

HIV & Aging



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The "Beard Conflict" Beard length is aging









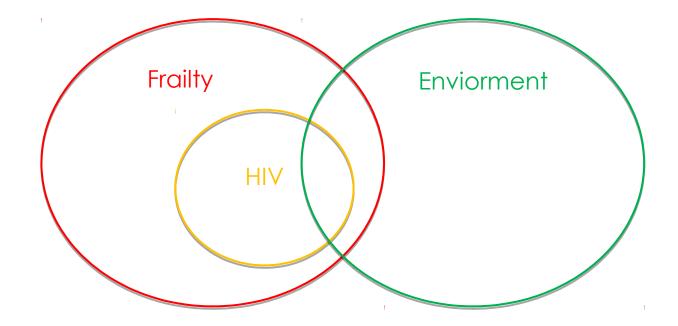


Prof Guaraldi received research grant from Gilead sciences, ViiV, MERCK, Jansen.

From the same companies he accepted travel sponsorship and speaker honorarium.

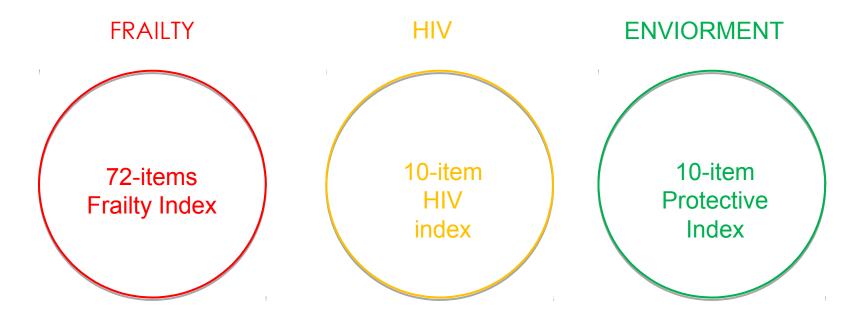
He attended advisory boards of Gilead sciences, ViiV and MERCK.

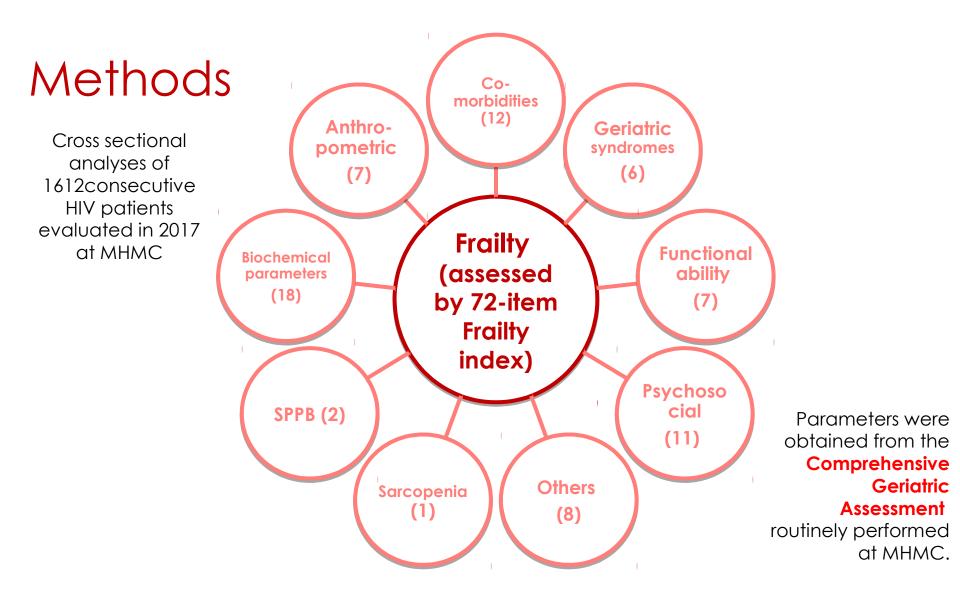
A conceptual approach: HIV in Frailty, not Frailty in HIV

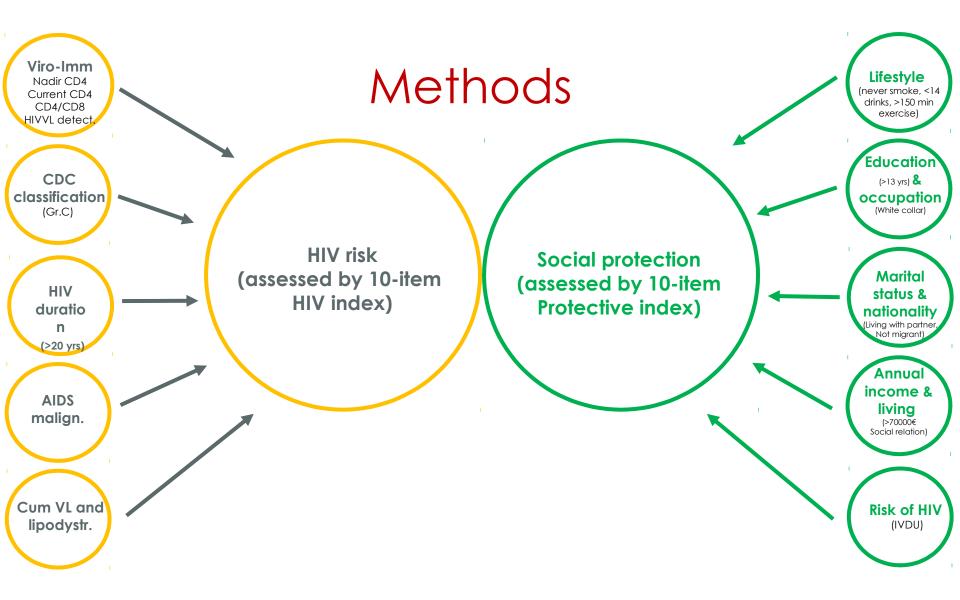


Study aim

Aim of this study was to evaluate the relationship between frailty, HIV and social vulnerability using two health indexes previously developed by our group, HIV and Protective Indexes, (HIVI, PI).



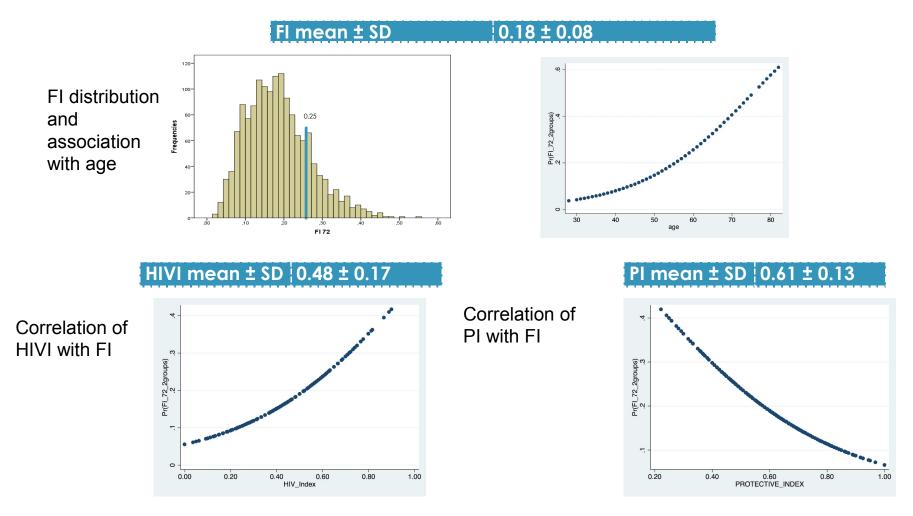




Patient disposition

Sample size (n)	1612	CDC classification n(%)	
Age mean ± SEM	53.13 ± 0.20	Α	698(43.3)
(years)		В	451(28)
Sex (men %)	73.9	С	362(22.5)
BMI (Kg/m ²)	24.43 ± 3.92	CD4 nadir mean ± SEM	225 ± 5
MultiMorbidity (≥ 2	975 (60.5)	(cell/mmc)	
comorbidities, n,%)		Current CD4 mean ±	748 ± 7
Alchool consumption		SEM (cell/mmc)	
n(%)	1132(70.8)	CD4/CD8 ratio ± SEM	0.98 ± 0.02
None	148(28)	Duration of HIV mean ±	20.83 ± 0.22
Mild	20(1.2)	SEM (years)	
Heavy			
Smoking habit n(%)			
None	1074(67.2)		
Mild	280(17.5)		
Heavy	245(15.2)		

Frailty index construct validity and relationship with HIVI and PI



Logistic regression model was used to assess the probability of being frail in relation to HIV index and Protective index

Frailty index	Coefficient	95% confidence Interval	Р
Protective index	-2.58	-3.711.44	<0.001
HIV index	2.00	0.98 - 3,02	<0.001
age	0.06	0.04 – 0.08	<0.001

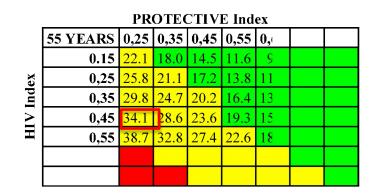
 $\Pr(Frailty / Age, PI, HIVI) = \frac{exp(-4.31+0.06Age-25.98I+2.0HIVI)}{1 + exp(-4.31+0.06Age-2.58PI+2.0HIVI)}$ $\Pr(Pr(Prailty / Age, PI, HIVI) = \frac{exp(-4.31+0.06Age-2.58PI+2.0HIVI)}{1 + exp(-4.31+0.06Age-2.58PI+2.0HIVI)}$ $= \frac{-4.31+0.06Age-2.58PI+2.0HIVI)}{-4.31+0.06Age-2.58PI+2.0HIVI)}$ We genrated tables which shows $\frac{1}{14}$ = -4.31+0.06Age-2.58PI+2.0HIVI)}{1 + exp(-4.31+0.06Age-2.58PI+2.0HIVI)} $= \frac{-4.31+0.06Age-2.58PI+2.0HIVI)}{-4.31+0.06Age-2.58PI+2.0HIVI}$

Probability of being frail according to different levels of PI and HIV index stratified by age categories

	PR	OTE	CTIV	E Ind	ex		
25 YEARS	0,25	0,35	0,45	0,55	0,65	0,75	
0.15	4.3	3.3	2.6	2.0	1.6	1.2	
0,25	5.2	4.0	3.2	2.5	1.9	1.5	
0,35	6.2	4.9	3.8	3.0	2.3	1.8	
0,45	7.5	5.9	4.6	3.6	2.8	2.2	
0,55	9.0	7.1	5.6	4.4	3.4	2.7	
0,65	10.8	8.6	6.8	5.3	4.1	3.2	
0 75	12.9	10.3	R 1	64	5.0	30	

	PROTECTIVE Index							
	45 YEARS	0,25	0,35	0,45	0,55	0,65	0,75	
	0.15	13.3	10.6	8.4	6.6	5.2	4.1	
ех	0,25	15.8	12.6	10.1	8.0	6.3	4.9	
HIV Index	0,35	18.6	15.0	12.0	9.5	7.5	5.9	
Σ	0,45	21.8	17.8	14.3	11.4	9.1	7.1	
Η	0,55	25.4	20.9	16.9	13.6	10.9	8.6	
	0,65	29.4	24.4	19.9	16.1	12.9	10.3	
	0.75	33.7	<mark>28 2</mark>	23.3	19 N	15 4	123	

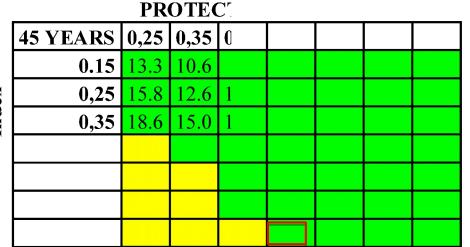
		PR	OTEC	CTIV	E Ind	ex		
	35 YEARS	0,25	0,35	0,45	0,55	0,65	0,75	
	0.15	7.6	6.0	4.7	3.7	2.9	2.2	
ex	0,25	9.2	7.2	5.7	4.5	3.5	2.7	
HIV Index	0,35	11	8.7	6.9	5.4	4.2	3.3	
Σ	0,45	13.1	10.4	8.3	6.5	5.1	4.0	
Η	0,55	15.5	12.5	9.9	7.8	6.2	4.8	
	0,65	18.4	14.8	11.8	9.4	7.4	5.8	
	0.75	21.5	17.5	14 1	113	8 9	7.0	

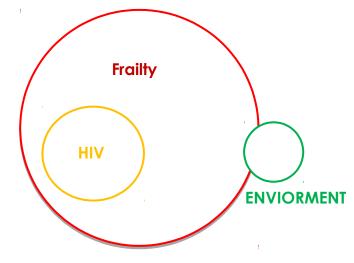


		PR	OTE	CTIV	E Ind	ex	
	65 YEARS	0,25	0,35	0,45	0,55	0,	
	0.15	34.5	28.9	23.9	19.5	15	
eх	0,25	39.1	33.2	27.7	22.9	18	
Index	0,35	44.0	37.8	31.9	26.6	21	
HIV	0,45	49.0	42.6	36.4	30.7	25	
Η	0,55	54.0	47.5	41.2	35.1	29	

Color code for Frailty risk probability: low (<.20%), intermediate (20-40%) and high (>40%)

Probability of being frail at the age of 45 years



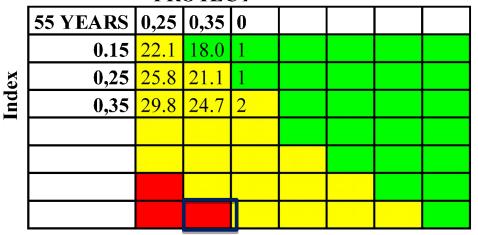


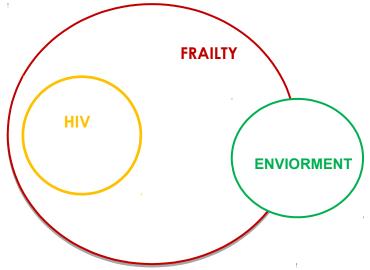


At the age of 45 years, frailty probability increases, mostly **driven by high HIVI**, while low PI alone still places individual at low risk of frailty.

Color code for Frailty risk probability: low (<.20%), intermediate (20-40%) and high (>40%)

Probability of being frail at the age of 55 years PROTECT







At the age of 55 years, HIV index still prevails in the contribution to frailty, nevertheless **an interaction HIVI and PI is substantial**

PI=0.35

Color code for Frailty risk probability: low (<.20%), intermediate (20-40%) and high (>40%)

4

Comprehensive Assessment for Patients with HIV

	Compre	enensive Asse	essment for Pati	ents with HIV		
NadirCD4+ □ ≥350 cell/mL (0) □ <350 cell/mL (1)	CDC □ A (0) □ B (0) □ C (1)	Duration of HIV □ <20 years (0) □ ≥20 years (1)	Detectable HIV-Viral Load □ No (0) □ Yes (1)	time between diagnosis and ARV initiation \Box No (0) \Box Yes (1)		
Lipodystrophy □ No (0) □ Yes (1)	3 rd line ARV □ No (0) □ Yes (1)	CD4+ □ ≥500 cell/mL (0) □ <500 cell/mL (1)	CD4/CD8 □ ≥0.8 (0) □ <0.8 (1)	AIDS malignancy requiring chemotherapy or radiotherapy \square No (0) \square Yes (1)		
HIV TOTAL SCOR	<u>RE:</u> / 10	1				
Comorbidities	 None (0) CKD (1) 	© COPD (1) © DM (1)	 Osteoporosis (1) CVD/HTN/DLP (1) 	Cancer (1 <u>) dyslipidemia</u> NAFLD/cirrhosis (1)		
Falls (past year) □ No (0) □ Yes (1)	Medications $\Box < 5 (0)$ $\Box \ge 5 (1)$	Exercise □ ≥150min/week (0) □ Less or none (1)	BMI (Kg/m ²) □ 18.5-25 (0) □ <18.5 (1) □ >25 (1)	WBC □ 4000-10000 (0) □ <4000 />10.000 (1)		
Systolic BP □ 80-120 mmHg (0) □ <80 mmHg (1) □ >120 mmHg (1)	Diastolic BP □ 60-90 mmHg (0) □ <60 mmHg (1) □ >90 mmHg (1)	Hemoglobin □ Normal (0) □ Low (1) □ High (1)	Glucose Normal (0) Low (1) High (1)	PLT □ Normal (0) □ Low (1) □ High (1)		
Bilirubin Dia Normal (0) High (1)	GGT □ Normal (0) □ High (1)	Creatinine □ Normal (0) □ High (1)	GPT/ALT □ Normal (0) □ High (1)	Total Cholesterol □ Normal (0) □ High (1)		
Cough No/rarely (0) Sometimes (1) Most times (1) 	Happy Do/rarely (0) Sometimes (1) Most times (1)	Lonely No/rarely (0) Sometimes (1) Most times (1) 	Bothered by things that de □ No/rarely (0) □ Sometimes (1) □ Most times (1)	on't usually bother		
Poor appetite No/rarely (0) Sometimes (1) Most times (1) 	Self-care □ Good (0) □ Fair (1) □ Poor (1)	Mobility Independent (0) Mild dependent (1) Total dependent (1) 	Usual activities independent (0) indicemendent (1) Total dependent (1)			
FRAILTY INDEX	TOTAL SCORE:	/ 30				
Alcohol (past week) □ ≥14 drinks (0) □ <14 drinks (1)	Smoking □ Current (0) □ Past (0) □ Never (1)	Education □ <13 years (0) □ 13-16 years (1) □ >16 years (1)	Marital status <u>widow</u> Single/divorced(0) Partner /Married (1) (1)	Occupation □ White collar (0) □ Blue collar (1) □ Unemployed/retired (1)		
Nationality □ Other (0) □ Italian (1)	Living □ Alone (0) □ With others (1)	Risk of HIV □ IDU (0) □ Other (1)	Annual income (Euro) □ ≤10.000 (0) □ 30.000-70.000 (1) □ 10.000-30.000 (0) □ ≥70.000 (1)	Unintentional weight loss □ <4.5Kg/past year (0) □ ≥4.5Kg/past year (1)		

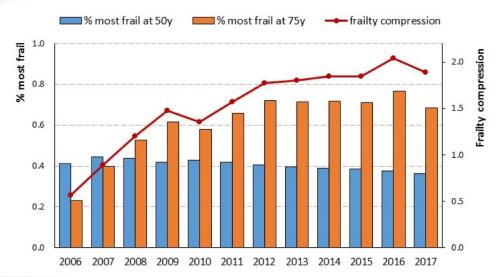
HIV Score /10

Frailty Index score /30

Protective index score /9

PROTECTIVE INDEX TOTAL SCORE:_/ 9

HIV& ARV impact frailty



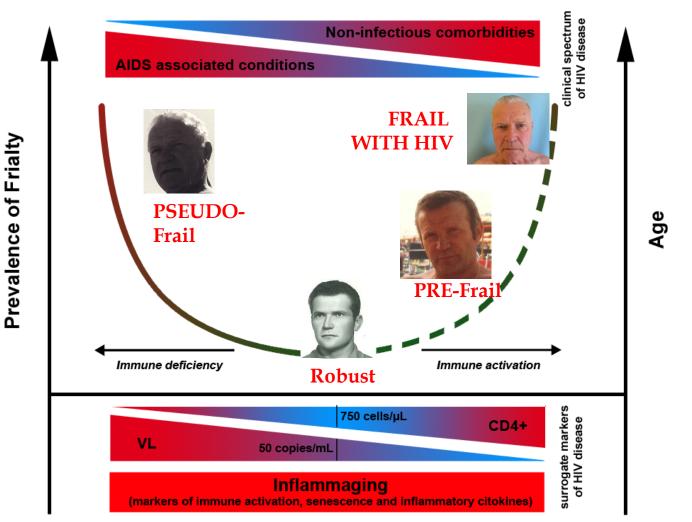
Frailty Compression: is the ratio of the proportion of frail individuals at the age of 75 and at the age of 50 years at any given year.

The frailty compression score increased from 0.56 to 1.89

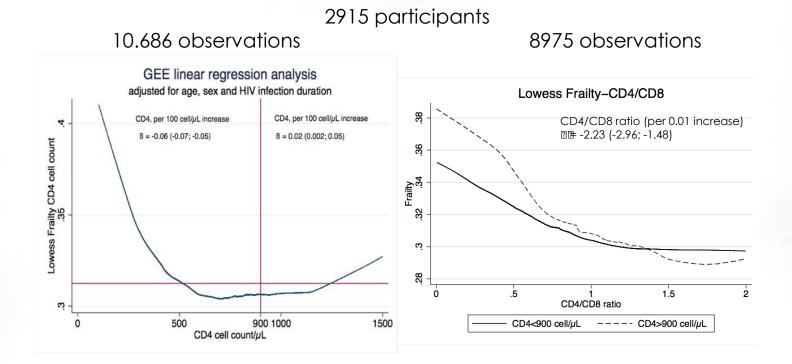
Predictors of FRAILTY COMPRESSION sat multivariable analyses:

- ✓ male patients (p=0.02), age (p<0.001)</p>
- ✓ nadir CD4+ T cell count (p<0.001)</p>
- ✓ proportion of patients with HIV duration more than 20 years (p=0.001)

Hypothetical association between frailty, HANA and immune activation / inflammation



The dynamic association between Frailty, CD4 and CD4/CD8 ratio in people aging with HIV



We found a dynamic relationship between current CD4 count and frailty Lower CD4/CD8 ratio, a surrogate marker of immune senescence, is associated with severity of frailty both below and above this cut-off of 900 CD4 cells/µL.



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The Journal of Frailty & Aging©

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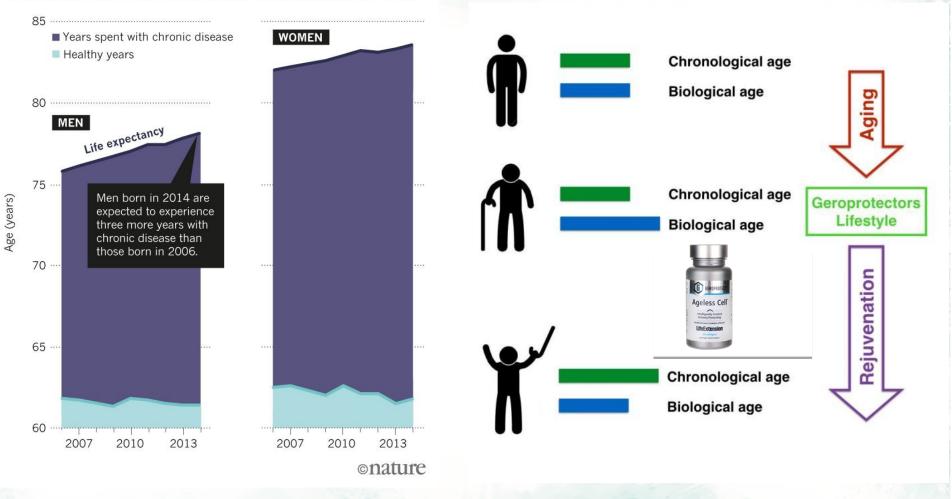
SPECIAL ARTICLE

THE MANAGEMENT OF GERIATRIC AND FRAIL HIV PATIENTS. A 2017 UPDATE FROM THE ITALIAN GUIDELINES FOR THE USE OF ANTIRETROVIRAL AGENTS AND THE DIAGNOSTIC-CLINICAL MANAGEMENT OF HIV-1 INFECTED PERSONS

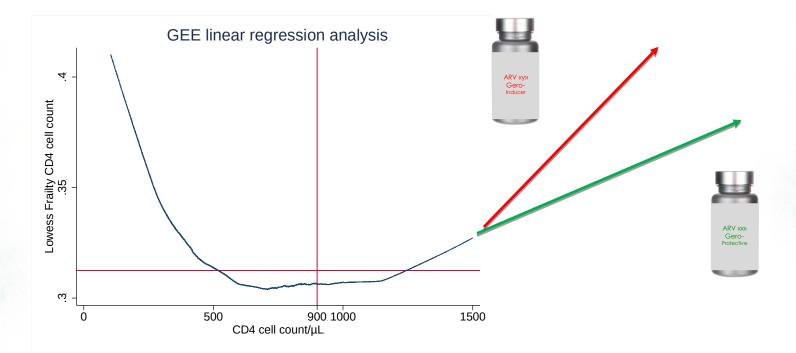
	Recommendation (Strength of evidence)
Host-related	
Limited CD4+ T cell count recovering with ageing	
Superior virological response (due to higher treatment adherence) with ageing	[AII]
Higher risk of progression compared to those below 50 years of age	
Higher risk of mortality related to non-AIDS conditions	[AII]
Higher risk of ART interruption due to toxicity	[AII]
Treatment-related	
The ART decisions should consider multi-morbidity and polypharmacy, as well as virological efficacy	[AII]
When virological suppression is achieved, NRTI-sparing, boosted-free regiments or even a simplification in mono or dual therapy should be considered in multi-morbidity and/or polypharmacy conditions	[BII]
TAF should be preferred to TDF	[AI]

MORE YEARS OF WHAT?

In Europe, men and women are living longer. They are also spending more years with chronic conditions such as diabetes, cancer and Alzheimer's disease.



Can we test Geroprotective effect o ARVs



The dynamic association between Frailty and CD4 in people aging with HIV.



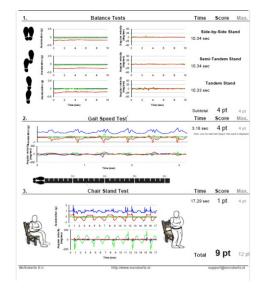
16 December 2015 EMA/CHMP/778709/2015 Committee for Medicinal Products for Human Use (CHMP)

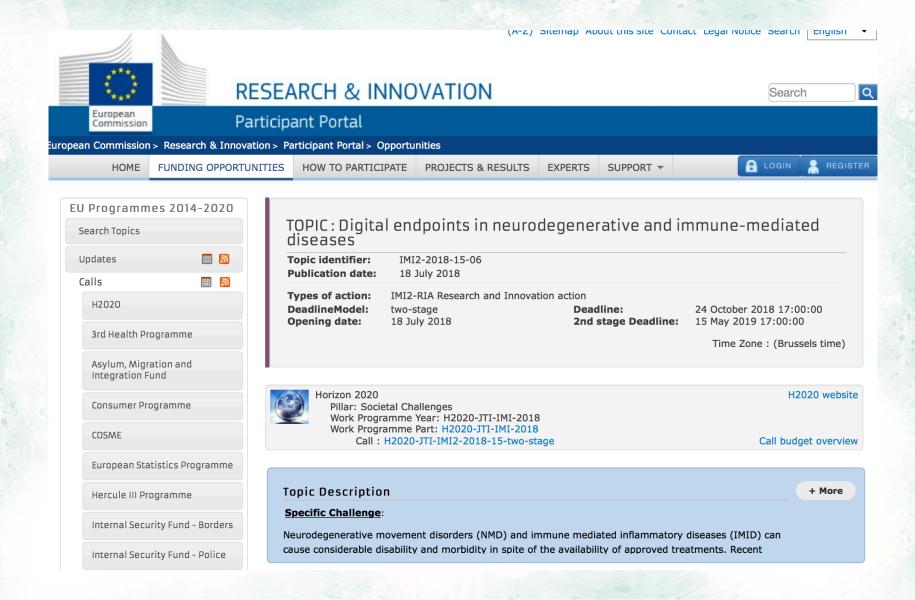
Points to consider on frailty: Evaluation instruments for baseline characterisation of clinical trial populations

The following aspects of frailty are considered; ✓ physical frailty ✓ cognitive dysfunction

- ✓ malnutrition
- ✓ multi-morbidity

The Short Physical Performance Battery (SPPB) is identified as the scale providing the overall best predictive value for the baseline characterization of the (physical) frailty of older people enrolled in a clinical trial.





Three natients



Case «A» Mirella, 80 years,	Co-morbidities: ✓ MetS (HTN,
HIV duration 14 years	DLP)
CD4=478/microL	🗸 Ostepenia
CD4/CD8=0.7	✓ CKD
HIV VL<40 c/mL (ND)	✓ CAC 206↑

Three patients





Case «A» Mirella, 80 years,	Co-morbidities: ✓ MetS (HTN,	Case B John, 63 years,	Co-morbidities: ✓ T2DM
HIV duration 14 years	DLP)	HIV duration 23 years	✓ DLP
CD4=478/microL	✓ Ostepenia	CD4=407/microL	🗸 Osteonecrosis
CD4/CD8=0.7	✓ CKD	CD4/CD8=0.6	✓ MI
HIV VL<40 c/mL (ND)	✓ CAC 206↑	HIV VL<40 c/mL (ND)	✓ CKD
	·		

Three patients







Case «A» Mirella, 80 years,	Co-morbidities: ✓ MetS (HTN,
HIV duration 14 years	DLP)
CD4=478/microL	✓ Ostepenia
CD4/CD8=0.7	✓ CKD
HIV VL<40 c/mL (ND)	✓ CAC 206↑

	Case B John, 63 years,
	HIV duration 23 years
	CD4=407/microL
	CD4/CD8=0.6
	HIV VL<40 c/mL (ND)
-	

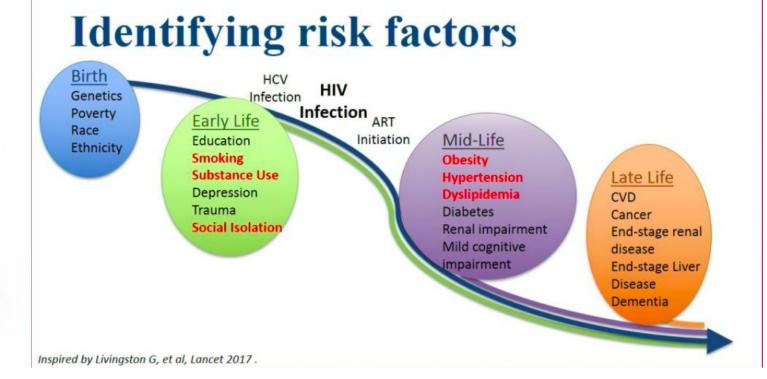
Co-morbidities:
✓ T2DM
✓ DLP
✓ Osteonecros
is
✓ MI
✓ CKD

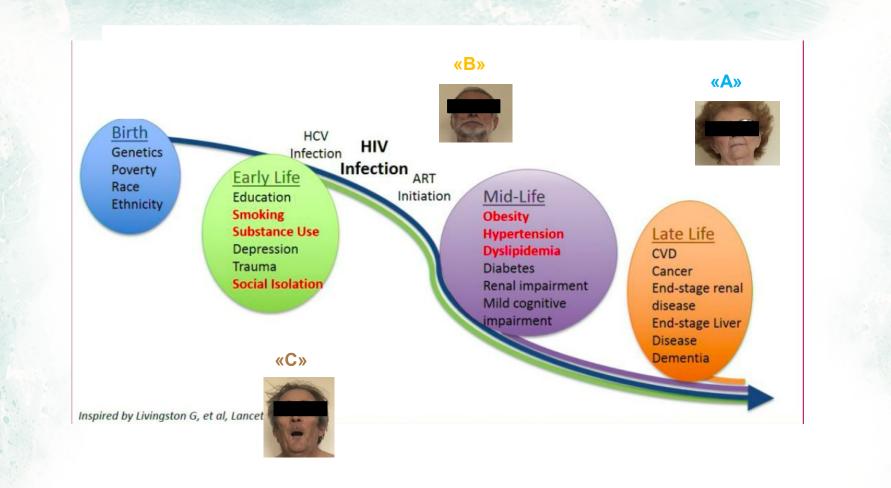
Case «C»	
Angelo, 55	years,

HIV duration 21 years CD4=408/microL CD4/CD8=0.7 HIV VL<40 c/mL (ND)

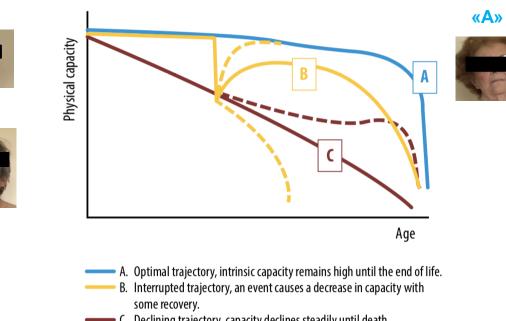
Co-morbidities:

- ✓ Cancer
- ✓ T2DM
- ✓ Fractures
- ✓ COPD





Trajectories of Healthy Ageing



«B»

«C»

 C. Declining trajectory, capacity declines steadily until death. The dashed lines represent alternative trajectories.

Three frail patients







Case «A» Mirella, 80 years,	M- Morbidity√
Geriatric Syndromes	Disability x
F. Phenotype 3/5 ✓	Functional ability (Pt. expectation:
FI=0.39√	
Slow walk ✓	Attend charity meeting in parish

Case B John, 63 years		M-I Dise
Geriatric Syndromes		
F. Phenotype 3/5 ✓		Func
FI=0.35✓		(Pt. e
Falls ✓		Atter
Viusual imp. 🗸	L	even
Slow walk √		

	M-Morbidity 🗸 Disability 🗶	Case «C» Angelo, 55 years,	
nes	,	Geriatric Syndromes	
✓	Functional ability (Pt. expectation:	F. Phenotype 4/5 ✓	
	1 · · · · · · · · · · · · · · · · · · ·	FI=0.39√	
	Attend cultural events	Falls 🗸	
		Urinary incont. 🗸	

Slow	walk	
210W	waik	•

Functional ability
Disability 🗸
M-Morbidity 🗸
M Marbidity (

(Pt. expectation:

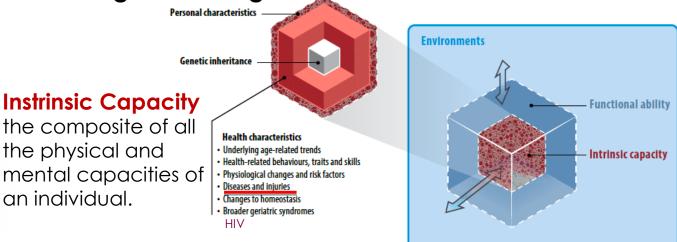
Follow soccer game (Milan) in a bar



Heart and stroke foundation. Published on February 4, 2013 https://www.youtube.com/watch?v=Qo6QNU8kHxl World Health Organization



Healthy Ageing: the process of developing and maintaining the functional ability that enables wellbeing in older age.

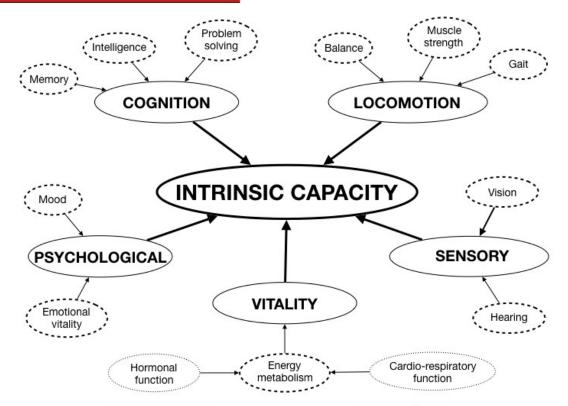


Functional ability: the health-related attributes that enable people to be and to do what they have reason to value. It is made up of the *intrinsic capacity* of the individual, relevant *environmental characteristics* and the interactions between the individual and these characteristics.

The Journals of GERONTOLOGY®

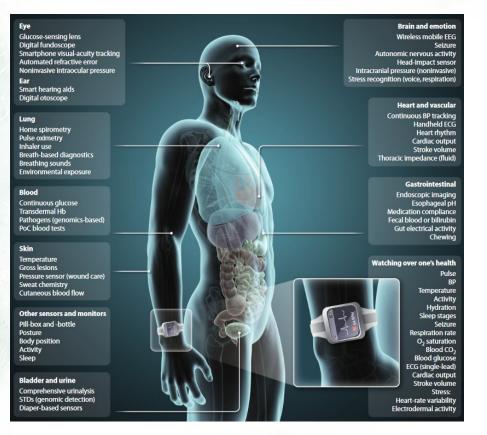
Evidence for the Domains Supporting the Construct of Intrinsic Capacity

Matteo Cesari, MD, PhD 📾, Islene Araujo de Carvalho, MD, MPH, Jotheeswaran Amuthavalli Thiyagarajan, MSC, PhD, Cyrus Cooper, MD, FMedSci, Finbarr C Martin, MD, MSc, Jean-Yves Reginster, MD, PhD, Bruno Vellas, MD, PhD, John R Beard, MBBS, PhD



Cesari M et al. J Gerontol 2018

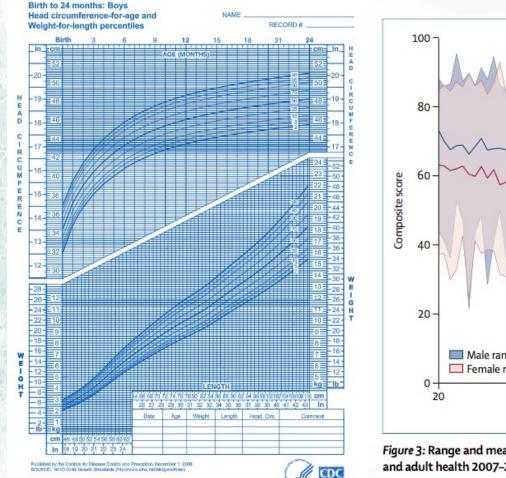
Internet of Medical Things (IoMT) is the future of healthcare



IoMT Framework

- Big data management
- Real time collection variables
- Integration of physiological parameters and patient related outcomes (ePRO)

Normogram of Intrisic capacity in aging trajectories



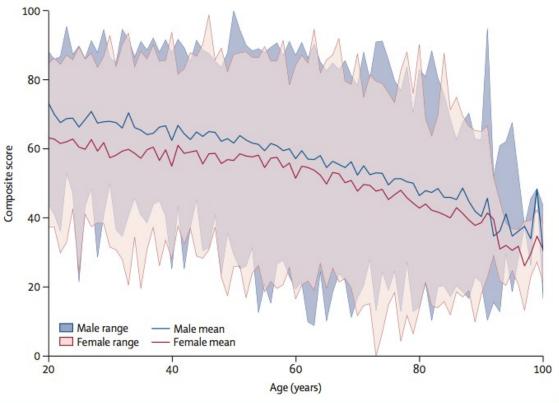
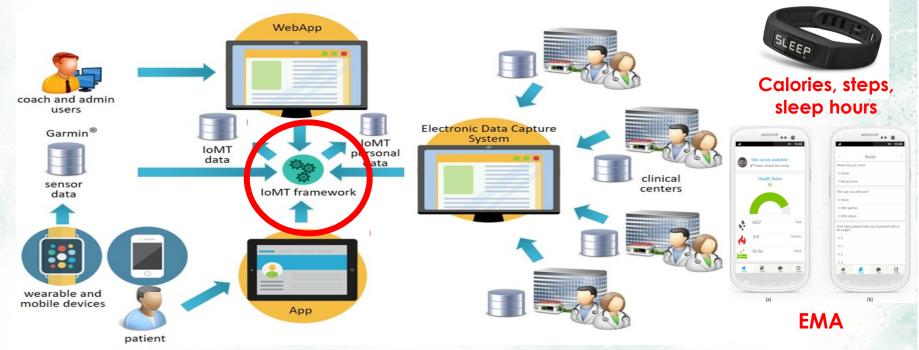


Figure 3: Range and mean intrinsic capacity of men and women in countries in the Study on global AGEing and adult health 2007-2010 (wave 1)⁴² Beard JR, et al. *Lancet* 2015;387:2145-2154

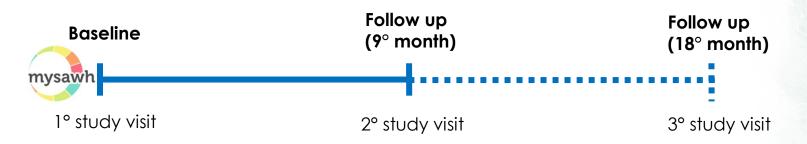
My Smart Age With HIV

mysawh

MySAwH is a 18 months multi-center prospective ongoing study designed to empower older adults living with HIV (OALWH) to achieve Healthy Ageing



Methods



Inclusion Criteria

- Age > 50;
- undergoing stable ART;
- routine access to a smartphone and willingness to use the fitness tracking device;
- willingness to be trained to use an interactive mobile application (MySAwH App).

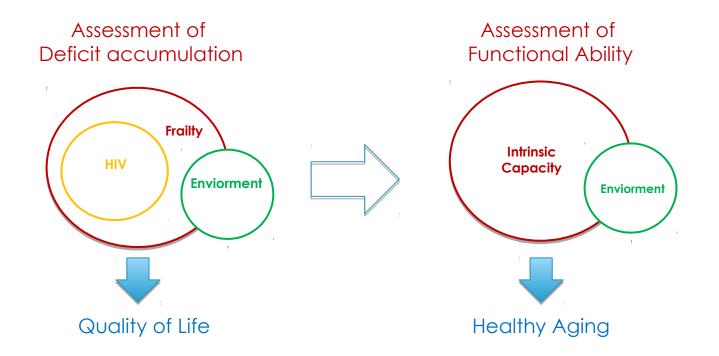
Population

224 OALWH

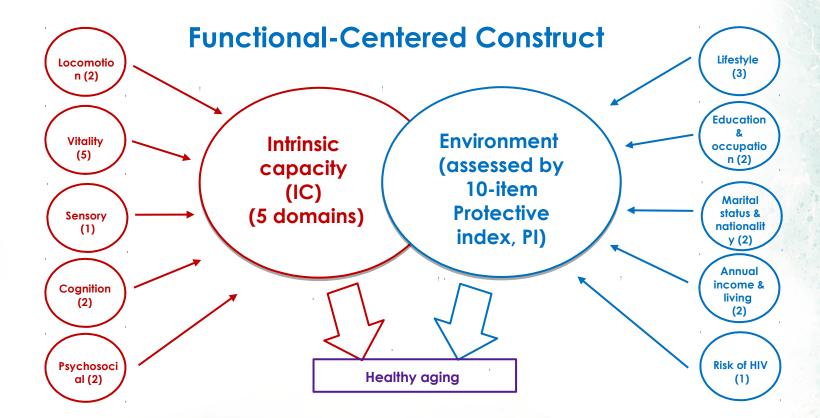
117 (52.23%) from Modena (Italy) 82 (36.61%) from Sidney (Australia) 25 (11.16%) from Hong Kong (China).

- Median age was 58.57 (5.74) years;
- 190 (86.76%) patients were man;
- Mean CD4 was 658.5 (480.25-817.75);
- 204 (91.07%) patients had undetectable HIV viral load.

Conceptual models to disease and health



Methods



Intrinsic capacity

Domains	Assessment
Locomotion	 ✓ Number of daily steps (Vivofit) ✓ SPPB (short physical performance battery)
Vitality	 ✓ Eating Behaviours questionnaire (EMA) ✓ Sleep Quality (EMA) ✓ Number of daily sleeping hours (Vivofit) ✓ Sexual Function Questionnaire (SFQ) ✓ Hand grip
Sensory	 ✓ Hearing handicap inventory for the elderly (HHIE)
Cognition	 ✓ PAOFI questionnaire ✓ GDS generated with Cogstate battery
Psychosocial	 ✓ Stress level questionnaire (EMA) ✓ Depression questionnaire (CES-D)

Cesari, M. et al. Evidence for The Domains Supporting The Construct of Intrinsic Capacity. J. Gerontol. A. Biol. Sci. Med. Sci. (2018).

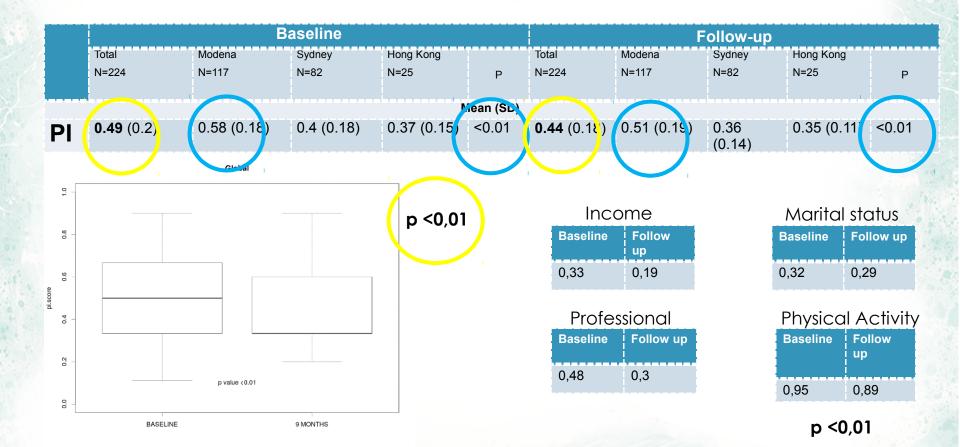
Protective Index

Protective Index domains	Assessment
Education	Elementary school
	High school
	Junior high School
	No formal education
	Post-secondary Educartion
Profession	Employed
	Retired
	Unemployed
Marital Status	Divorced
	Married & living together
	Married but living separated Never married
	Registered partnership
	Widowed
Income	20th percentile or lower
	Higher than the 20th percentile
Alchool use	How many drinks containing alcohol do you have on a typical day when you are drinking? or ≥2
Smoking	Yes/No
ntra-Venous Drug Use	Yes/No
Physical activity (METS)	≥ 150 min/Week
	Less
	None
Nationality	Same of the site/Other
_iving alone	Yes/No

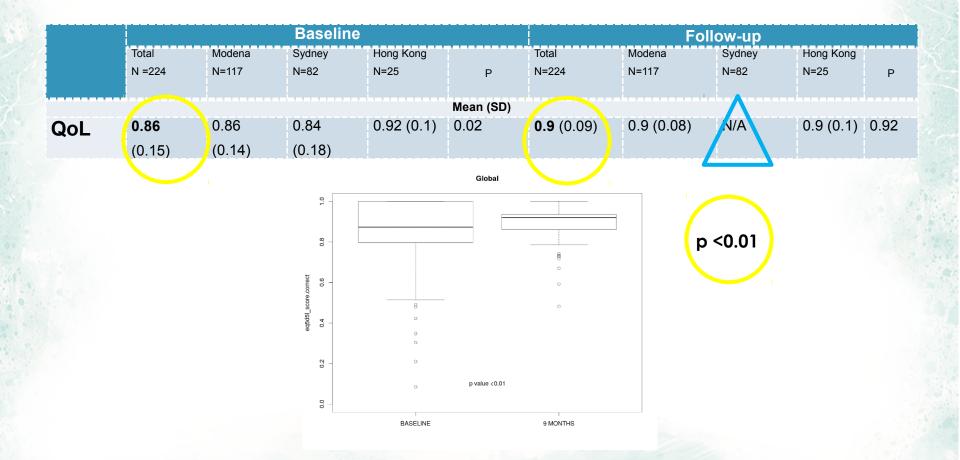
Results



Results

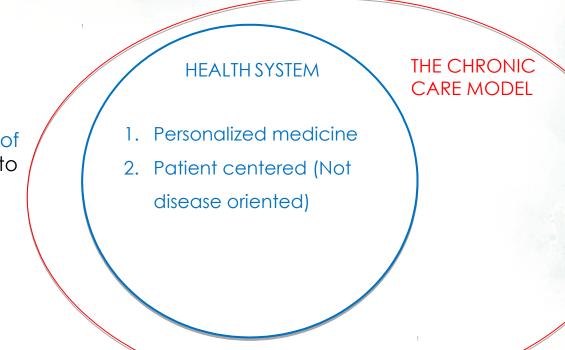


Results



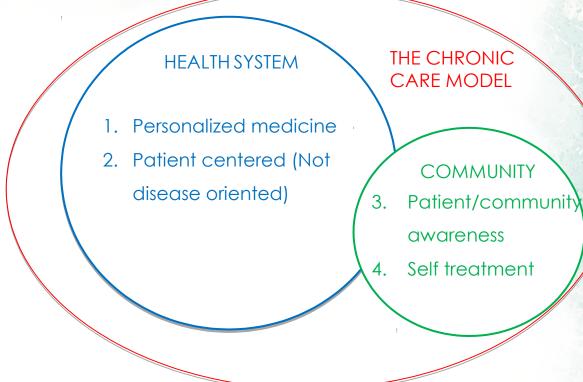
Total Patient care

Total Patient Care is a comprehensive patient approach which considers the physical, emotional, social, economic, and spiritual needs of the person; his or her response to illness;



Total Patient care

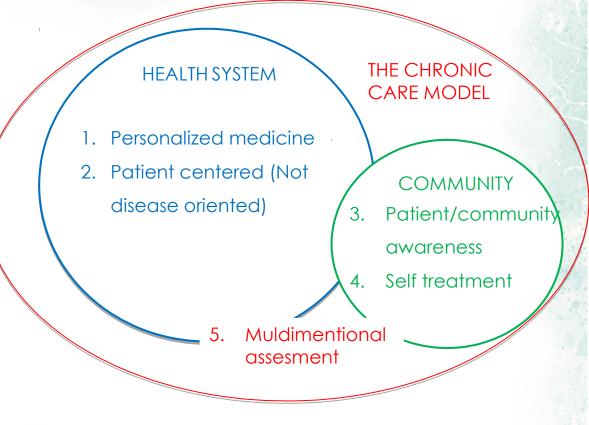
Total Patient Care is a comprehensive patient approach which considers the physical, emotional, social, economic, and spiritual needs of the person; his or her response to illness; and the effect of the illness on the ability to meet selfcare needs.



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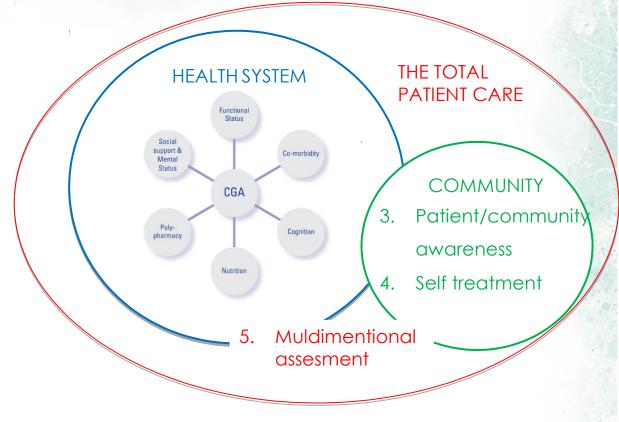
It means a transition away from a model of single referral center for care provision to a system of comprehensive coordinated care able to provide both primary and specialized support for PLWH



THE COMPREHENSIVE GERIATRIC ASSESSMENT (CGA)

The CGA is what better reproduce a Total Patient Care Model suitable to:

- ✓ Assess functional capacities
- Address a comprehensive coordinated care



Take home messages

- It is time to reshape healthcare system and define new relevant clinical outcomes based on a total patient care paradigm
- ✓ HIV care goes beyond obtaining HIV undetectability
- Assessment implies a switch from a multidisciplinary approach of HIV disease into a Multidimensional assessment of functional ability, through a comprehensive geriatric assessment

The ultimate goal for our patient (and for us) is HEALTHY AGING

