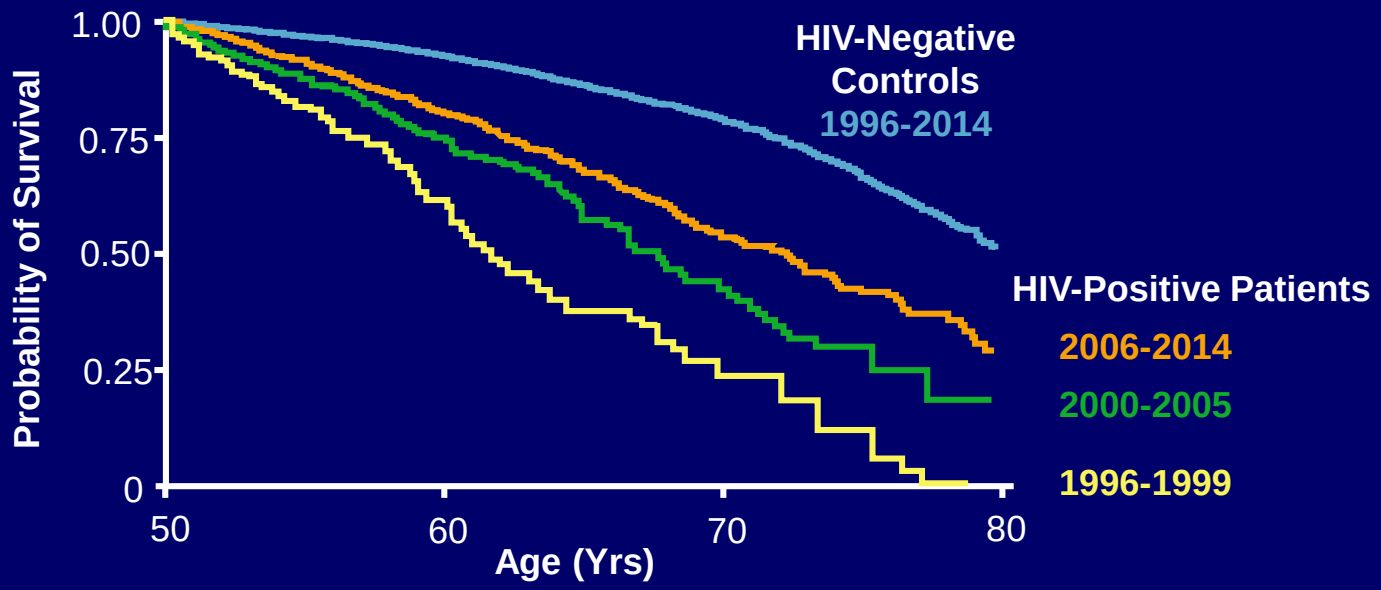
Life Expectancy in Patients With HIV Is Increasing: The "Graying" of the HIV Epidemic



Marcus JL, et al. J Acquir Immune Defic Syndr. 2016;73:39-46.

Life Expectancy With HIV Still Not the Same as Life Expectancy Without HIV

- Population-based cohort study of survival in HIV-infected patients (n = 2440) and uninfected controls matched by age and sex (n = 14,588) in Denmark



Legarth RA, et al. J Acquir Immune Defic Syndr. 2016;71:213-218.

Le stime dell'invecchiamento

I dati ICONA all'ultimo aggiornamento del luglio 2017 mostrano come il **36% dei pazienti nella coorte abbia attualmente più di 50 anni e l'11% superi i 60 anni.**
Un recente studio condotto sempre a partire dai dati della stessa coorte stima che **nel 2035 il 76%** dei soggetti seguiti per HIV in Italia avrà età >50 anni (27% >65 anni) e **l'89% di questi avrà almeno una comorbilità**, con un conseguente **raddoppio stimato dei costi** per il trattamento delle comorbidità non infettive.

SIMIT
Società Italiana di Malattie infettive e Tropicali

Italian Cohort
I. C O.
N A.
Naive Antiretrovirals

Elementi di specificità del paziente anziano

Relativi all'ospite

- Minore recupero dei CD4+.
- Migliore risposta virologica (migliore aderenza al trattamento)
- Maggiore rischio progressione rispetto < 50 anni.
- Maggiore rischio mortalità non AIDS.
- Maggiore rischio interruzione ART per tossicità

Relativi al trattamento

- Multimorbidità e politerapia devono guidare la scelta della terapia ART alla pari dell'efficacia virologica.
- Nella fase di mantenimento terapeutico (ossia stabile soppressione virologica), la scelta di regimi NRTI-sparing o booster-free - anche in semplificazione in mono o duplice - deve essere considerata in condizioni di multimorbidità e/o politerapia.
- TAF deve essere preferito a TDF.

"Traditional" Risk Factors Conspire with HIV to increase Morbidity and Mortality

Smoking is prevalent in most HIV cohort studies

- North American and European PLHIV risk losing more years of life due to smoking related illnesses than due to HIV in NA (AIDS 2015, 29:221–229)

Hypertension

- Prevalence in PLHIV vary by setting, unclear whether HIV directly increases the risk or response to anti-hypertensive therapy.

Diabetes

- Growing rates of diabetes in population globally in the background of HIV

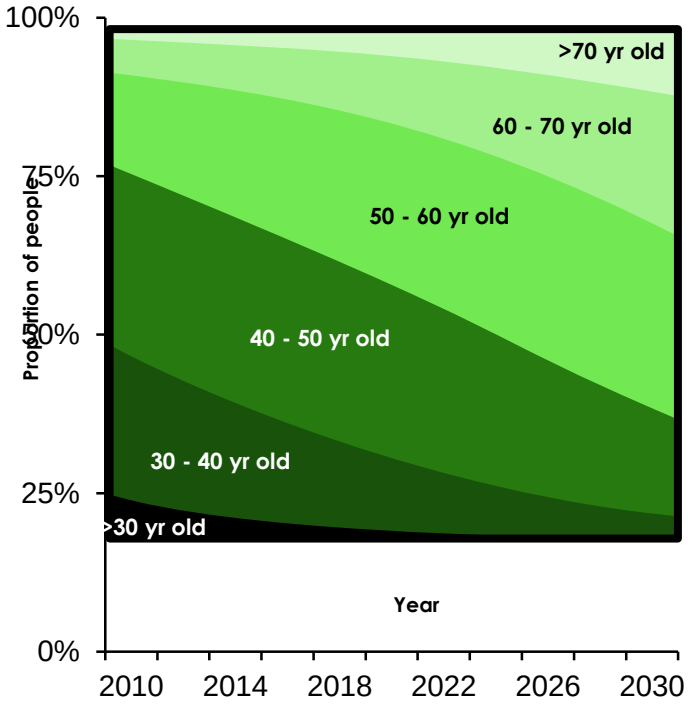
Obesity

- Growing rates in the general population globally in the background of HIV

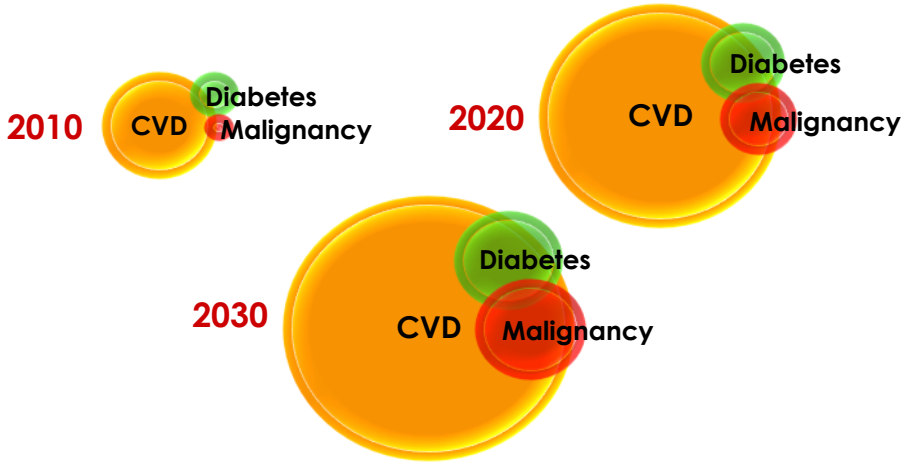
Clinical Implications of an Ageing HIV Population: ATHENA Cohort

An individual-based model of an ageing HIV-population following patients on treatment as they age, develop NCDs and start co-administered medications

Future Age Distribution of HIV Patients in the Netherlands



Changes in Relative Number of Patients with Specific NCDs



- **In the ATHENA cohort, proportion of patients on ART aged ≥50 years old will increase from 28% to 73% between 2010 and 2030**
- **Burden of NCDs mostly driven by larger increases in cardiovascular disease compared with increases in other comorbidities**
- **Polypharmacy is being driven by increase in cardiovascular medications**

Linee Guida Italiane sull'utilizzo della Terapia Antiretrovirale e la gestione diagnostico-clinica delle persone con infezione da HIV-1

«A tal proposito va introdotta la distinzione tra **età cronologica e ed età biologica**, identificando quest'ultima come il tempo che separa il soggetto dal decesso. La **fragilità**, definita come stato di vulnerabilità del paziente e conseguente aumentato rischio di eventi clinici negativi quali ospedalizzazioni, disabilità, delirium, cadute, istituzionalizzazione e morte, identifica un'età biologica più avanzata rispetto all'età anagrafica del paziente»

SIMIT
Società Italiana di Malattie infettive e Tropicali

Geriatric patient
(biologically aged)

versus

Older patient
(chronologically old)

DAY TO DAY MANAGEMENT OF HIV PATIENTS

2000	2005	2010	2014
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

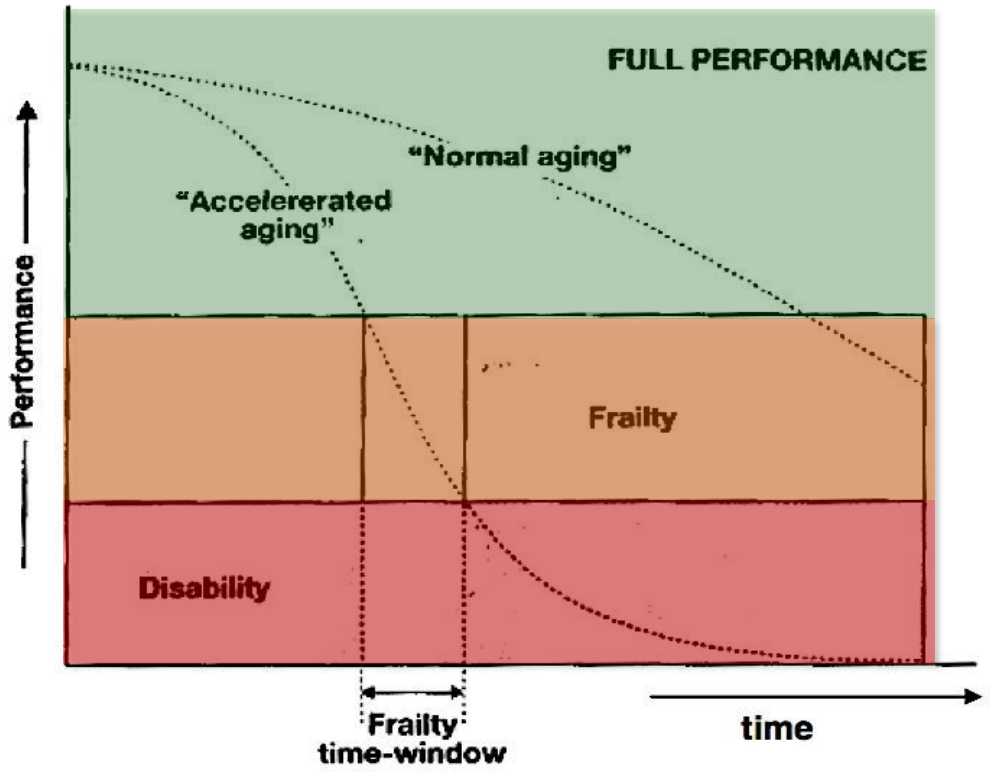
journal homepage: www.jamda.com

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 recognition in clinical practice

Frailty Related Phenotype[1]

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

Frailty as a deficit accumulation[2]

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

Can be summarised as a scale from Robust to Terminally Ill

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

1. Fried et al., J Gerontol Med Sc 2001; 2. Rockwood et al. Lancet 1999;353:205-6

Frailty is correlated to mortality

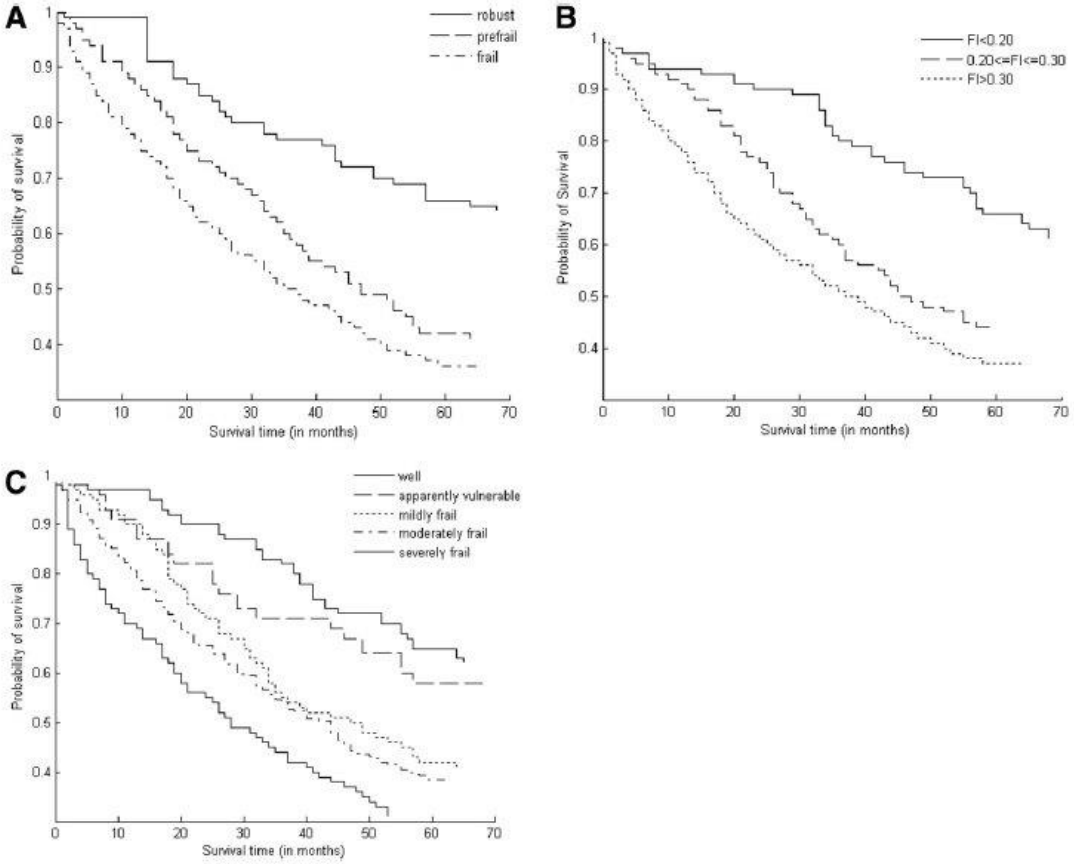


Fig 2. *Survival by grades of fitness/frailty. Panel A, The Cardiovascular Health Survey definition of frailty. The 3 lines refer to "robust," "pre-frail," and frail. Panel B, A 3-part stratification, based on the Frailty Index. The 3 lines refer to people with a Frailty Index Score of less than 0.20, between 0.20 and 0.30, or greater than 0.30. Panel C, A 5-part stratification based on the Canadian Study of Health and Aging Clinical Frailty Scale. Because of small numbers, the categories of "Very fit," "well," and "well with treated comorbid disease" were combined as one "well" category. The other lines represent groups who are "apparently vulnerable," "mildly frail," moderately frail," and "severely frail."*

Rockwood K et al. *J Am Med Dir Assoc* 2007;8:595-603

If Not Aging, What Is Causing This Increased Risk?

The virus

- HIV infection itself
- Late diagnosis, poor engagement in care
- Ongoing inflammation despite ART

The treatment

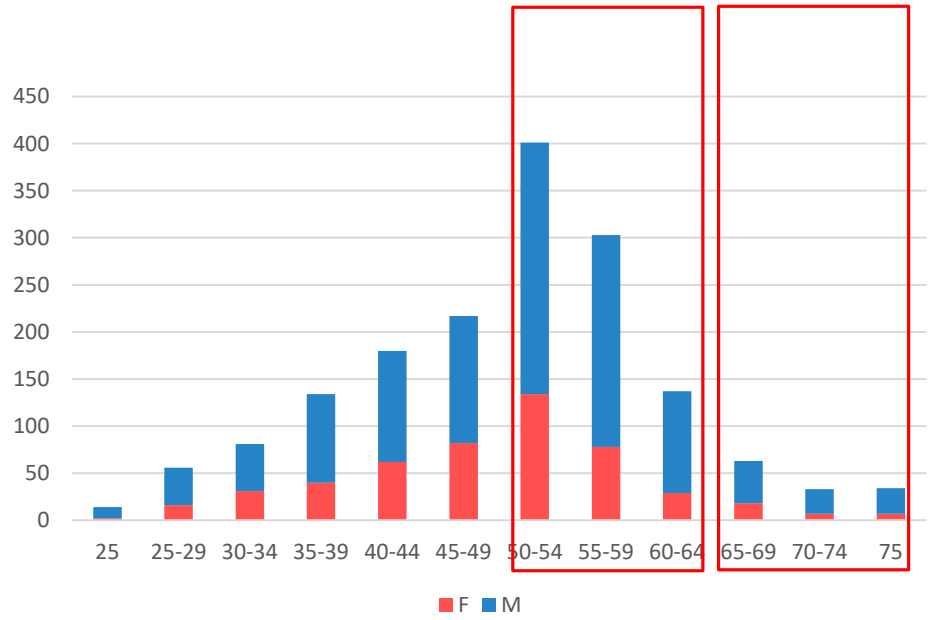
- ART and toxicity

Patient and social factors

- Higher rate of traditional risk factors: smoking, dyslipidemia, hypertension, diabetes
- Obesity
- Renal disease
- Poverty

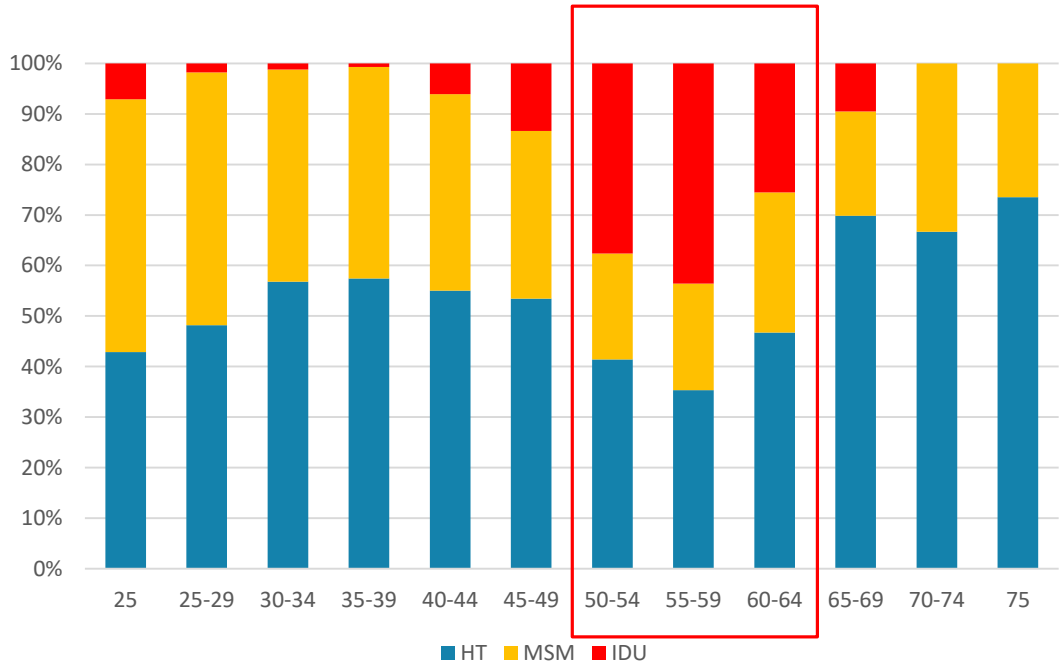
Fixing the “gap” requires addressing these factors

Anche i pazienti con malattia da HIV invecchiano



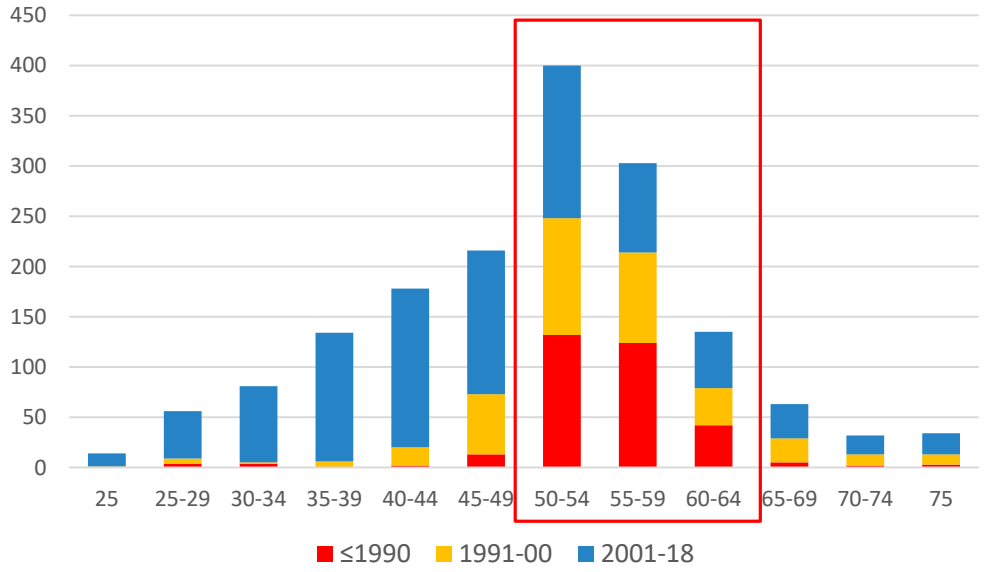
Il numero di pazienti con età >65 anni rappresenta, attualmente, il 6% della popolazione con infezione da HIV.
Nei prossimi 10 anni il numero sarà destinato a decuplicare grazie alla terapia anti-retrovirale. Il 75% delle persone affette sarà rappresentato genere maschile.

Anche i pazienti con malattia da HIV invecchiano



Nei prossimi anni il numero di persone che hanno contratto l'infezione dall'uso di droghe ev aumenterà, rappresentando quasi il 40% delle persone >65 anni. Di conseguenza aumenteranno le co-patologie ad esse associate (HCV, alcool, problemi psichiatrici).

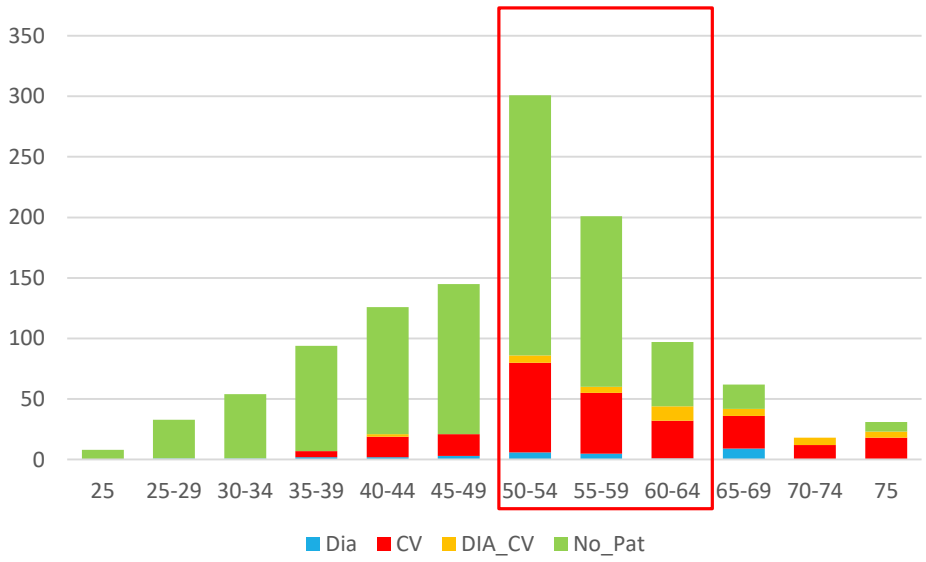
Anche i pazienti con malattia da HIV invecchiano



Le persone che entreranno nella fascia di età >65 anni avranno:

- Lungo periodo di infezione
- Lunga storia di terapia

Anche i pazienti con malattia da HIV invecchiano



Le persone che entreranno nella fascia di età >65 anni avranno:

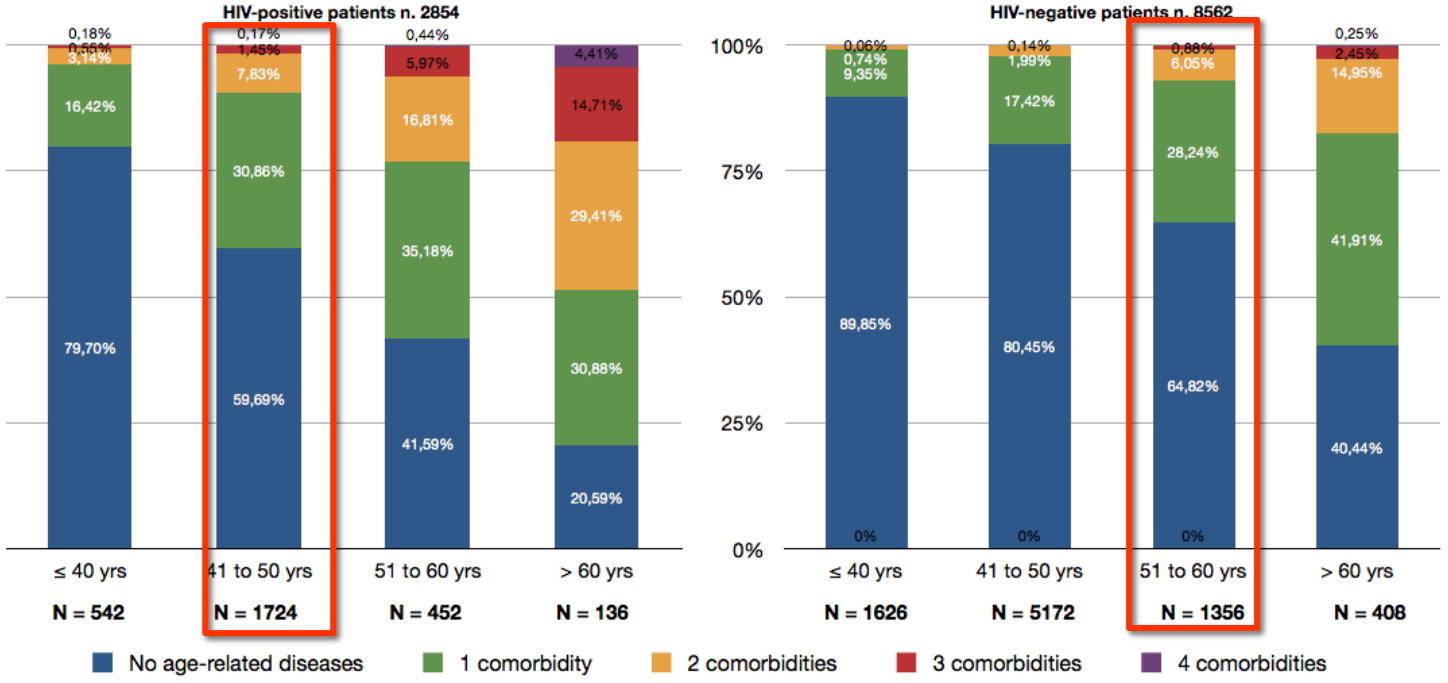
- Maggior frequenza di patologia CV e diabete
- (nel 30-40% dei casi si ha attualmente almeno una patologia nelle classi 50-60)

PATIENT AGEING TRAJECTORY

2000 2005 2010

Drug toxicities Co-morbidities Multi-morbidities

Premature Age-Related Comorbidities Among HIV-Infected Persons Compared With the General Population



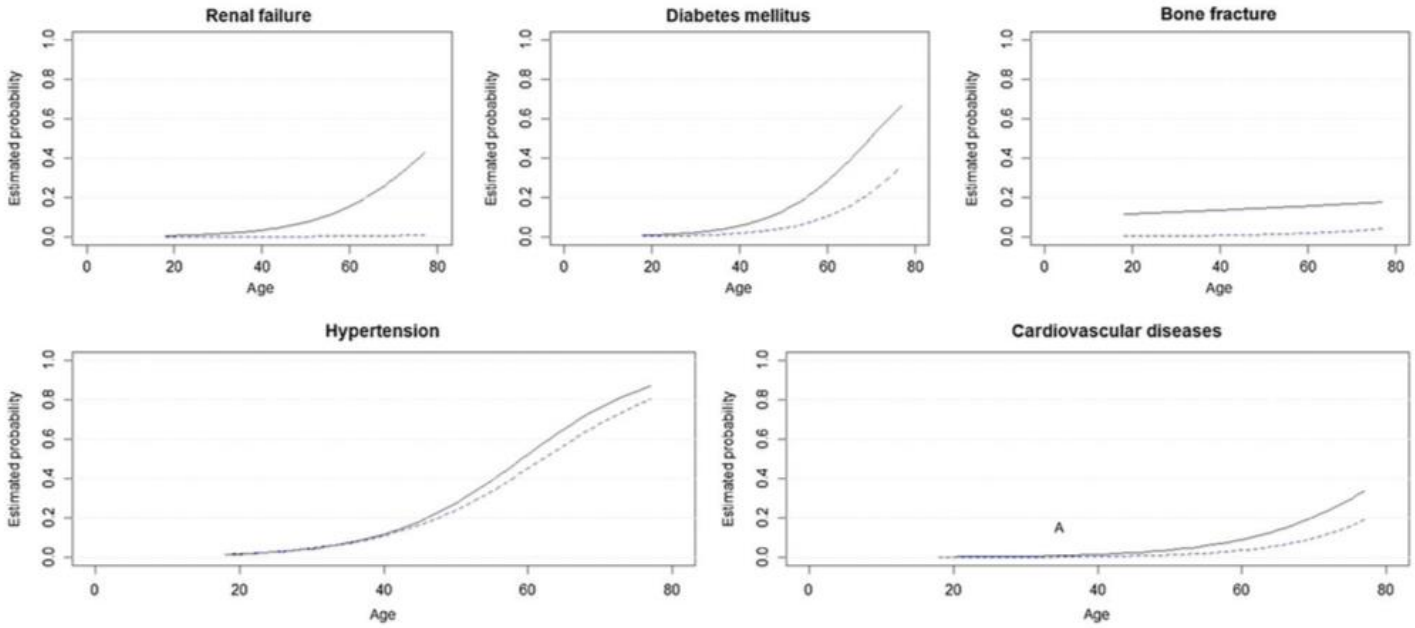
Guaraldi G. CID 2011 *53*(11), 1120–1126.

HIV/AIDS MAJOR ARTICLE

Premature Age-Related Comorbidities Among HIV-Infected Persons Compared With the General Population

Giovanni Guaraldi,[1] Gabriella Orlando,[1] Stefano Zona,[1] Marianna Menozzi,[1] Federica Carli,[1] Elisa Garlassi,[1] Alessandra Berti,[2] Elisa Rossi,[2] Alberto Roverato,[3] and Frank Palella[4]

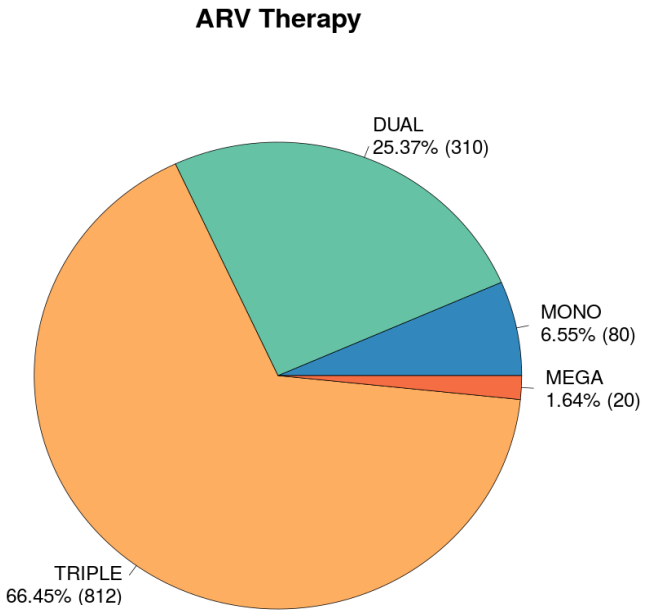
Comparative risk of co-morbidities by age, among patients versus control subjects



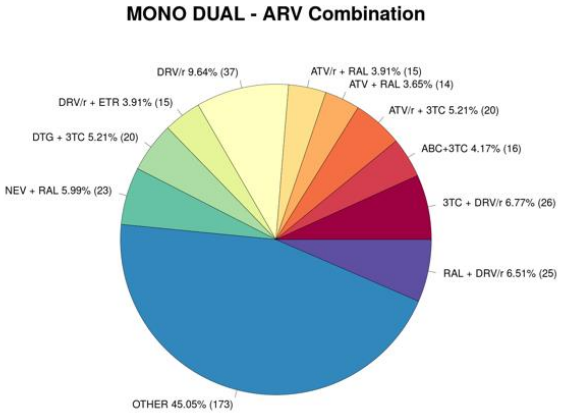
Guaraldi G. CID *53*(11), 1120–1126.

J Antimicrob Chemother
doi:10.1093/jac/dkx169 *2017 Jun 10*

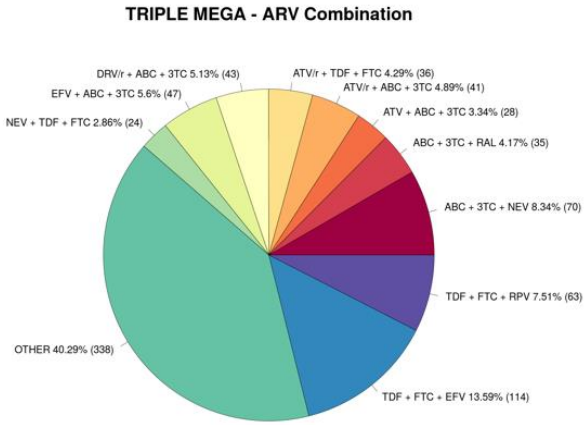
Antiretroviral therapy in geriatric HIV patients: the GEPPO cohort study



In the triple/mega group 839 patients, there were 113 different ARV regimens



In mono/dual therapy for 384 patients, there were 68 different ARV regimens



ARV Combination 113 on 839 pz

High prevalence of non conventional ARV regimens in elderly HIV pateinbts suggests that clinicians try to tailor ARV regimens according to age, HIV duration, MM and PP

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3. **Presa incarico e gestione paziente**
4. **Erogazione interventi personalizzati**
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Obiettivi:

-Responsabilizzare tutti gli attori coinvolti

-Integrare le Cure Primarie e le Cure Specialistiche

Possibili modelli di gestione della cronicità HIV

- Gestione esclusiva da parte dell'infettivologo
- Gestione integrata da parte dell'infettivologo (case manager) con altri specialisti ± MMG
- Gestione integrata da parte del MMG (case manager) con infettivologo ed altri specialisti.
- Gestione esclusiva da parte del MMG

Approccio multidisciplinare

In questo contesto un approccio multidisciplinare, consente di costruire un percorso di cura nel quale si integrano le competenze dello specialista HIV con quelle altri specialisti.

I risultati sono stati positivi laddove la gestione della terapia HIV è rimasta di pertinenza dello specialista in HIV.

Una recente metanalisi ha analizzato il modello assistenziale che demanda la gestione del paziente al medico di medicina generale, con risultati negativi a conferma del ruolo centrale dello specialista HIV nel percorso diagnostico che terapeutico.

Interazione tra le reti della cronicità

Chi gestisce le co-morbosità?

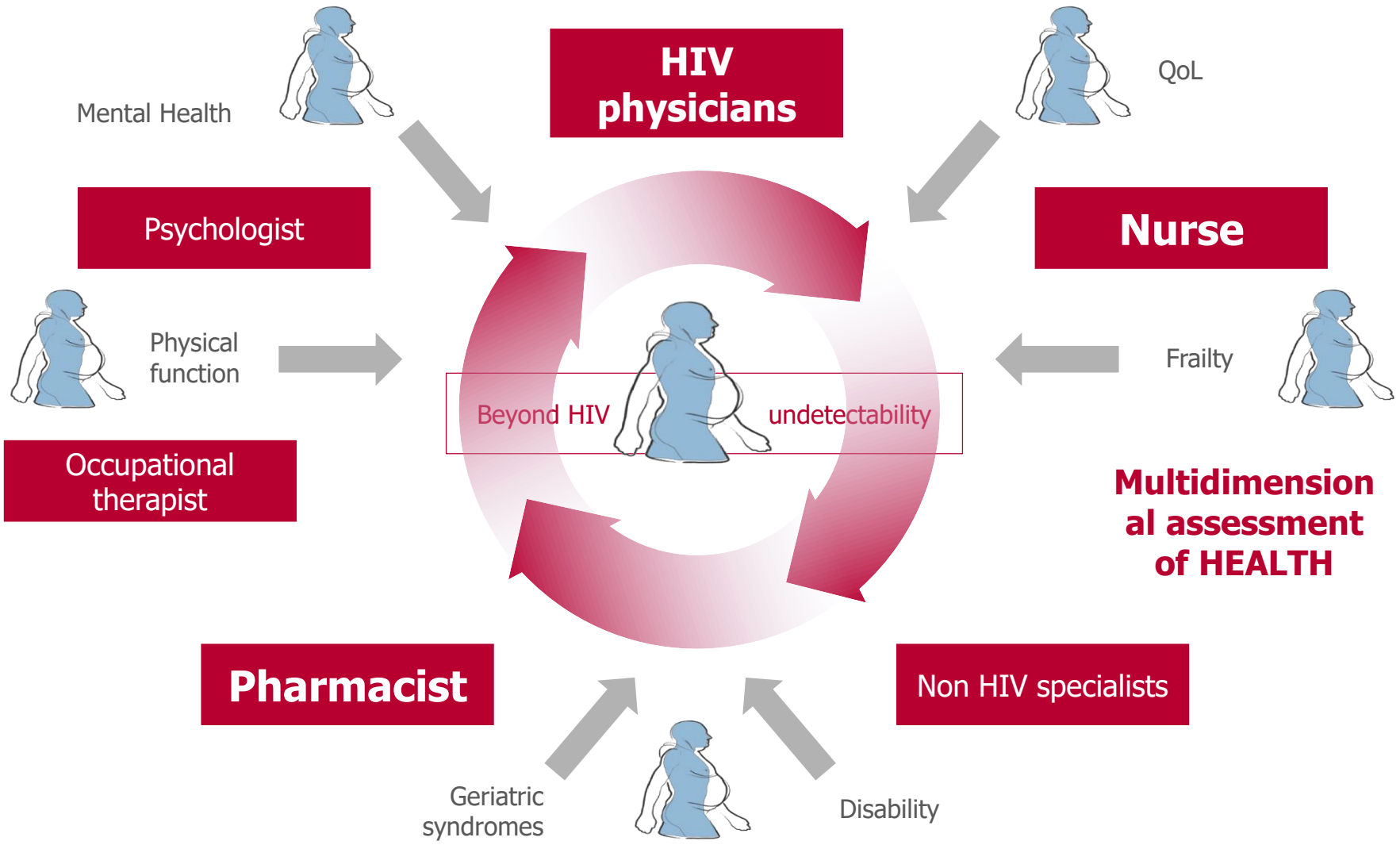
- Da infettivologo ad internista
- Il pellegrinaggio nei CUP

Rapporti con MMG

Rapporti con le reti della cronicità

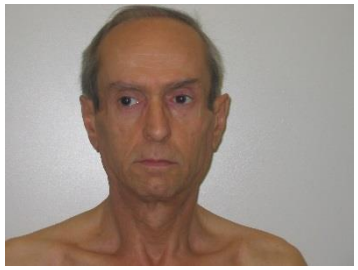
- Centro antidiabetico
- Ambulatori di cardiologia, nefrologia, pneumologia, etc

TOTAL PATIENT CARE: a patient cantered **multidimentional** assessment of HEALTH



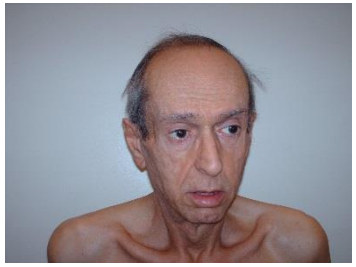
Day to Day Management of HIV Patients

2000	2005	2010	2014	2018
Drug Toxicities	Co-morbidities	Multi-morbidities	Frailty	Disability



2005

CD4=232/microL
VL<40 c/mL (ND)

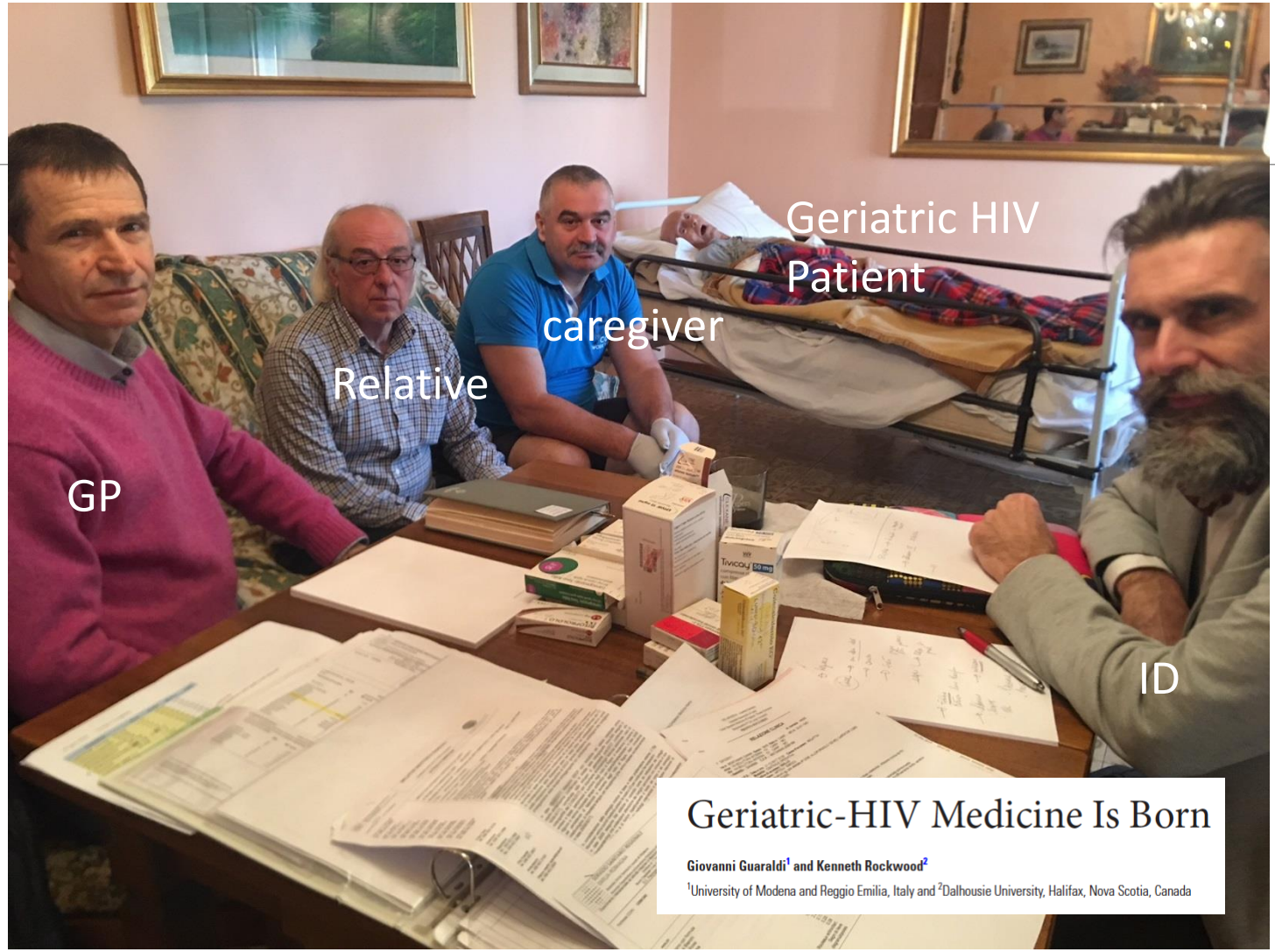


2008

CD4=279/microL
CD4/CD8=0.2
HIV VL<40 c/mL (ND)

2018

CD4=164/microL
CD4/CD8=0.2
HIV VL<40 c/mL (ND)


Geriatric HIV
Patient
caregiver
Relative
GP
ID
Geriatric-HIV Medicine Is Born
Giovanni Guaraldi[1] and Kenneth Rockwood[2]
[1]University of Modena and Reggio Emilia, Italy and [2]Dalhousie University, Halifax, Nova Scotia, Canada

To manage declines in the instrinsic capacity of older people

- Improve musculoskeletal function, mobility and vitality
- Maintain older adults' capacity to see and hear
- Prevent severe cognitive impairment & promote psychological well-being
- Manage age-related conditions such as urinary incontinence
- Prevent falls
- Support caregivers

The new target

~~90-90-90-90-90~~

90% diagnosed

90% on treatment

90% virally suppressed

90% fit at 90 years

Thanks to Giovanni Guaraldi for his works on frialty and iconografy.

Thank you….
…and stay fit!