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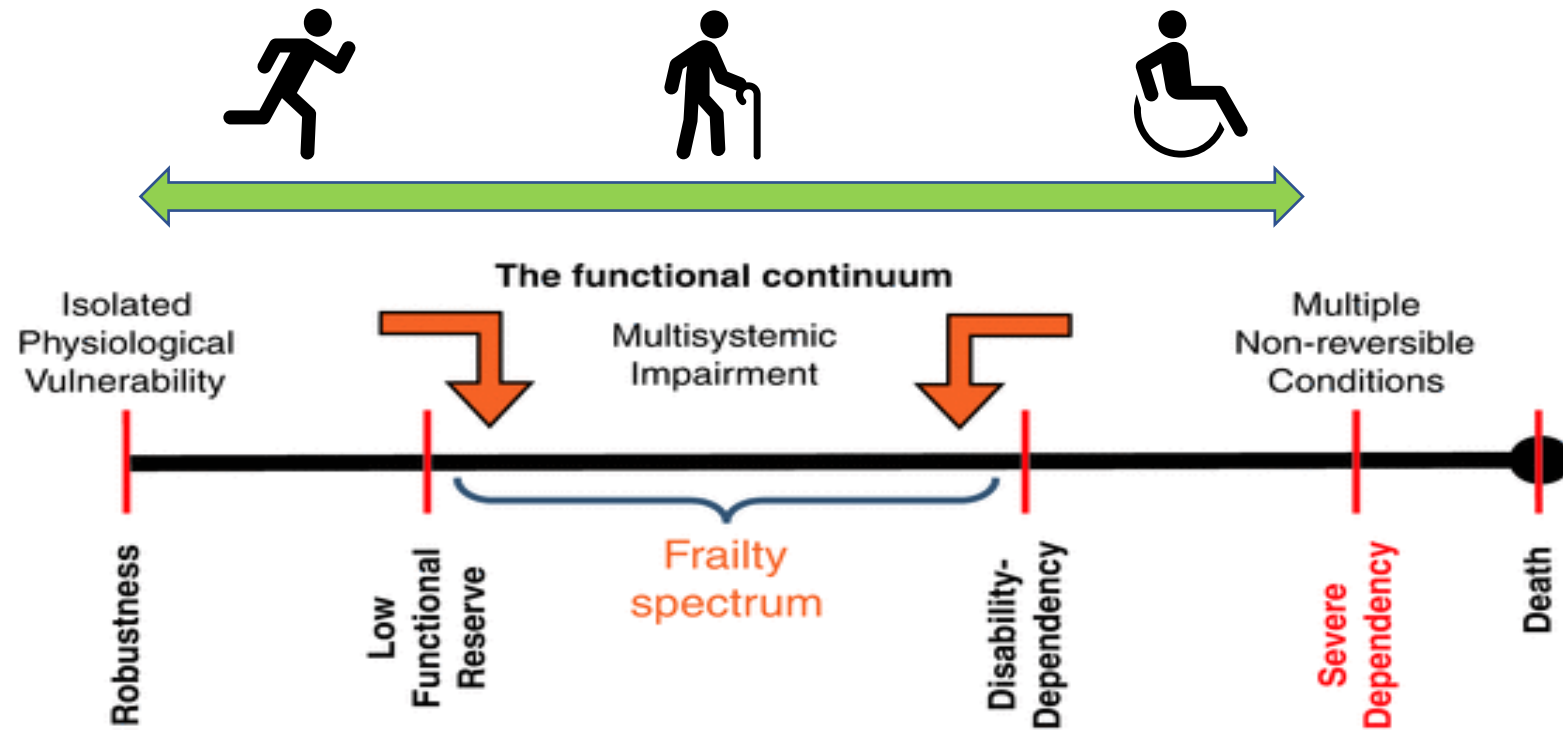


Investigating and Modifying Frailty in PLWHIV

Dr Liam Townsend, MB PhD

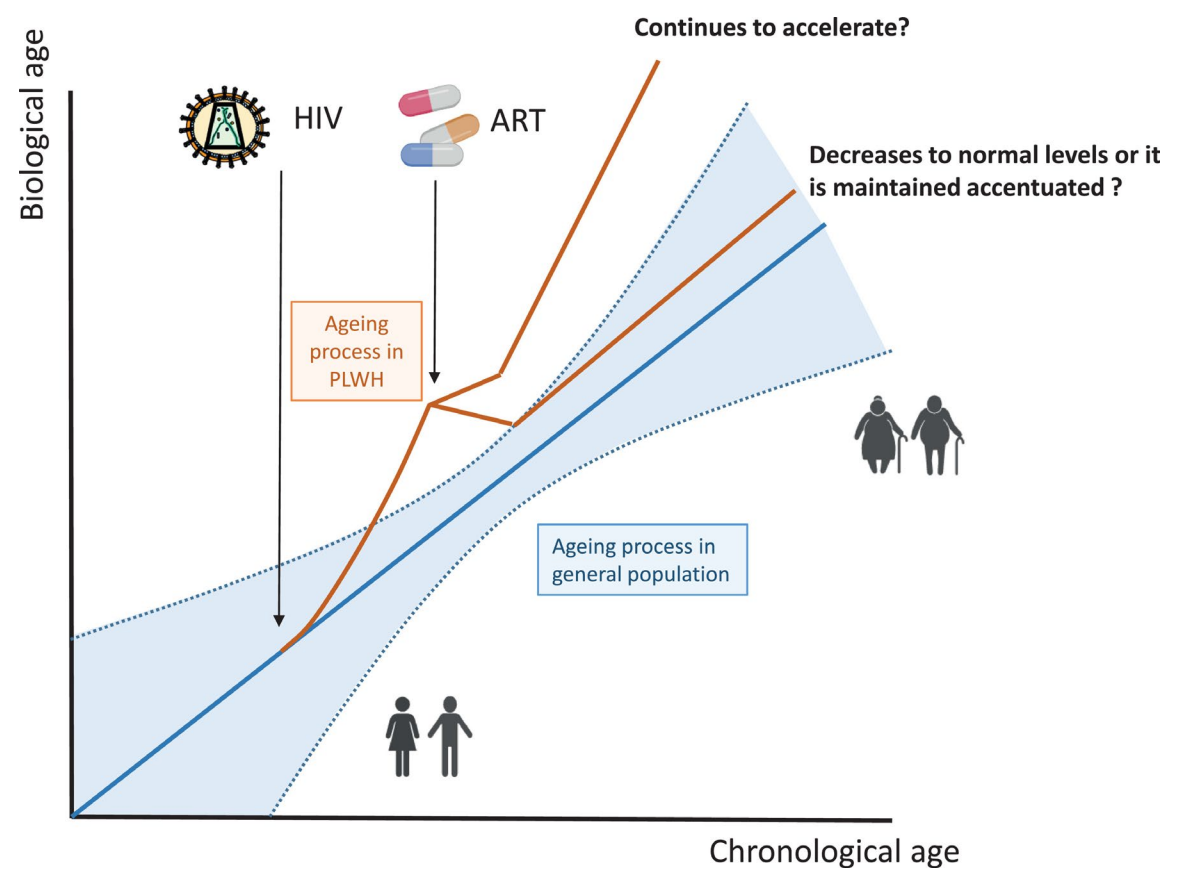
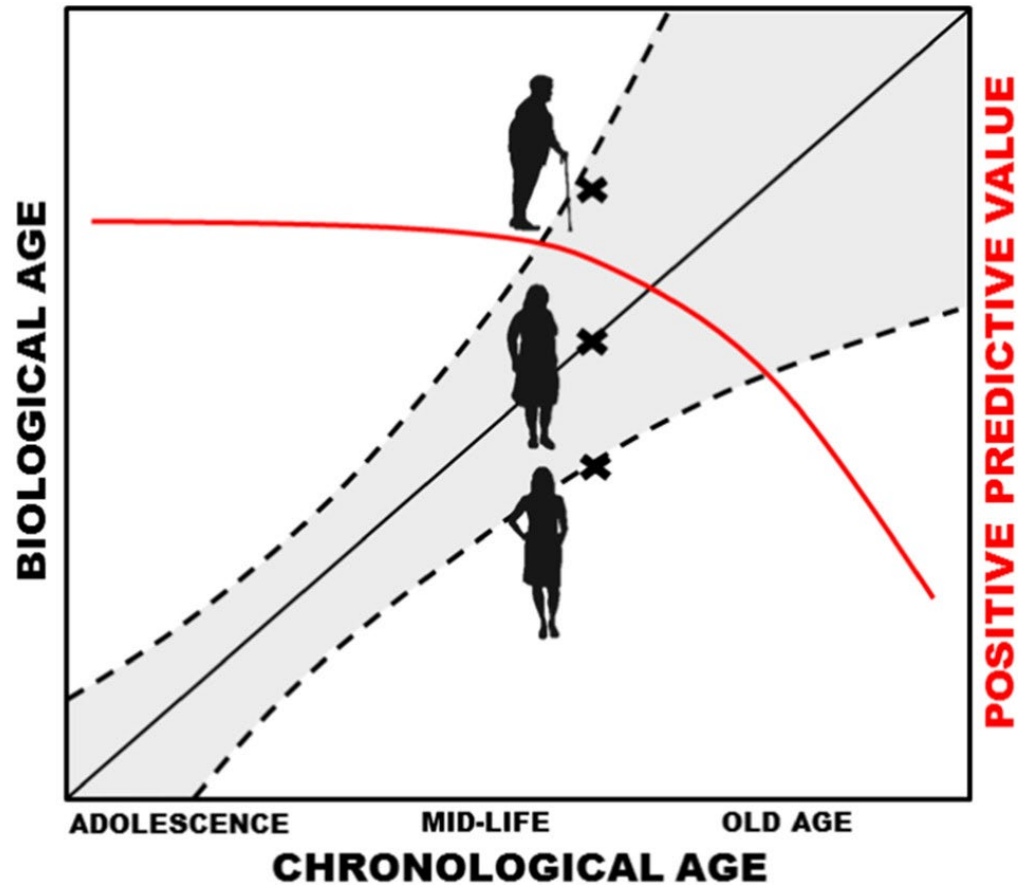
St James's Hospital, Dublin, Ireland

Frailty

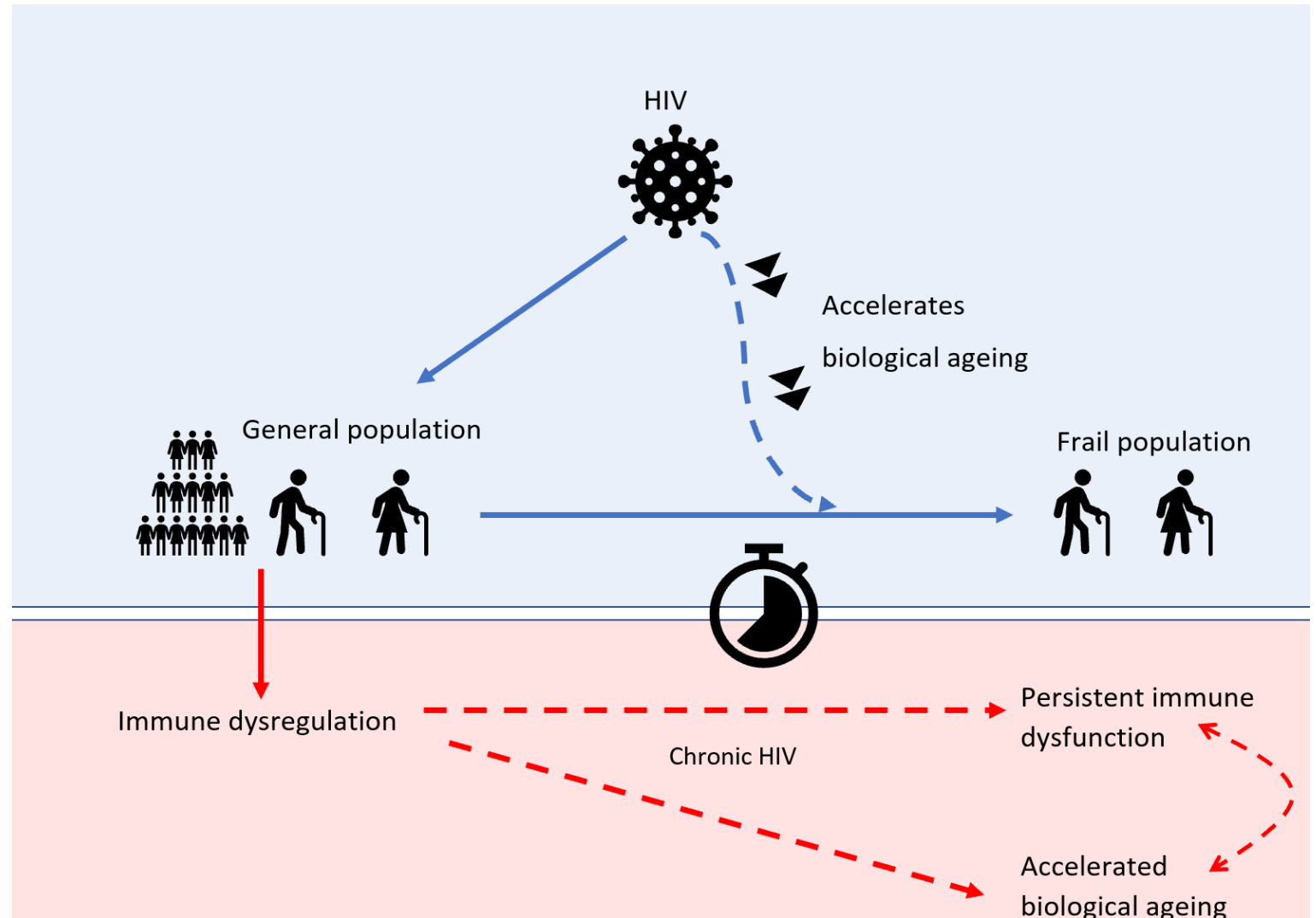


Rodriguez-Mañas, L. and Mora, M.A.C., The Concept of Frailty and Functional Decline.

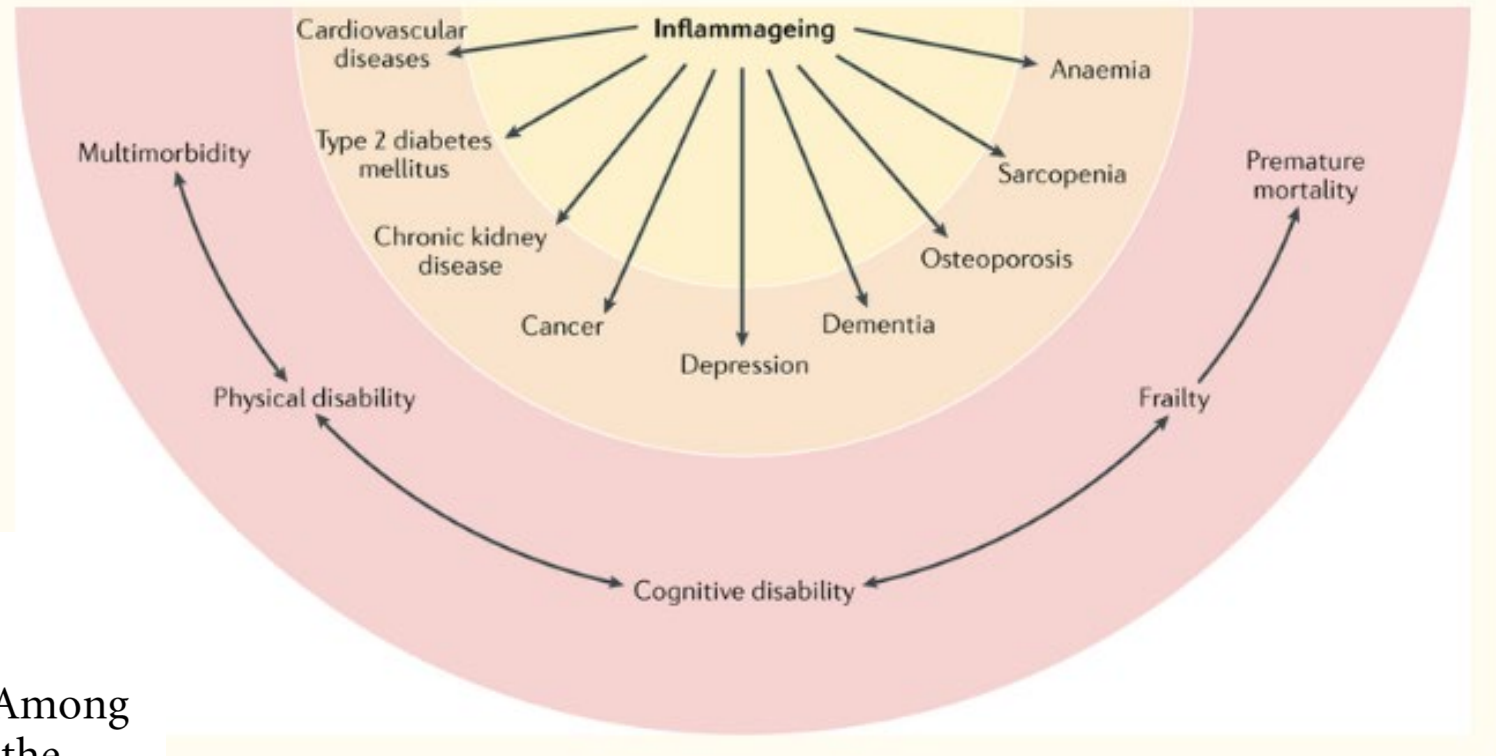
Types of Ageing



Proposed mechanisms of HIV-associated frailty



Inflammageing



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 Palella⁴

Prevalence of HIV and chronic comorbidities among older adults

Joel Negin^a, Alexandra Martiniuk^{a,b,c}, Robert G. Cumming^a, Nirmala Naidoo^d, Nancy Phaswana-Mafuya^{e,f}, Lorna Madurai^g, Sharon Williams^h and Paul Kowal^d

Contributions of traditional and HIV-related risk factors on non-AIDS-defining cancer, myocardial infarction, and end-stage liver and renal diseases in adults with HIV in the USA and Canada: a collaboration of cohort studies

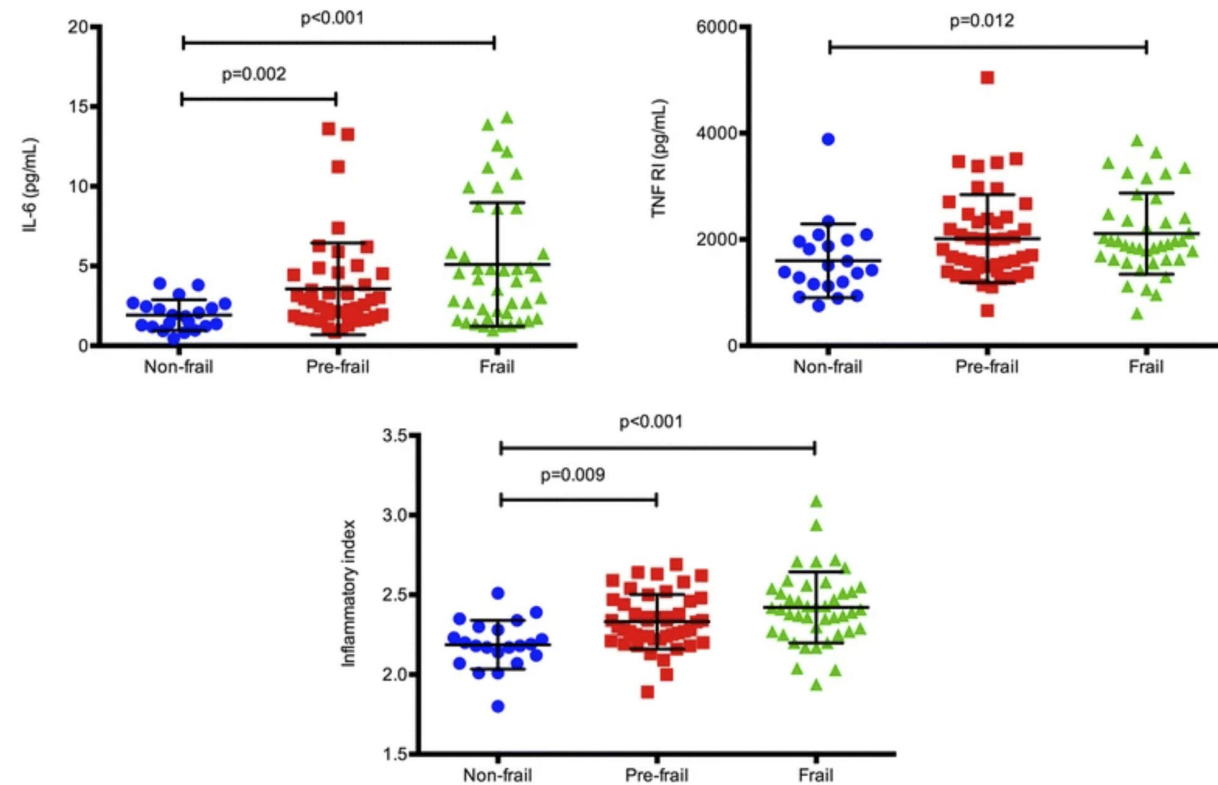
Keri N Althoff, Kelly A Gebo, Richard D Moore, Cynthia M Boyd, Amy C Justice, Cherise Wong, Gregory M Lucas, Marina B Klein, Mari M Kitahata, Heidi Crane, Michael J Silverberg, M John Gill, William Christopher Mathews, Robert Dubrow, Michael A Horberg, Charles S Rabkin, Daniel B Klein, Vincent Lo Re, Timothy R Sterling, Fidel A Desir, Kenneth Lichtenstein, James Willig, Anita R Rachlis, Gregory D Kirk, Kathryn Anastos, Frank J Palella Jr, Jennifer E Thorne, Joseph Eron, Lisa P Jacobson, Sonia Napravnik, Chad Achenbach, Angel M Mayor, Pragna Patel, Kate Buchacz, Yuezhou Jing, Stephen J Gange for the North American AIDS Cohort Collaboration on Research and Design



Evidence of inflammation

Odds of Frailty and Prefrailty by Level of Inflammation in ALIVE*

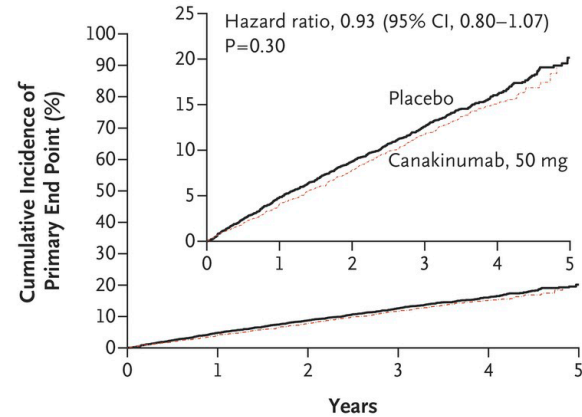
Model	Prefrail		Frail	
	Unadjusted	Adjusted [†]	Unadjusted	Adjusted [†]
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
IL-6	1.13 (0.99–1.29)	1.09 (0.95–1.26)	1.40 (1.17–1.68)	1.33 (1.09–1.61)
sTNFR1	1.08 (0.93–1.24)	1.03 (0.89–1.19)	1.40 (1.17–1.66)	1.25 (1.04–1.51)
Inflammatory index score	1.13 (0.99–1.30)	1.08 (0.94–1.25)	1.53 (1.28–1.83)	1.39 (1.14–1.68)



Type	Biomarker	Hallmarks of cell ageing covered
<i>Nucleic acid-based</i>	Telomere length	Telomere attrition
	Epigenetic clocks	Epigenetic alterations
	Mitochondrial DNA	Mitochondrial dysfunction
<i>Protein-based</i>	Apolipoprotein J/Clusterin (ApoJ/CLU)	Cellular senescence
	Proteasome subunits	Loss of proteostasis
<i>Metabolic-based</i>	NAD/NADH ratio	Mitochondrial dysfunction
	Lipid alterations in plasma	Deregulated nutrient sensing
	Plasma levels of essential amino-acids	Deregulated nutrient sensing
<i>Immunologic</i>	Soluble inflammatory markers (sCD14, sCD163, IL-6, hsCRP, D-dimer)	Inflammageing
	Cell surface molecules (CD28, CD96)	Cellular senescence and exhaustion
<i>Integrative</i>	MARK-AGE	Epigenetic alterations Mitochondrial dysfunction Deregulated nutrient sensing Inflammageing

Modifiable?

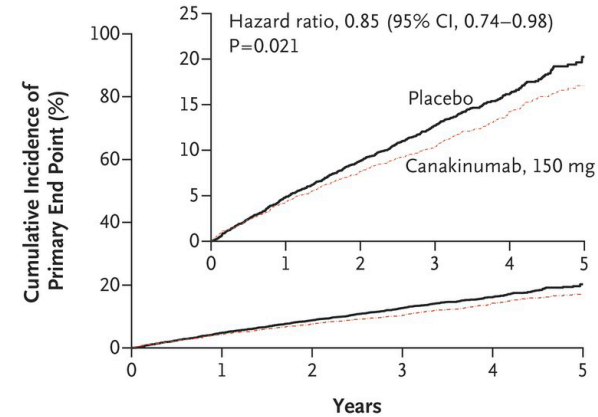
A Primary End Point with Canakinumab, 50 mg, vs. Placebo



No. at Risk

Placebo	3344	3141	2973	2632	1266	210
Canakinumab	2170	2057	1950	1713	762	47

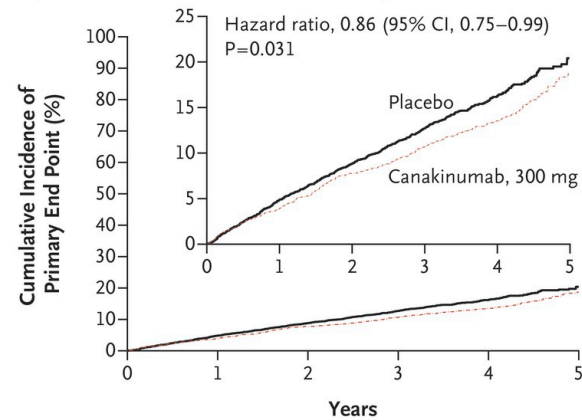
B Primary End Point with Canakinumab, 150 mg, vs. Placebo



No. at Risk

Placebo	3344	3141	2973	2632	1266	210
Canakinumab	2284	2151	2057	1849	907	207

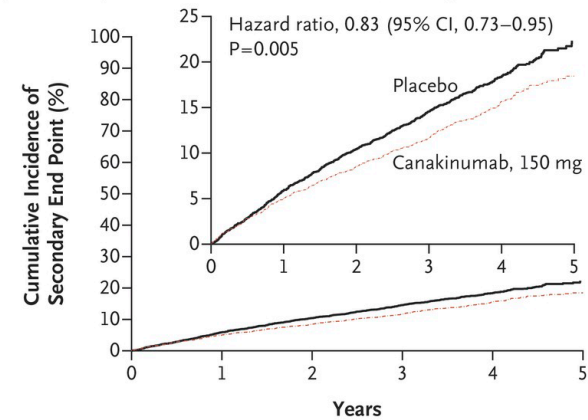
C Primary End Point with Canakinumab, 300 mg, vs. Placebo



No. at Risk

Placebo	3344	3141	2973	2632	1266	210
Canakinumab	2263	2149	2038	1819	938	199

D Key Secondary End Point with Canakinumab, 150 mg, vs. Placebo



No. at Risk

Placebo	3344	3107	2921	2578	1238	206
Canakinumab	2284	2135	2039	1824	892	201



Modifications

- MDT....! (Geriatrician, physio, OT, dietician...)
- Medication optimisation
 - Deprescribing
- Comorbidity management
- Physical function interventions
- Peer support groups

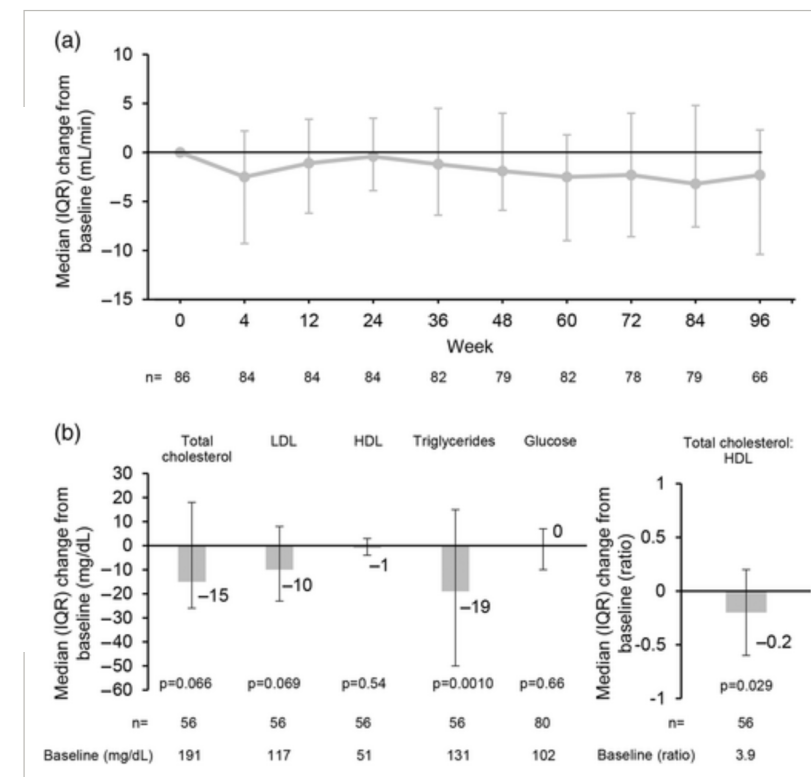
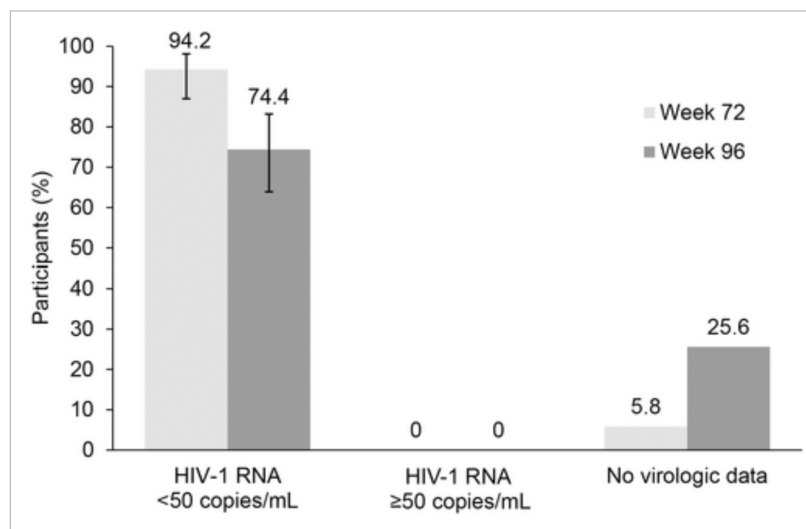
- Advance care planning...

ART Optimisation in Frailty & Increasing Age

Bictegravir/emtricitabine/tenofovir alafenamide in older individuals with HIV: Results of a 96-week, phase 3b, open-label, switch trial in virologically suppressed people ≥ 65 years of age

Franco Maggiolo, Giuliano Rizzardini, Jean-Michel Molina, Federico Pulido, Stephane De Wit, Linos Vandekerckhove, Juan Berenguer, Michelle L. D'Antoni, Christiana Blair ... See all authors \vee

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Conclusions



NO AGREED NON-PHENOTYPIC
ASSESSMENT OF FRAILITY



CHRONIC INFLAMMATION



NO PHARMACOLOGICAL
INTERVENTIONS FOR *FRAILITY*



PHENOTYPIC APPROACH AND
FUNCTIONAL INTERVENTIONS
REMAIN MAINSTAY OF THERAPY