



***HIV & Aging in the era of ART
and COVID19***
an Inter-CFAR Virtual Symposium



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AIDS Research

**Resilience and frailty in people living with HIV during the COVID era:
two complementary constructs?**



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ACCEPTED MANUSCRIPT

HIV care models during the COVID-19 era ^{FREE}

Giovanni Guaraldi, Jovana Milic, Esteban Martinez, Adeeba Kamarulzaman, Cristina Mussini, Laura Waters, Anton Pozniak, Patrick Mallon, Jürgen Rockstroh, Jeffrey V Lazarus ✉

Clinical Infectious Diseases, ciaa1864, <https://doi.org/10.1093/cid/ciaa1864>

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Telehealth can compensate the reduction of face-to-face patient-physician encounters, promoting collection of health domains useful to reshape HIV care models towards a patient centred approach.

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Clinical Infectious Diseases, ciaa1864,

	Assessment	Follow-up frequency (#)	F2F	Telehealth	Tool	Comment
Psychosocial	Current lifestyle (alcohol use, smoking, diet, exercise, drug use)	At 4- and 8-months post F2F		✓	Questionnaire	Adverse lifestyle habits should be addressed more frequently
	Employment	At 4- and 8-months post F2F		✓	Screening questions	Provide advice and support if needed
	Social and welfare			✓	Screening questions	
	Psychological morbidity			✓	Screening questions	
	Partner and children			✓	Screening questions	Test partner and children if at risk
Sexual and Reproductive Health	Sexual history	At 4- and 8-months post F2F		✓	Screening questions	Address issues concerning sexual dysfunction Risk of sexual transmission should be addressed
	Safe sex			✓	Screening questions	
	Partner status and disclosure			✓	Screening questions	Recommend starting ART in serodifferent couples
Frailty		At 4- and 8-months post F2F		✓	Screening questionnaire	PLWH aged>50 years

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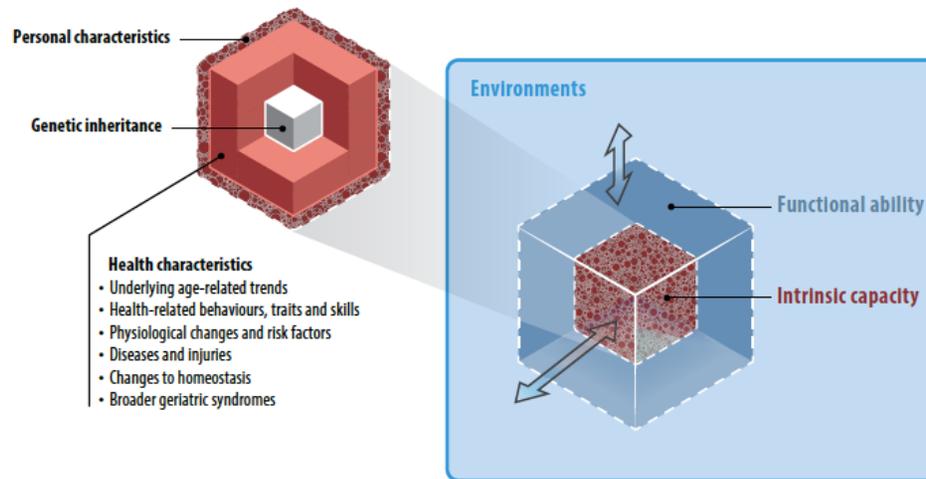
Clinical Infectious Diseases, ciaa1864,

	Assessment	Follow-up frequency (#)	F2F	Telehealth	Tool	Comment
Health-Related Quality of life		At 4- and 8-months post F2F		✓	Questionnaire	
Intrinsic capacity	Locomotion	At 4- and 8-months post F2F		✓	Screening questions	Refer to WHO ICOPE program https://www.who.int/ageing/health-systems/icope/en/
	Vitality	At 4- and 8-months post F2F		✓	Screening questions	
	Sensory	At 4- and 8-months post F2F		✓	Screening questions	
	Cognition	At 4- and 8-months post F2F		✓	Screening questions	
	Psychosocial	At 4- and 8-months post F2F		✓	Screening questions	



Healthy Aging : The process of developing and maintaining functional ability that enables wellbeing in older age

Functional ability: health-related attributes that **enable people to be and to do what they value in life**



INTRINSIC CAPACITY

Is the composite of all physical and mental capacities that an individual can draw upon during his/her life

Rationale

- COVID pandemic represents a common stressor which may impact differently vulnerable people.
- The relationship between resilience and frailty is poorly studied, both in the general population and in people living with HIV (PWH).

How to assess vulnerability

Frailty

is the **reduction of homeostatic reserves** exposing the individual to **higher risk of negative outcomes**.

It conceptualize the age-related increase of vulnerability and it is considered to be a measure of **biological age** of the individual

vs

Resilience

is the human **ability to adapt** in the face of significant life **stressors**

- (Physical) resilience is a characteristic at the whole person level which determines an individual's **ability to recover** physical health following a **stressor** (e.g. COVID disease)
- (Psychological) resilience refers to **effective coping and adaptation** although faced with **adversity**
- (e.g. COVID crisis)

Objective:

1. To characterize resilience in PLWH
2. To describe the relationship between frailty and resilience PLWH which identifies 4 different phenotypes which impact on QoL and Intrinsic capacity.

Methods:

In January 2021, PLWH attending MHMC at least once from during 2019, were offered to complete an electronic questionnaire including:

- **resilience score questionnaire: CD-RISC-25**
- **Frailty: 37-item frailty index**
- Insomnia Severity Index: ISI
- Depression Anxiety Stress: DASS
- Symptoms (Short form health survey): SF36
- health related quality of life: EQ 5D5L
- Intrinsic Capacity index: 29-item ICI

Tools to assess vulnerability

Frailty



Frailty was assessed by 37-item frailty index (FI)
FI was coded with the value of 1 when a deficit was present and 0 when absent

FI cut-offs:

- Fit: <0.25
- Frail: ≥ 0.25

vs

Resilience



Connor Davison resilience score questionnaire:
CD-RISC-25 score is from 0 to 100

Cut-offs:

- Resilient: ≥ 75.7
- Non resilient: < 75.7

The Connor Davidson + Brief Resilience Scales

The Connor Davidson Resilience Scale measures several components of resilience:

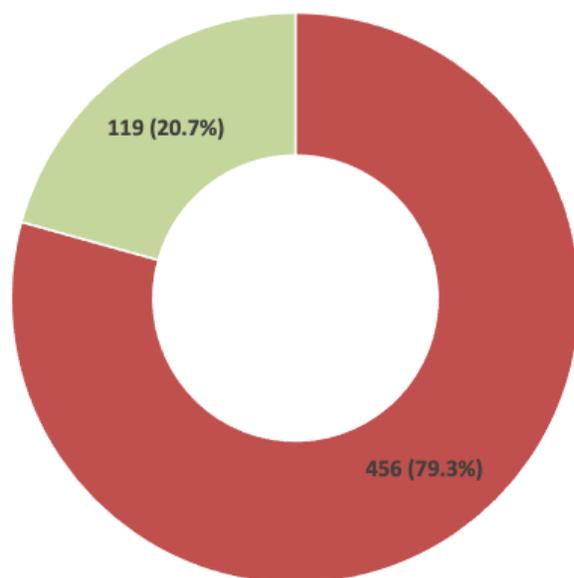
1. The ability to adapt to change.
2. The ability to deal with what comes along.
3. The ability to cope with stress.
4. The ability to stay focused and think clearly.
5. The ability to not get discouraged in the face of failure.
6. The ability to handle unpleasant feelings such as anger, pain or sadness.

Item No.	Item
Composite reliability	
1	Able to adapt to change
2	Close and secure relationships
4	Can deal with whatever comes
5	Past success gives confidence for new challenges
6	Try to see the humorous side of things
7	Coping with stress can strengthen me
8	Tend to bounce back after illness or hardship
10	Best effort no matter what
11	Can achieve goals despite obstacles
12	When things looks hopeless, I don't give up
13	Know where to turn for help
14	Can stay focused under pressure
15	Prefer to take the lead in problem solving
16	Not easily discouraged by failure
17	Think of self as a strong person
18	Make unpopular or difficult decisions
19	Can handle unpleasant feelings
21	Have a strong sense of purpose
22	In control of your life
23	I like challenges
24	You work to attain your goals
25	Pride in your achievements

Health outcomes



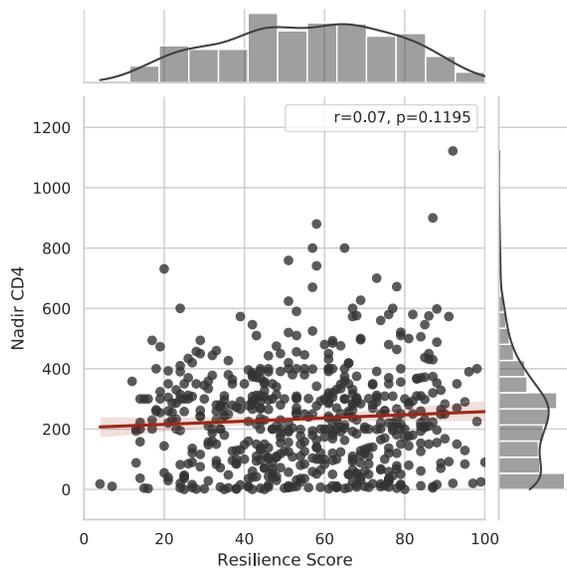
Out of 800 PLWH reached via mail, 575 (72%) completed the CD-RISC-25 questionnaire.



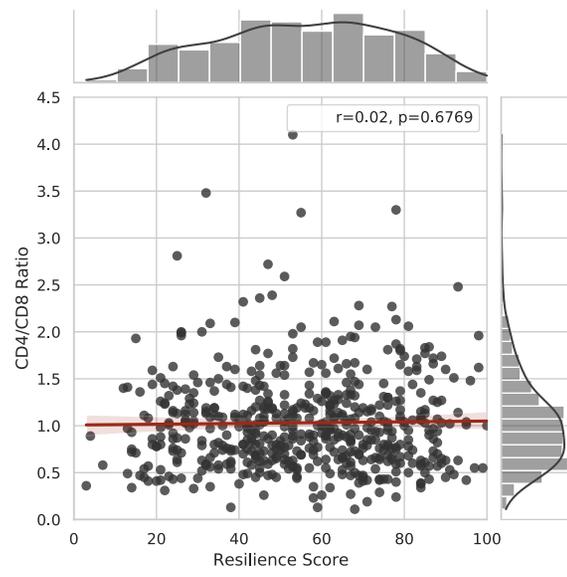
■ Non resilient (CD-RISC-25 score <75.7) ■ Resilient (CD-RISC-25 score ≥75.7)

	Resilient N=119 (20.7%)	Non resilient N=459 (79.3%)	p
Age, years, mean (±SD)	54.6 (8.4)	54.5 (7.2)	0.91
HIV duration, months, median (IQR)	272 (168 - 325)	301 (213 - 365)	0.007
Nadir CD4 cell count, c/microl, median (IQR)	221 (120 - 366)	222 (100 - 312)	0.11
Multimorbidity, %	98 (82.4%)	362 (79.4%)	0.55
Loneliness, %	11 (9.2%)	112 (24.6%)	<0.001

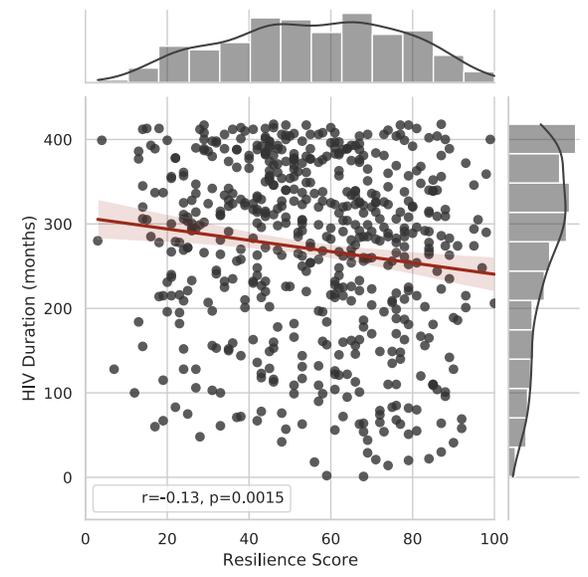
Is there an HIV specific biological correlate to psychological resilience?



Nadir CD4



Current CD4/CD8



HIV duration

Predictors of impaired psychological resilience

Univariate analysis

	ODDS RATIO	95% CI	p
Demographic characteristics and lifestyles			
Age > 50 years	1.64	1.04 – 2.61	0.03
Female sex	1.81	1.05 – 3.11	0.03
Migrant status	0.38	0.06 – 2.32	0.59
Employed	1.0	0.65 – 1.55	0.99
Education > 13 years	1.14	0.68 – 1.92	0.62
Alcohol consumption	1.12	0.70 – 1.79	0.63
Smoking	1.27	0.81 – 1.99	0.29
Physical activity	0.61	0.40 – 0.92	0.02

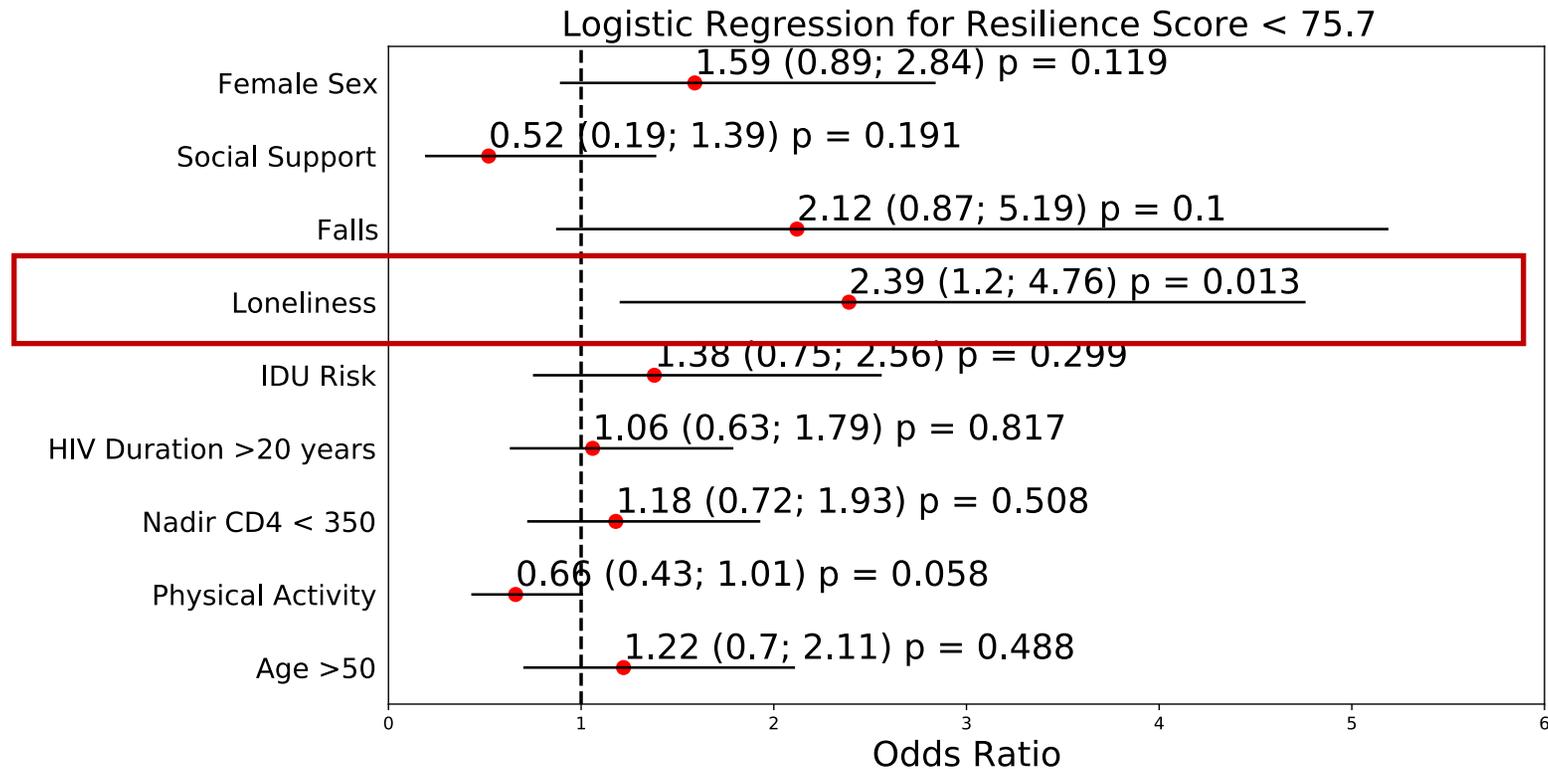
Predictors of impaired psychological resilience

Univariate analysis

	ODDS RATIO	95% CI	p
HIV characteristics			
CDC – C group	1.35	0.81 – 2.25	0.26
Nadir CD4 <350	1.53	0.97 – 2.43	0.07
HIV duration >20 years	1.48	0.98 – 2.24	0.06
CD4/CD8 ratio <1	1.17	0.78 – 1.77	0.44
HIV risk - IDU	1.69	0.96 – 2.95	0.07
Social characteristics			
Health costs difficulties	1.47	0.70 – 3.09	0.31
Loneliness	3.20	1.66 – 6.16	<0.001
Family and social support	0.31	0.12 – 0.80	0.01
Falls	2.96	1.25 – 7.03	0.01

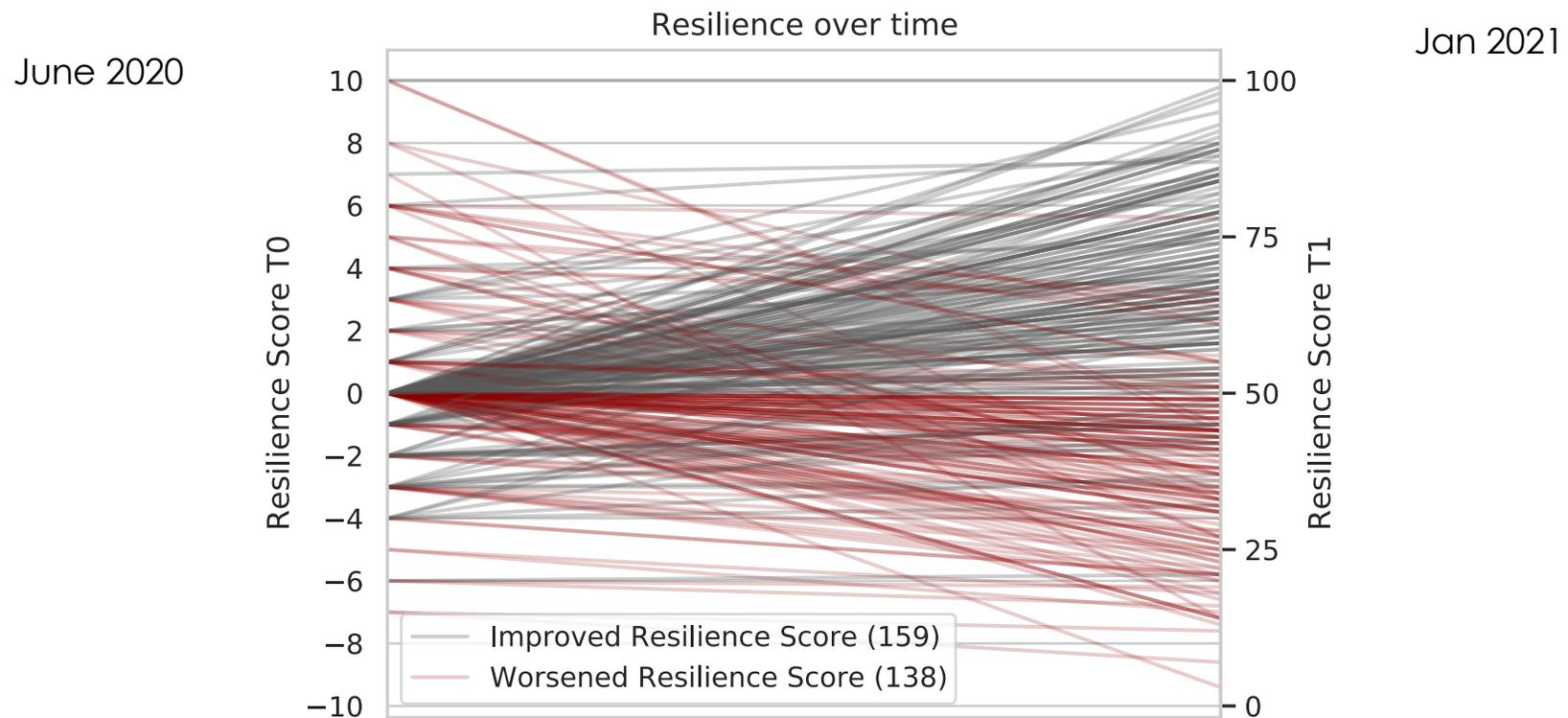
Predictors of scarce psychological resilience

Multivariate regression model

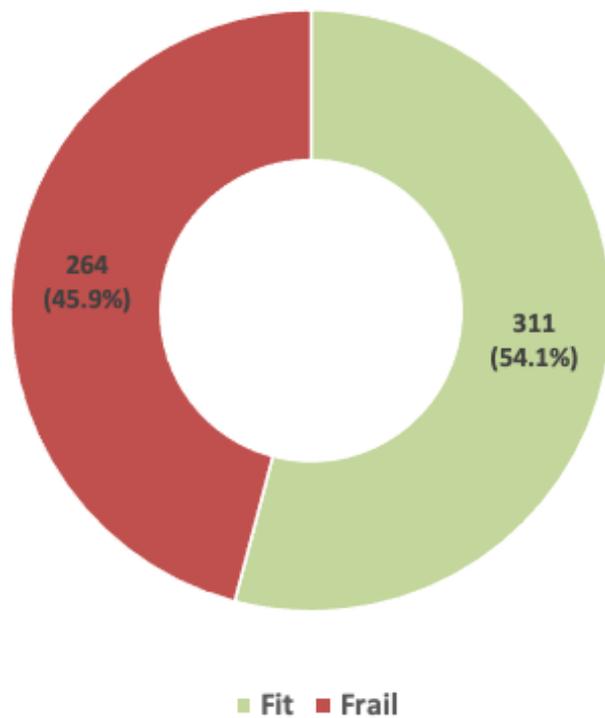


Does resilience vary over time?

In a subset of 297 PLWH in this cohort we compared results of “CD-risk-25” with “HIV resilience questionnaire” examined 6 months before



Frailty (defined as FI \geq 0.25) in PLWH

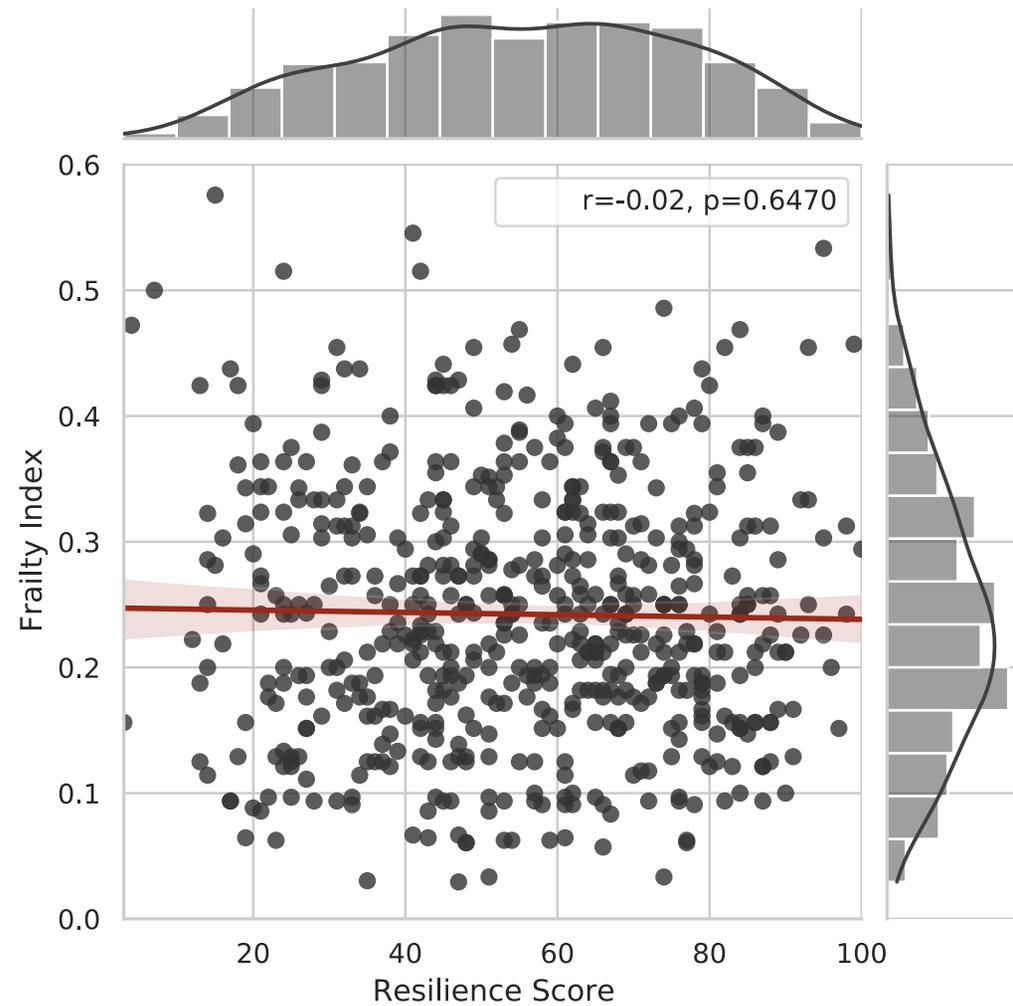


	Fit N=311 (65.1%)	Frail N=264 (45.9%)	p
Age, years, mean (\pm SD)	52.7 (7.8)	56.6 (6.5)	<0.001
HIV duration, months, median (IQR)	259 (149.5 - 326)	323 (263 - 381.5)	<0.001
Nadir CD4 cell count, c/microL, median (IQR)	254 (124.5 - 350)	191 (71.5 - 300)	<0.001
Multimorbidity, %	215 (69.1%)	245 (92.8%)	<0.001
Loneliness, %	60 (19.3%)	63 (23.9%)	0.22

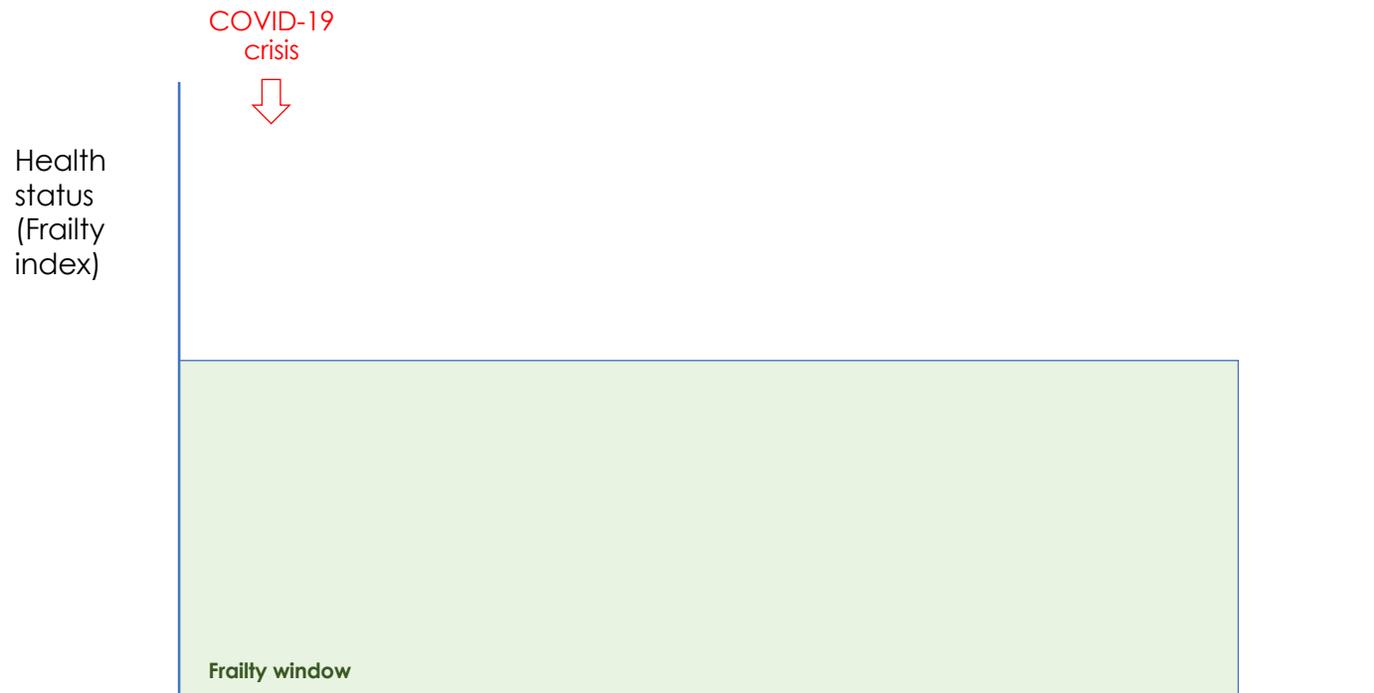
Drivers of frailty and resilience in PLWH

	FRAILITY	RESILIENCE
Age	✓	X
HIV duration	✓	✓
Nadir CD4 cell count	✓	X
Multimorbidity	✓	X
Loneliness	X	✓

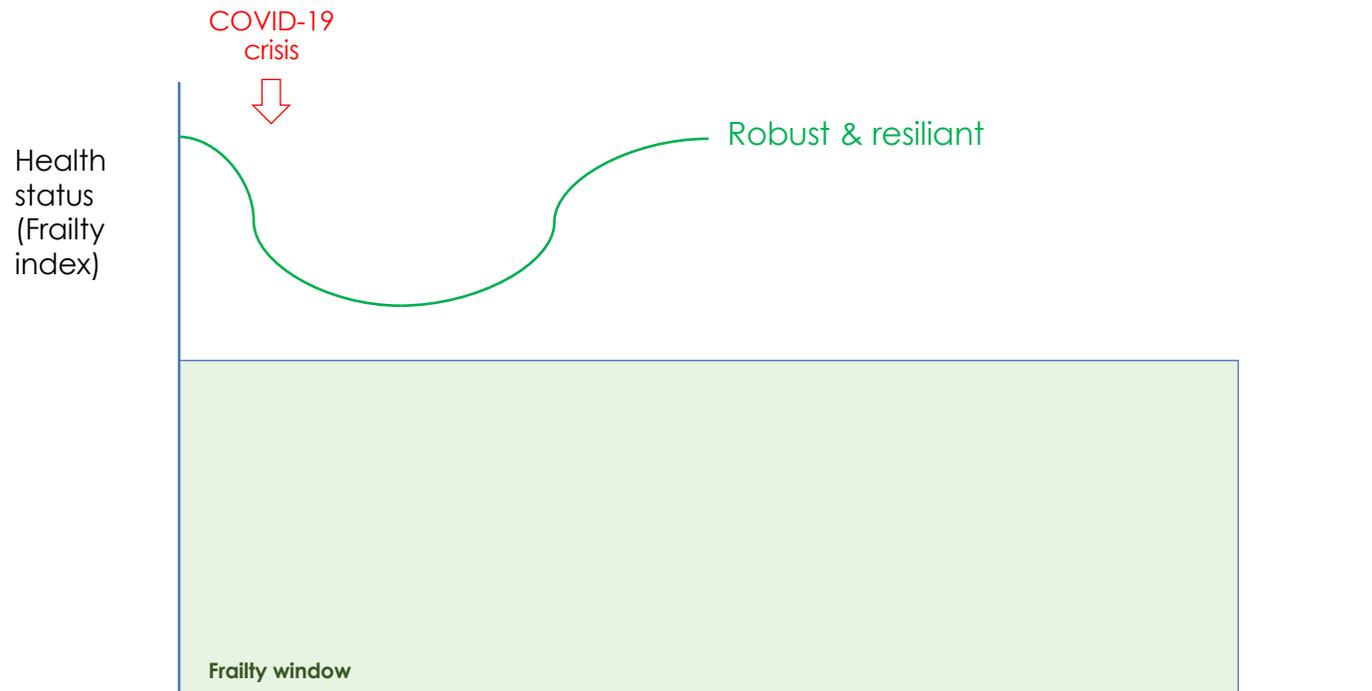
Frailty and Resilience are not overlapped health domains



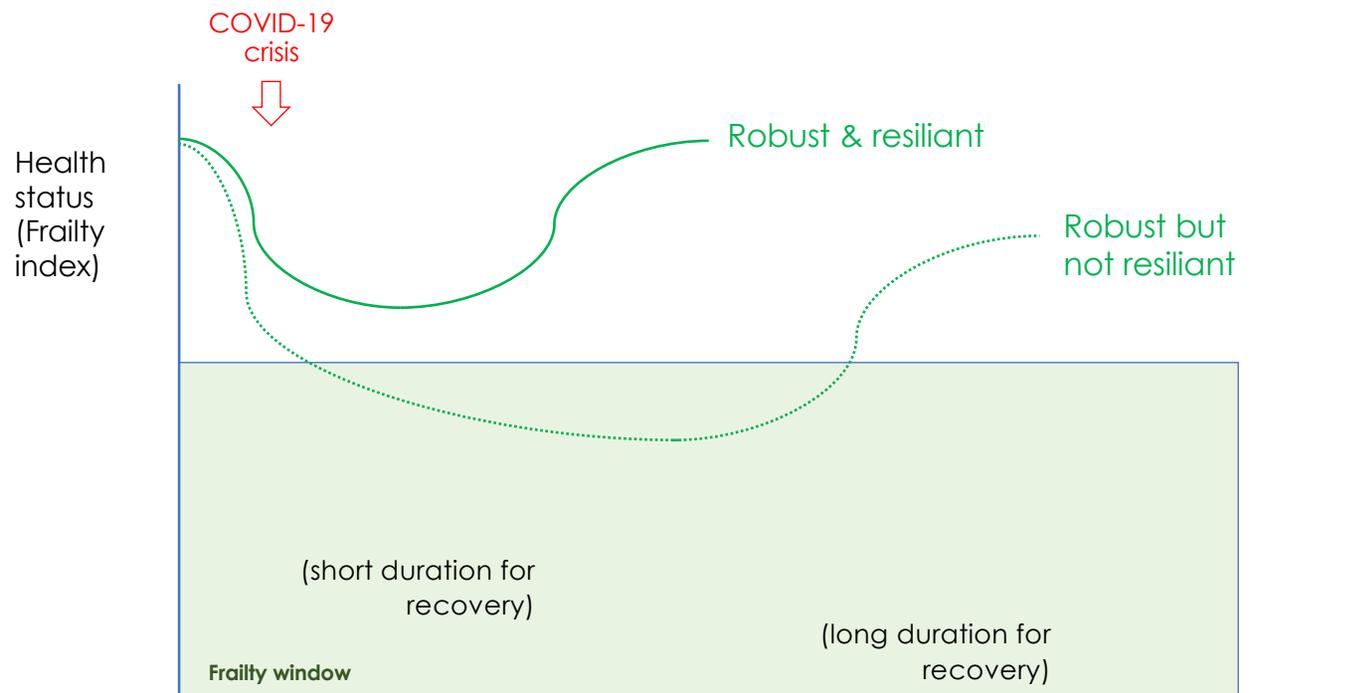
Conceptual model to combine Frailty and Resilience



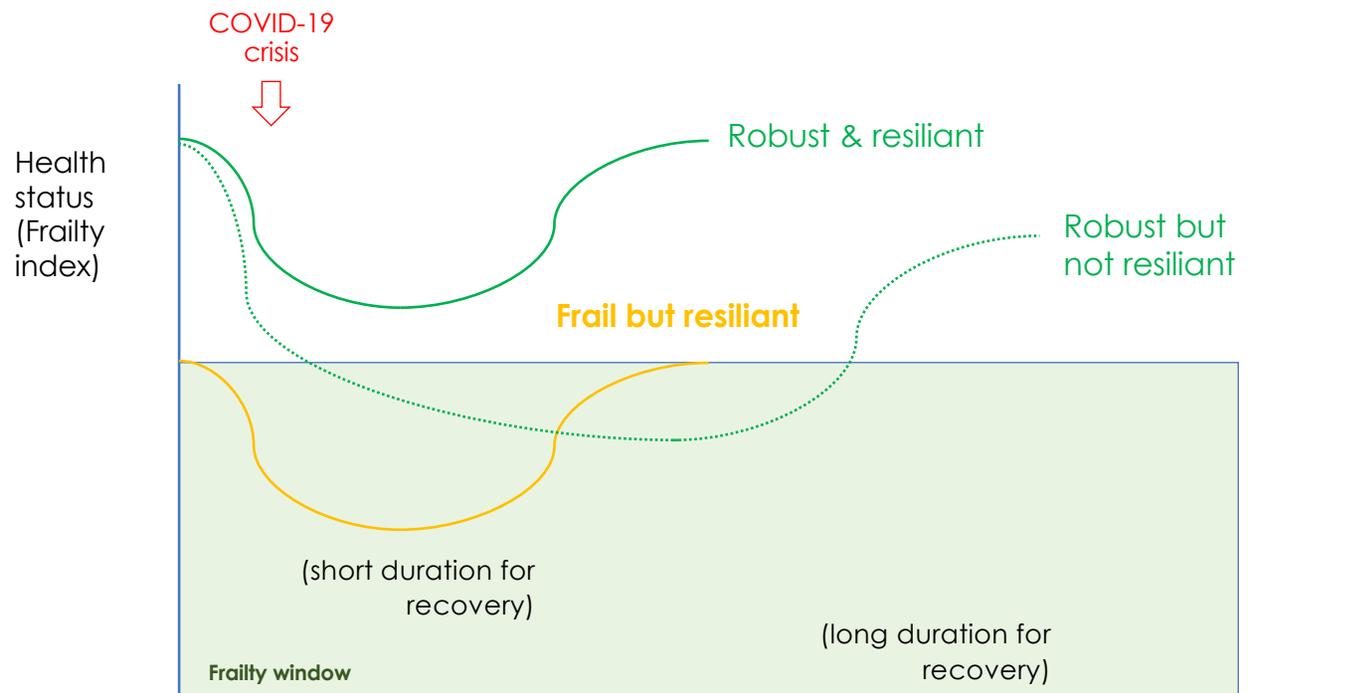
Conceptual model to combine Frailty and Resilience



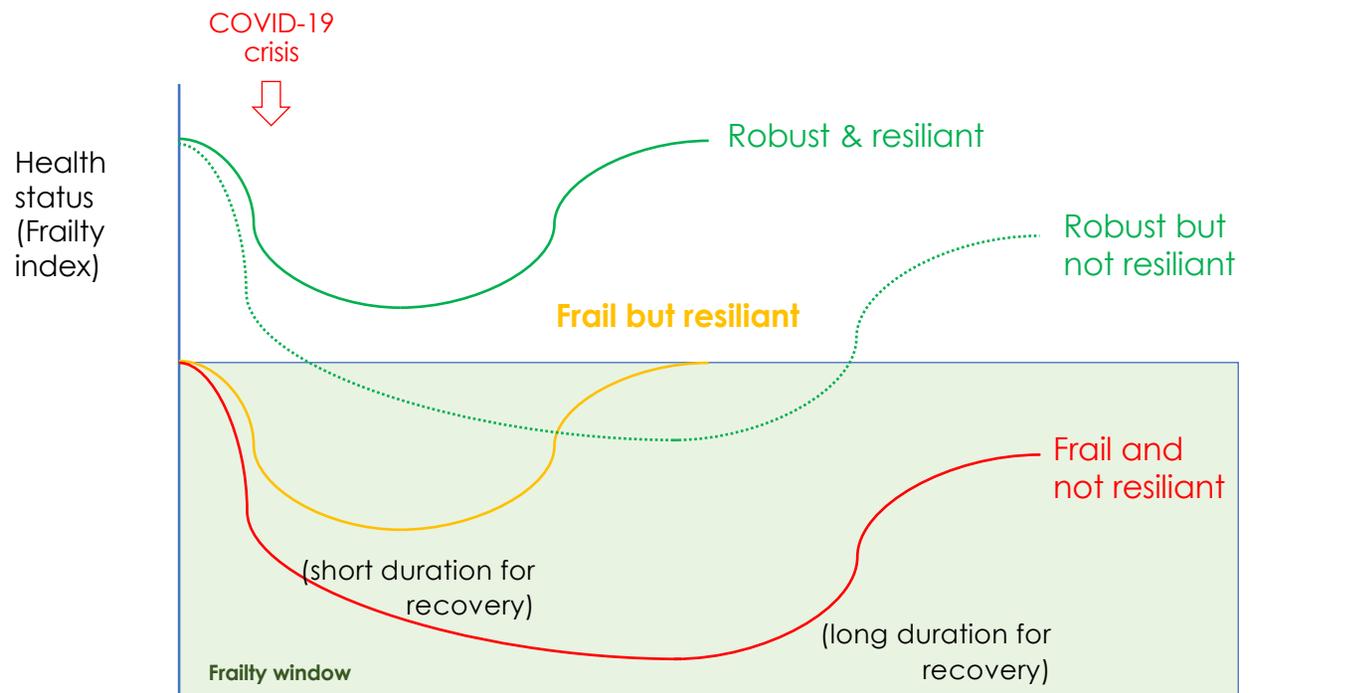
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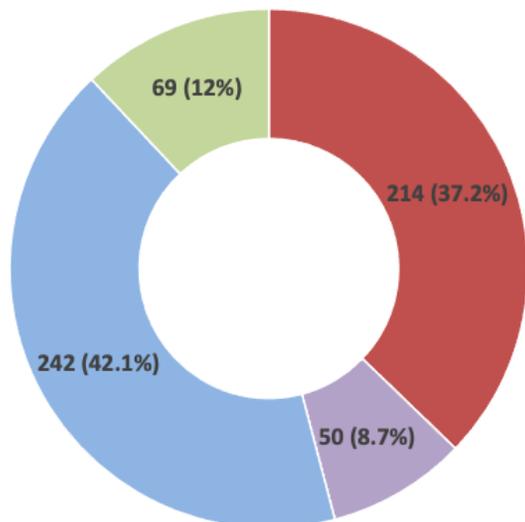
Conceptual model to combine Frailty and Resilience



Conceptual model to combine Frailty and Resilience



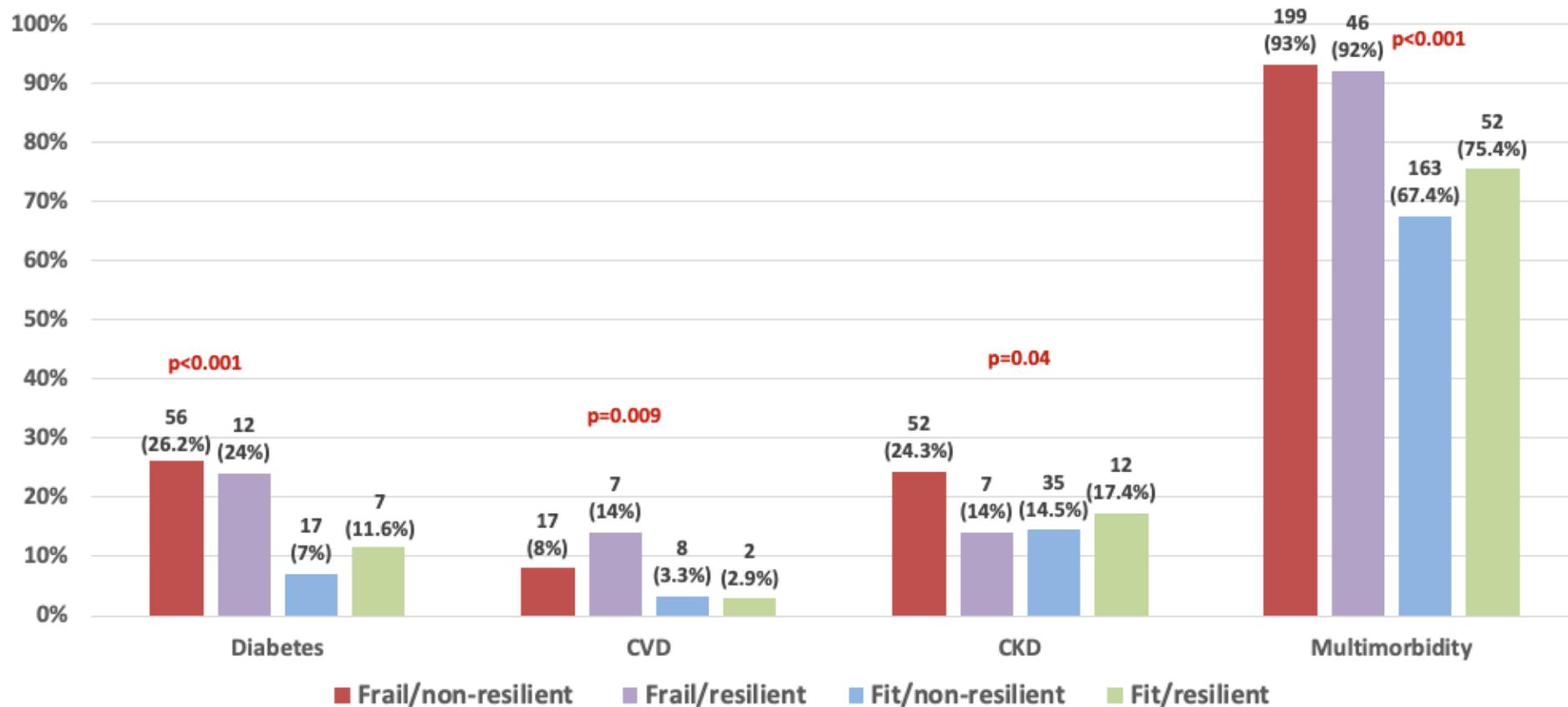
Out of 800 PLWH reached via mail, 575 (72%) completed the questionnaires. Frailty was assessed in 2019, at the closest visit prior to the onset of COVID pandemic.



	Fit & resilient N=69 (12%)	Fit & non resilient N=242 (42.1%)	Frail & resilient N=50 (8.7%)	Frail & non resilient N=214 (37.2%)	p
Age, years, mean (±SD)	52.9 (8.6)	52.7 (7.5)	56.9 (7.6)	56.5 (6.3)	<0.001
HIV duration, months, median (IQR)	246 (139 - 307)	263 (152 - 334)	290.5 (207.3 - 347.5)	326 (267 - 386)	<0.001
Nadir CD4 cell count, c/microl, median (IQR)	250 (162 - 361)	261 (127 - 350)	202.5 (84.8 - 363.5)	190.5 (66.3 - 284.8)	<0.001
Multimorbidity, %	52 (75.4%)	163 (67.4%)	46 (92%)	199 (92.9%)	<0.001
Loneliness, %	7 (10.1%)	53 (21.9%)	4 (8%)	59 (27.6%)	0.002

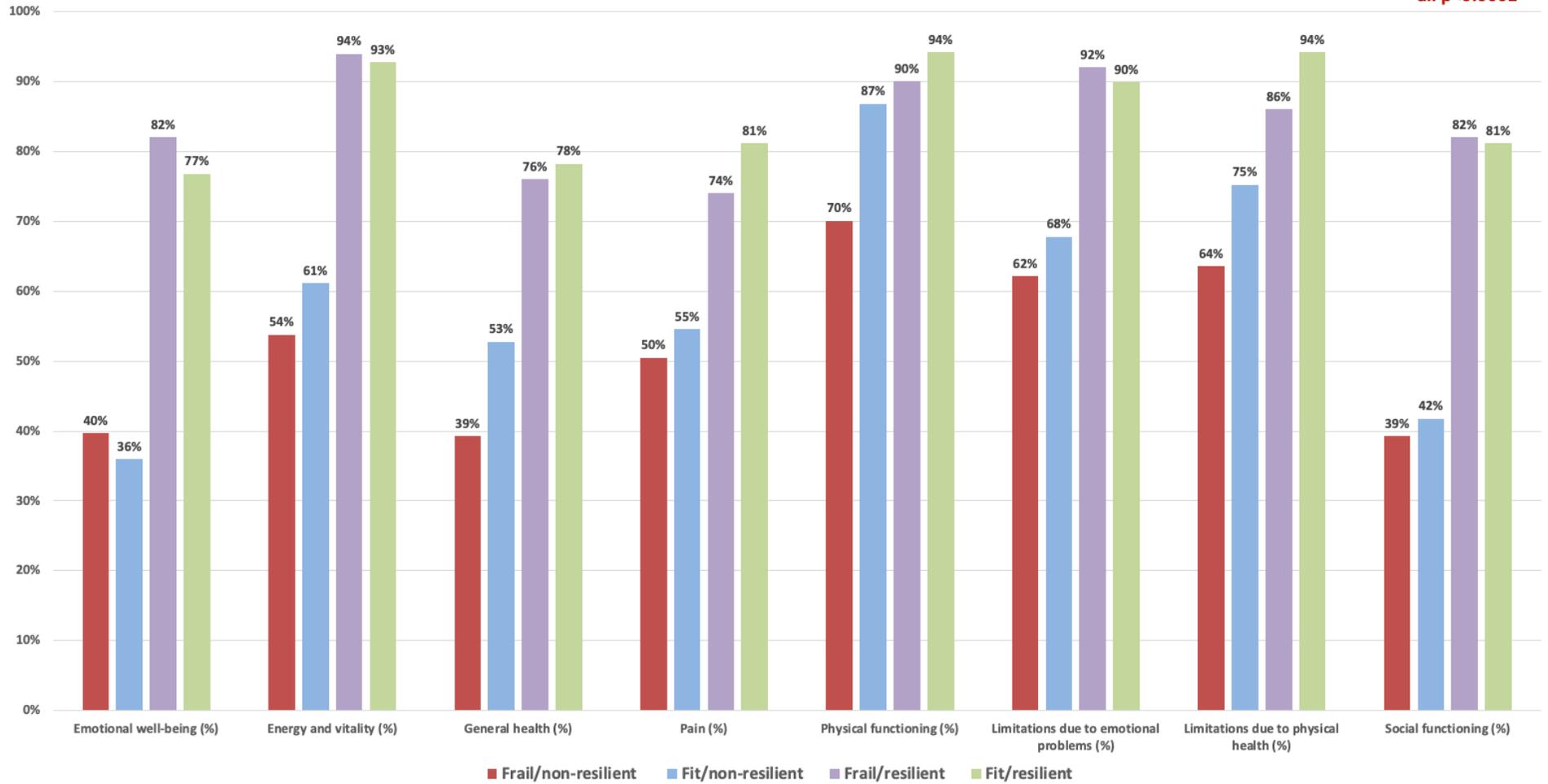
■ Frail/non-resilient ■ Frail/resilient ■ Fit/non-resilient ■ Fit/resilient

Prevalence of co-morbidities across frailty-resilience phenotypes

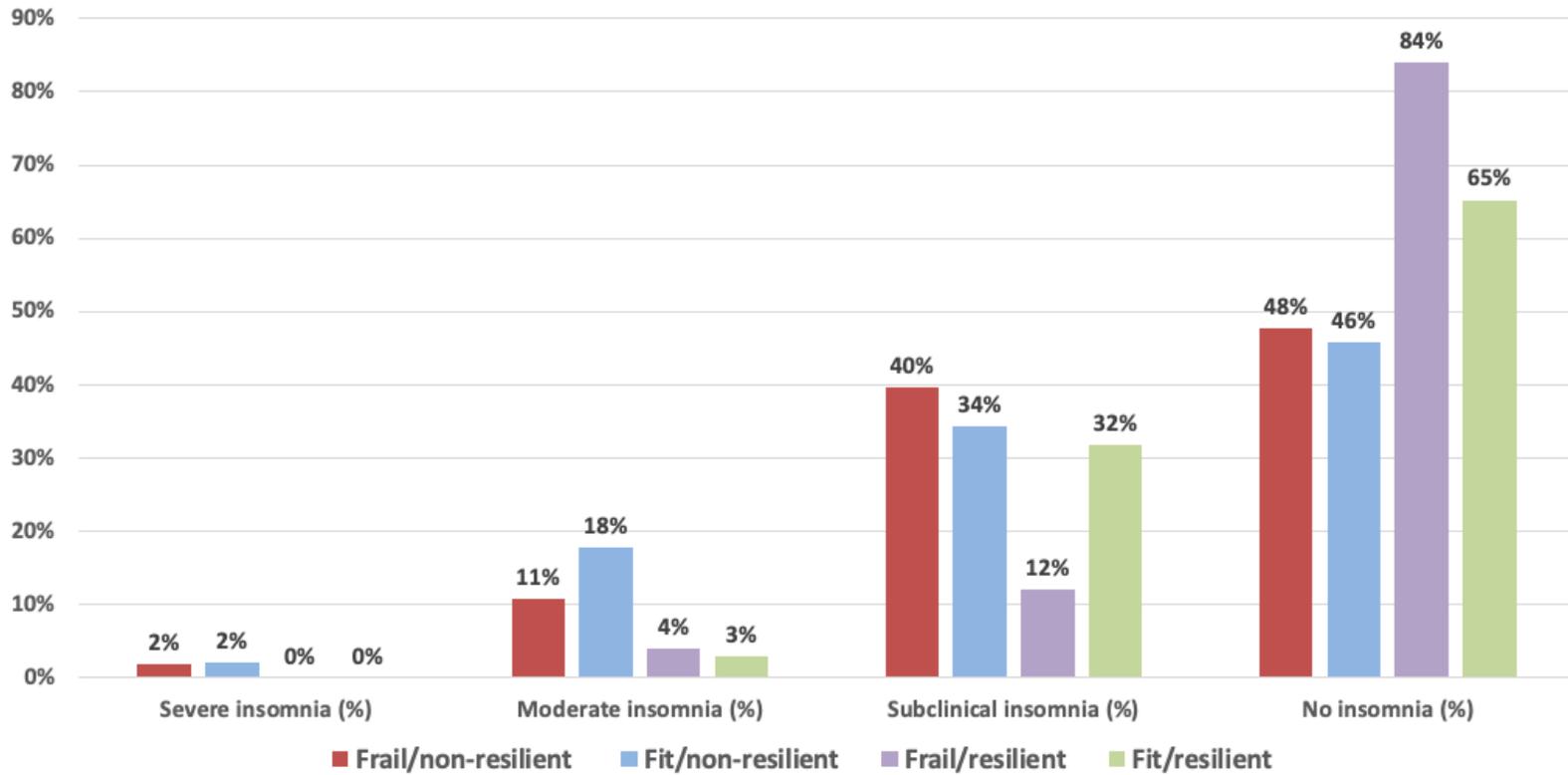


Domains of SF-36 across frailty/resilience phenotypes (% of PLWH with score above the average)

all p<0.0001

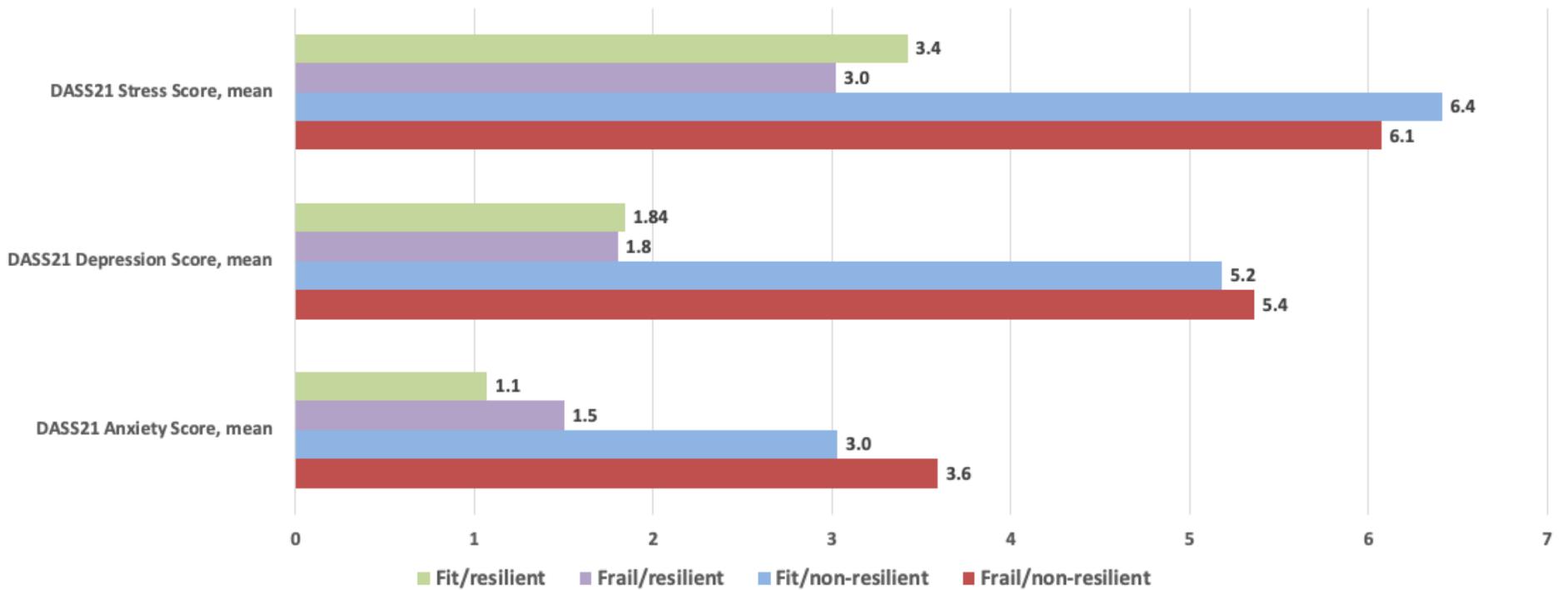


Insomnia severity index across frailty/resilience phenotypes $p < 0.001$

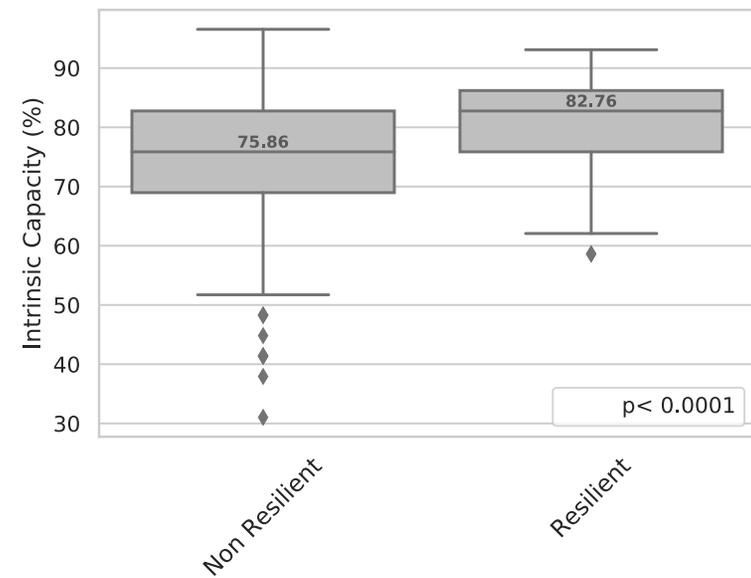
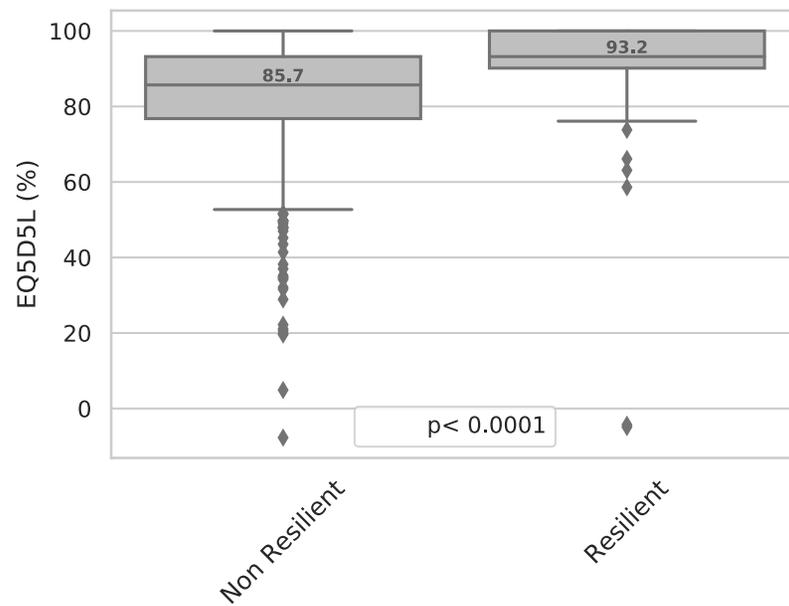


Depression, anxiety and stress score across frailty/resilience phenotypes

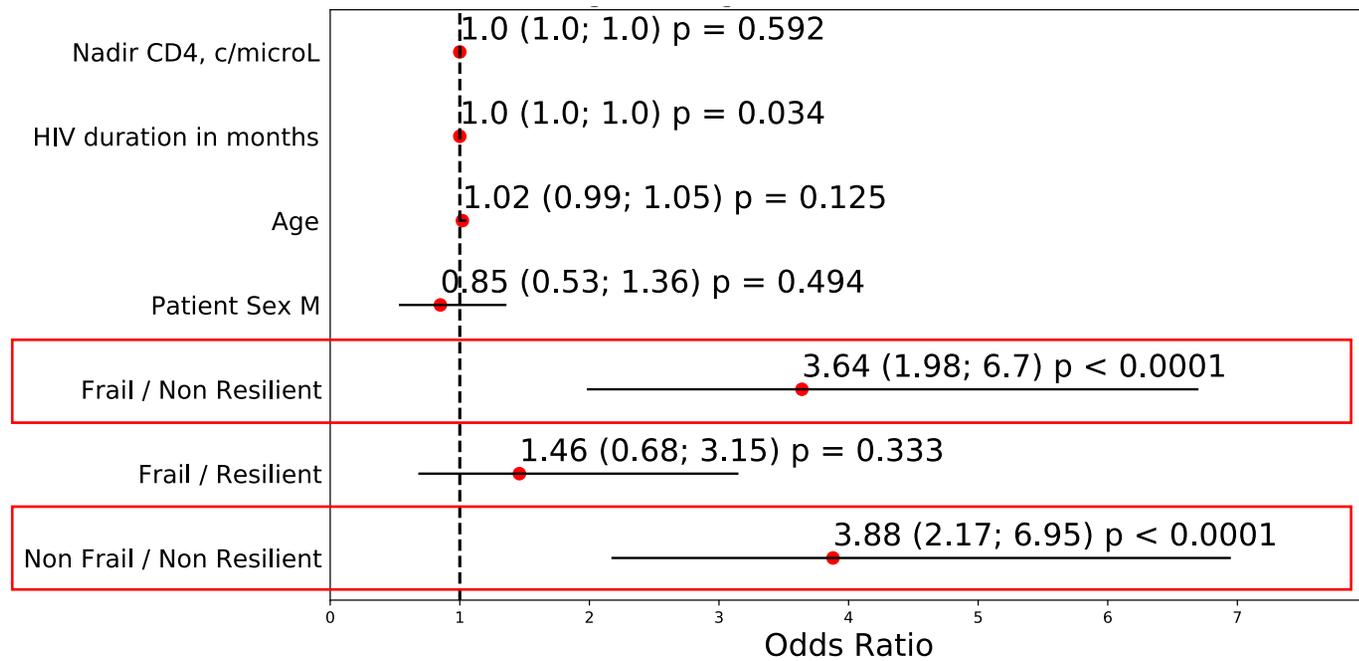
p<0.001



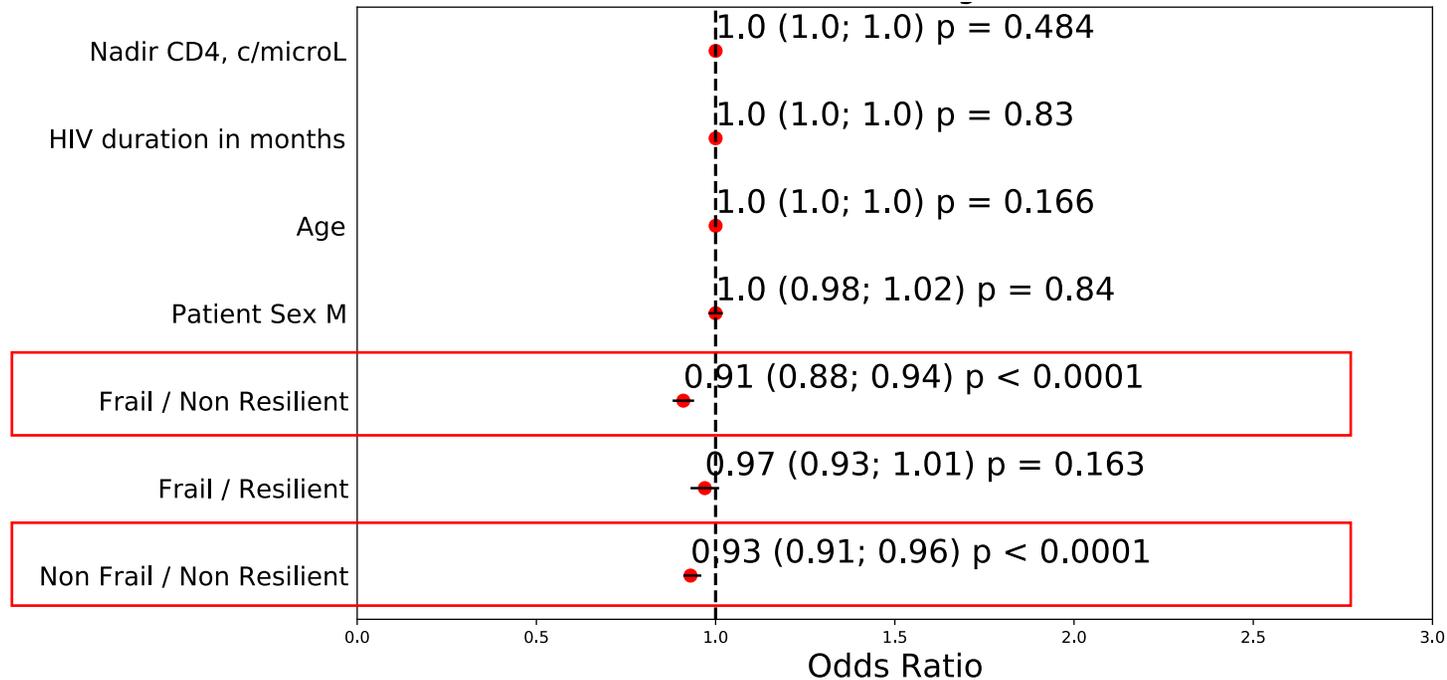
Relationship between resilience and HRQoL and IC at univariate analysis



Outcome 1: logistic regression model to predict EQ 5D5L<93% (4th quartile)



Outcome 2: multilinear regression model to predict intrinsic capacity index as a continuous variable (ranging from 0 the worst to 1 the best)



Take home message

- Resilience construct characterises health status and well-being of PLWH during COVID crisis.
- In an ongoing COVID crisis stress, prevalence of resilience tend to decrease over time
- This health outcome is complementary to frailty in the identification of clinical phenotypes with different impacts on relevant clinical outcomes including HRQoL and Intrinsic Capacity
- Frailty and resilience should be evaluated in PLWH to identify vulnerable individuals in order to priorities urgent health interventions.