

HIV: LA COMPLESSITA' IN EVOLUZIONE «L'invecchiamento»

Paolo Bonfanti

Unità Operativa Complessa di Malattie Infettive

Sistema Socio Sanitario



Regione
Lombardia

ASST Lecco



Disclosure

Dr Bonfanti has received grants from:

- ViiV Healthcare
- Gilead
- Janssen
- Merck



Outline

- The HIV-infected Population is Getting Older
- Accelerated or Accentuated Aging?
- Management Issues in Older HIV-Infected Patients
 - Development of a Comprehensive Approach for the Early Diagnosis of Geriatric Syndromes
 - A Different Approach to HIV Therapy



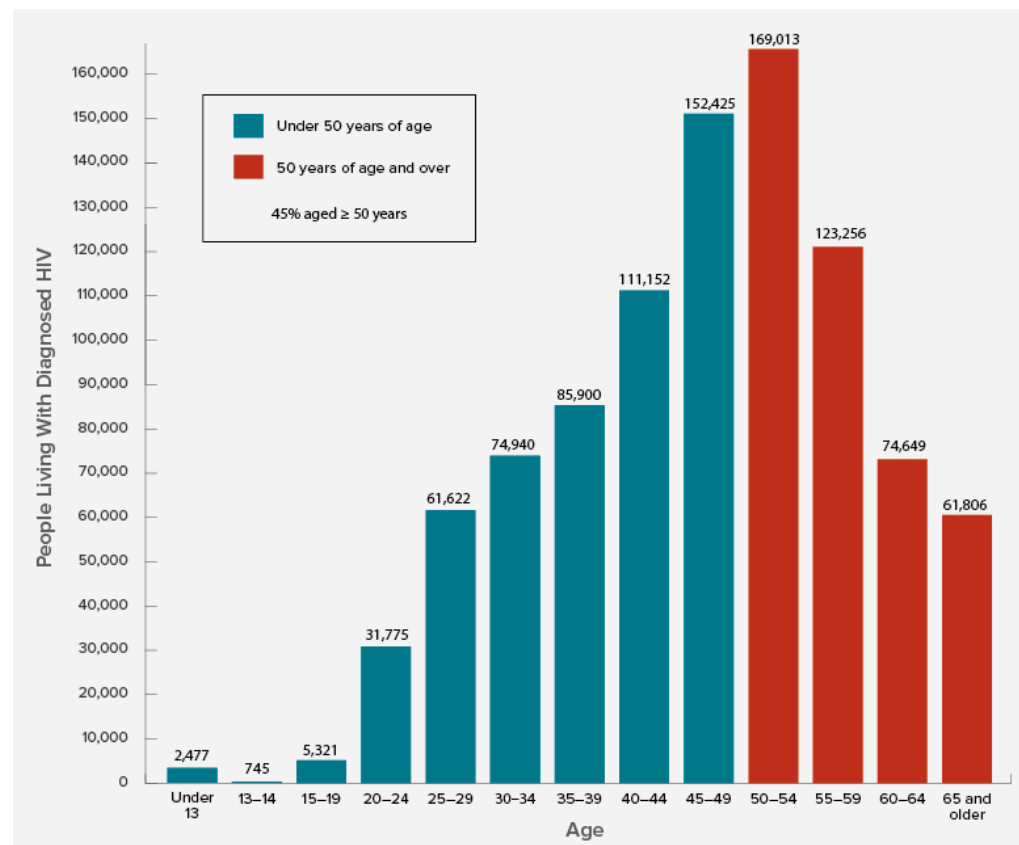
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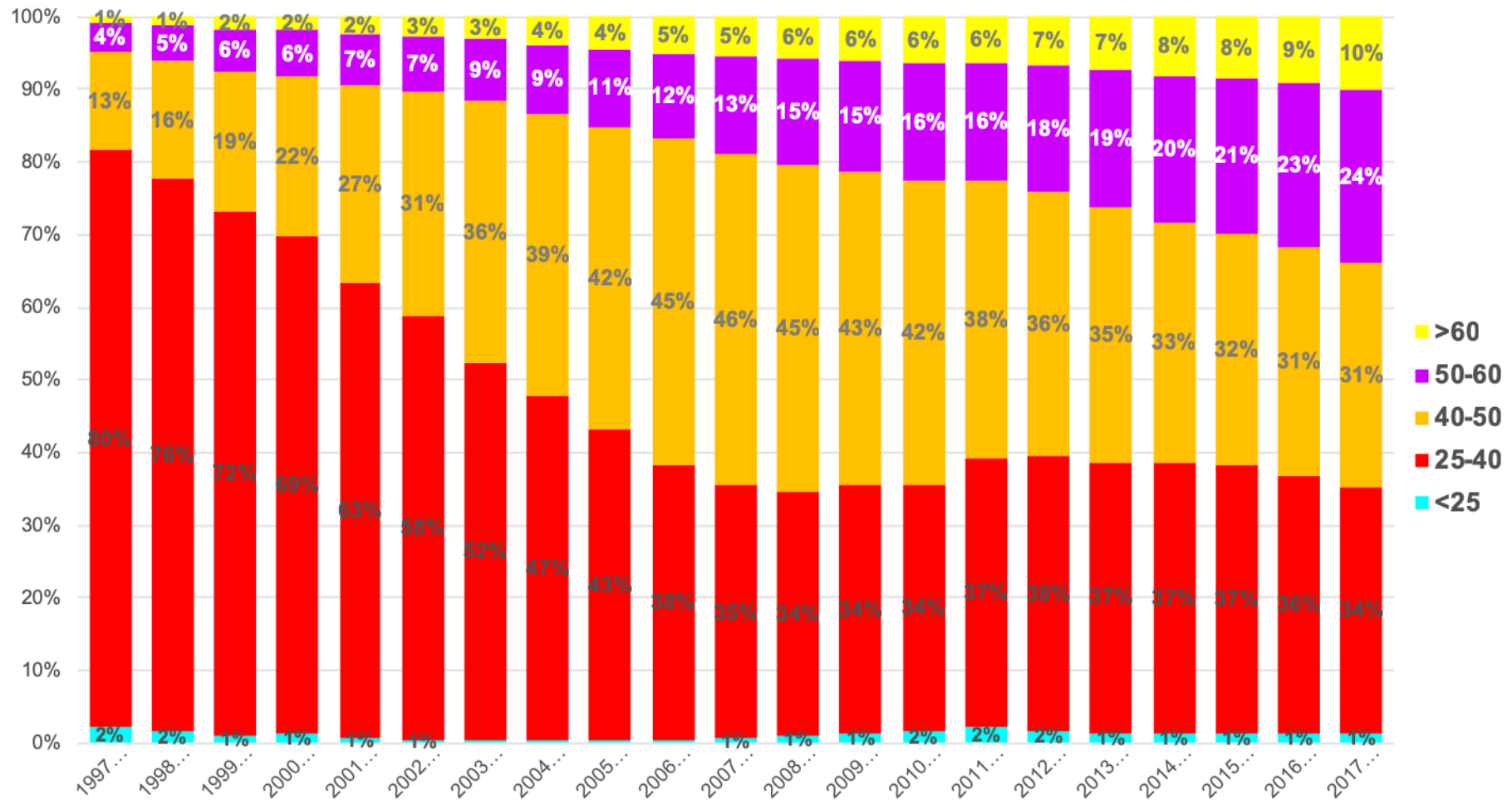
People Aged 50 or Older Living with HIV are Nearing a Majority

- Those infected with HIV at a younger age are successfully growing older
- Thousands of older people become infected with HIV every year
- **$\geq 45\%$ of people with HIV in the US are aged 50 or older**
- **Proportion of people living with HIV ≥ 50 years of age is estimated to reach $\sim 75\%$ by 2030**



HIV & Aging in Italy: Data from the ICONA Cohort

Age strata per calendar year in patients on follow-up



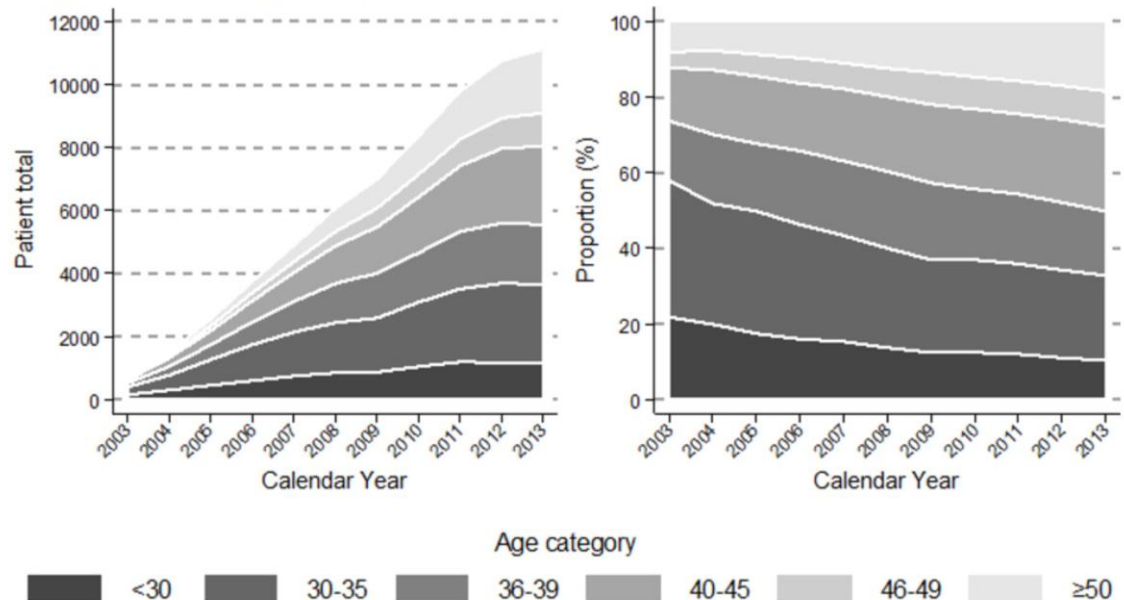
ICONA: 2018 Report



HIV & Aging In Resource-Limited Settings

- Proportion of those 50 years or older with HIV in sub-Saharan Africa has been slower to increase
 - Represents ~ 17% of the population but numerically is a great number than those in the developed countries
 - Estimated tripling by 2040

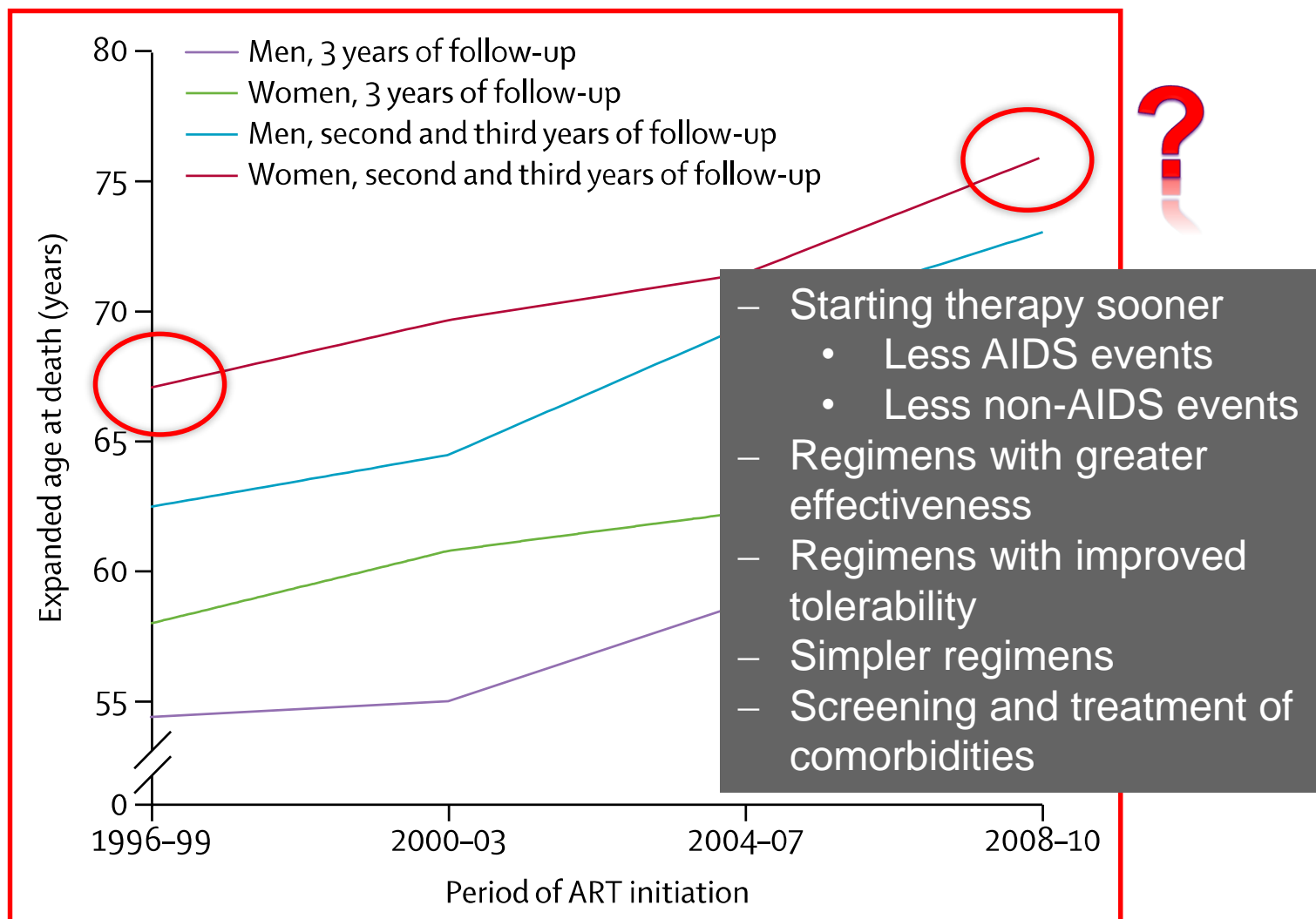
(B) Age of patients during follow-up



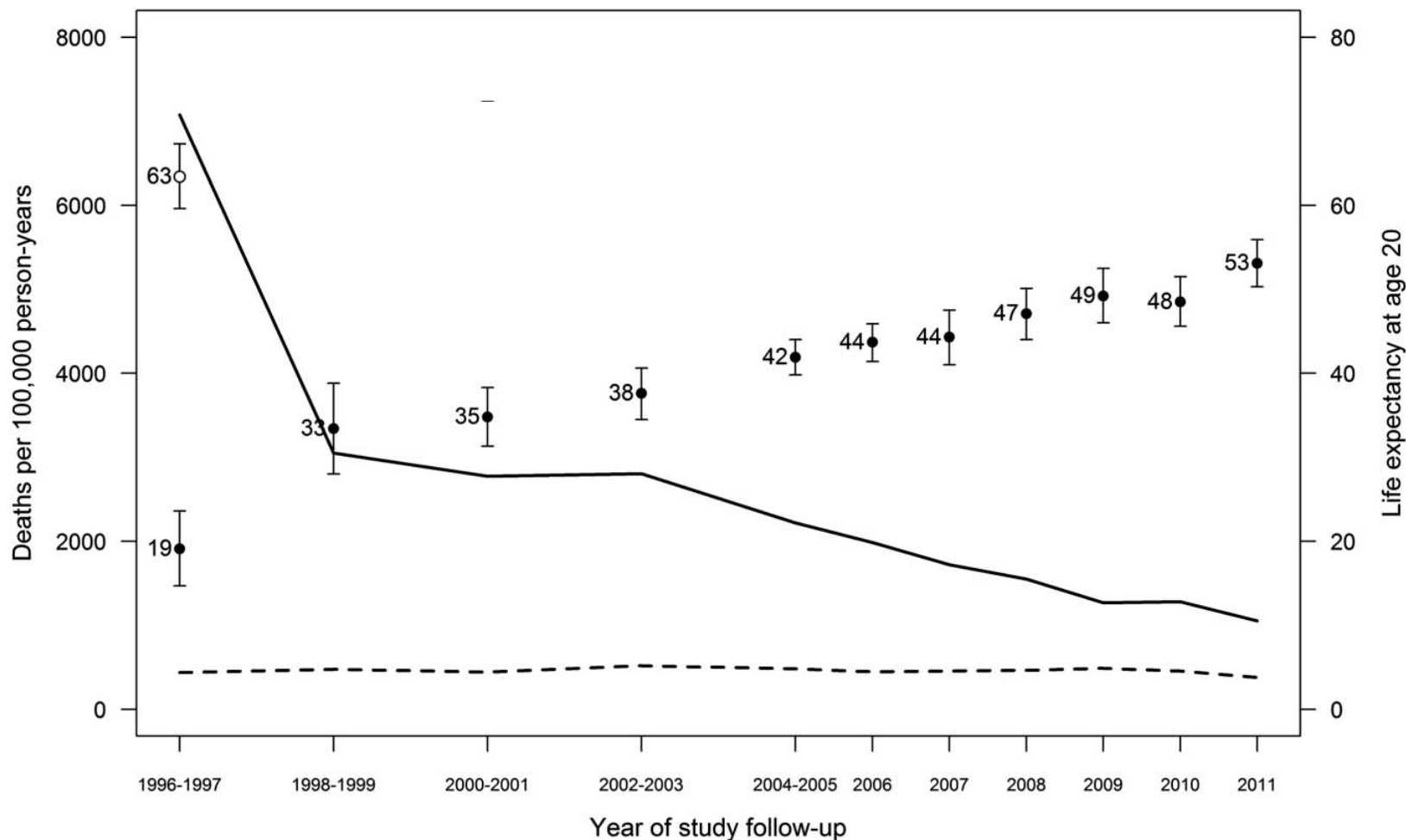
Negin J and Cumming RG, Bulletin of the WHO 88: 2010: 847-53;
De La Mata NL, et al. AIDS Care 2017; 29: 1243-54.



Expected age at death of men and women living with HIV starting antiretroviral therapy (ART) aged 20 years, by period of initiation



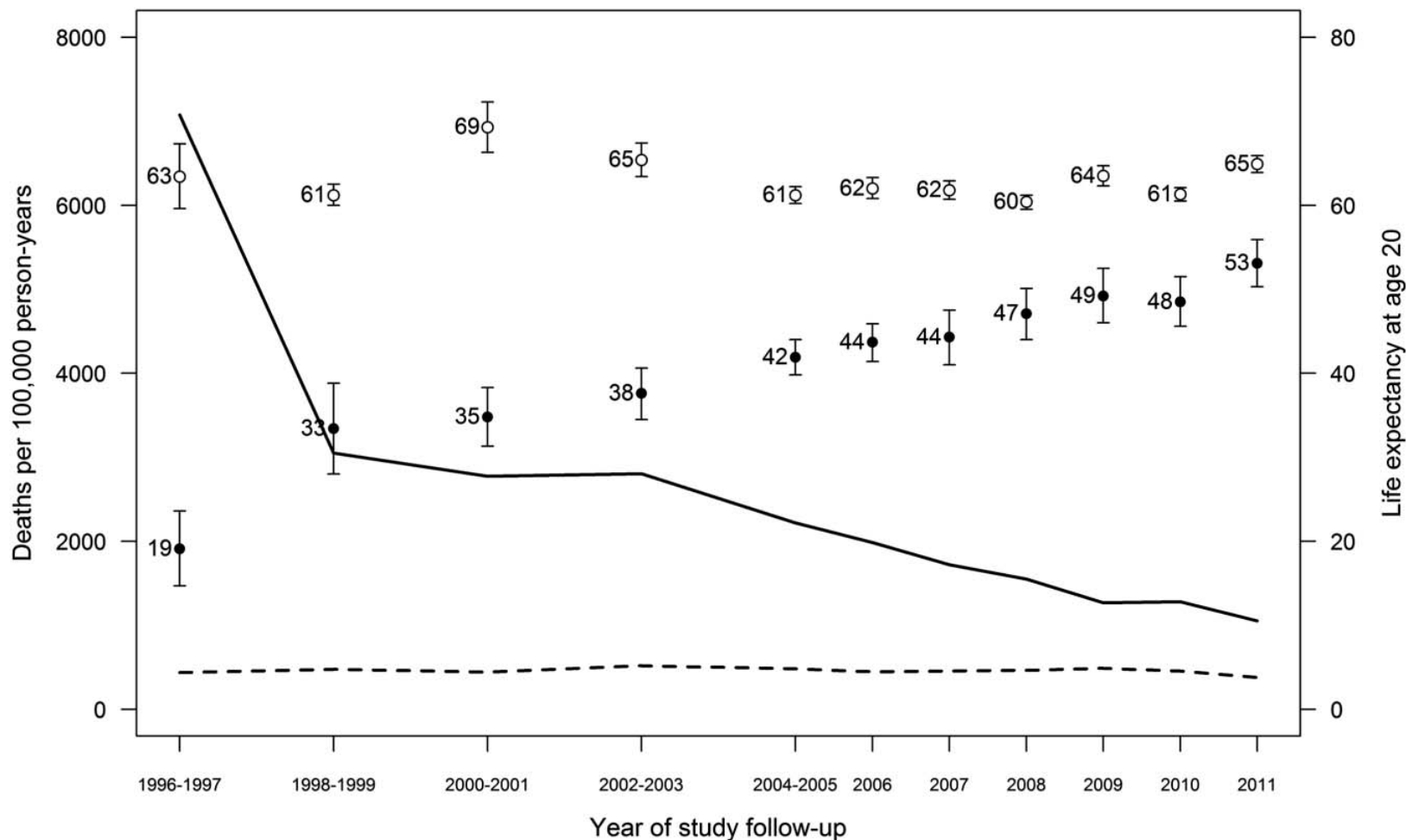
Life Expectancy in Patients With HIV



Marcus JL et al, *JAIDS* 2016



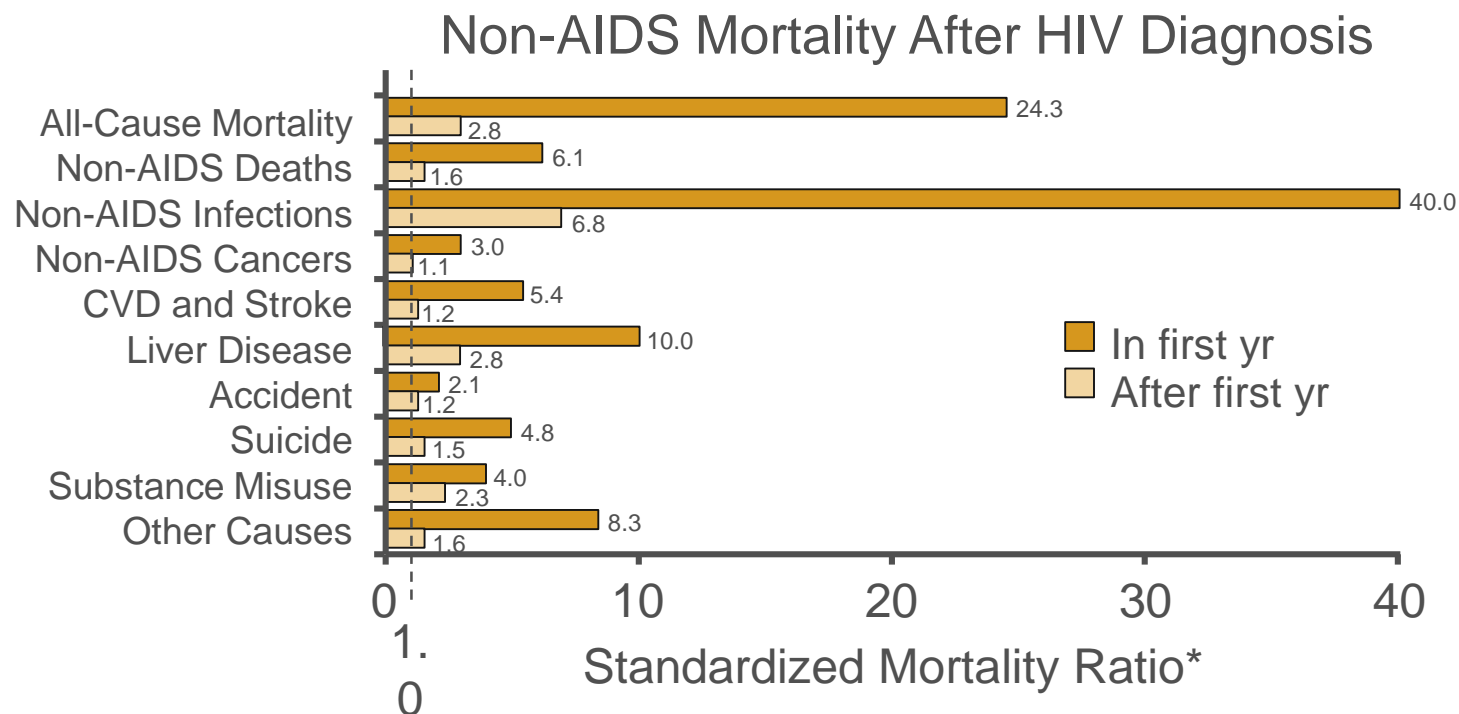
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Marcus JL et al, *JAIDS* 2016



Treatment Decreases Event Risk, Does Not Normalize Risk



*Ratio for individuals diagnosed with HIV vs general population 1997-2012 in England and Wales.

Croxford S, et al, *Lancet Public Health* 2017;2:e35-e46.

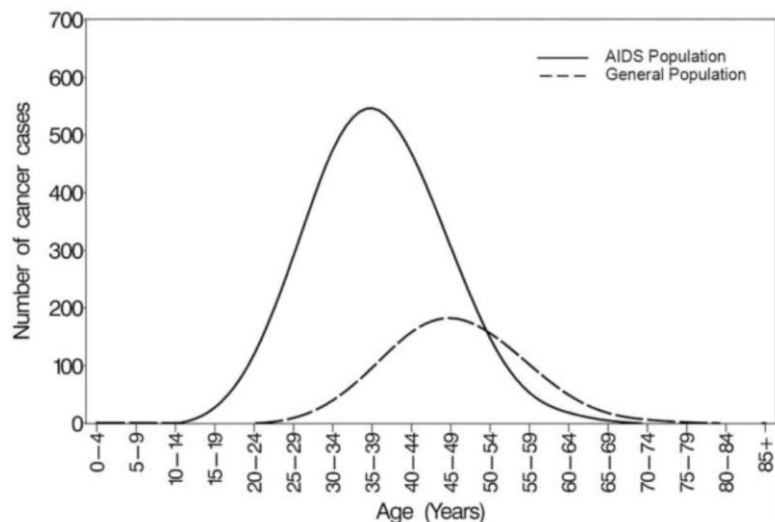


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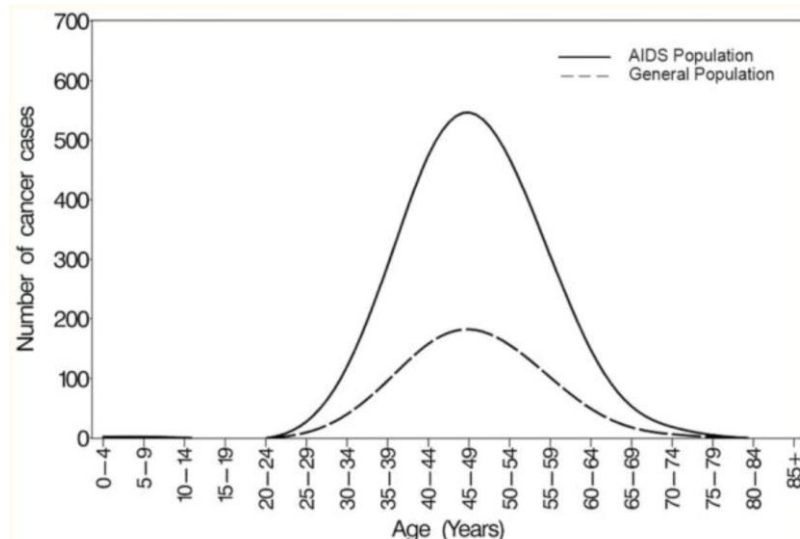


Accelerated or Accentuated Aging?



Accelerated:

age-associated condition
occurs *earlier* than controls



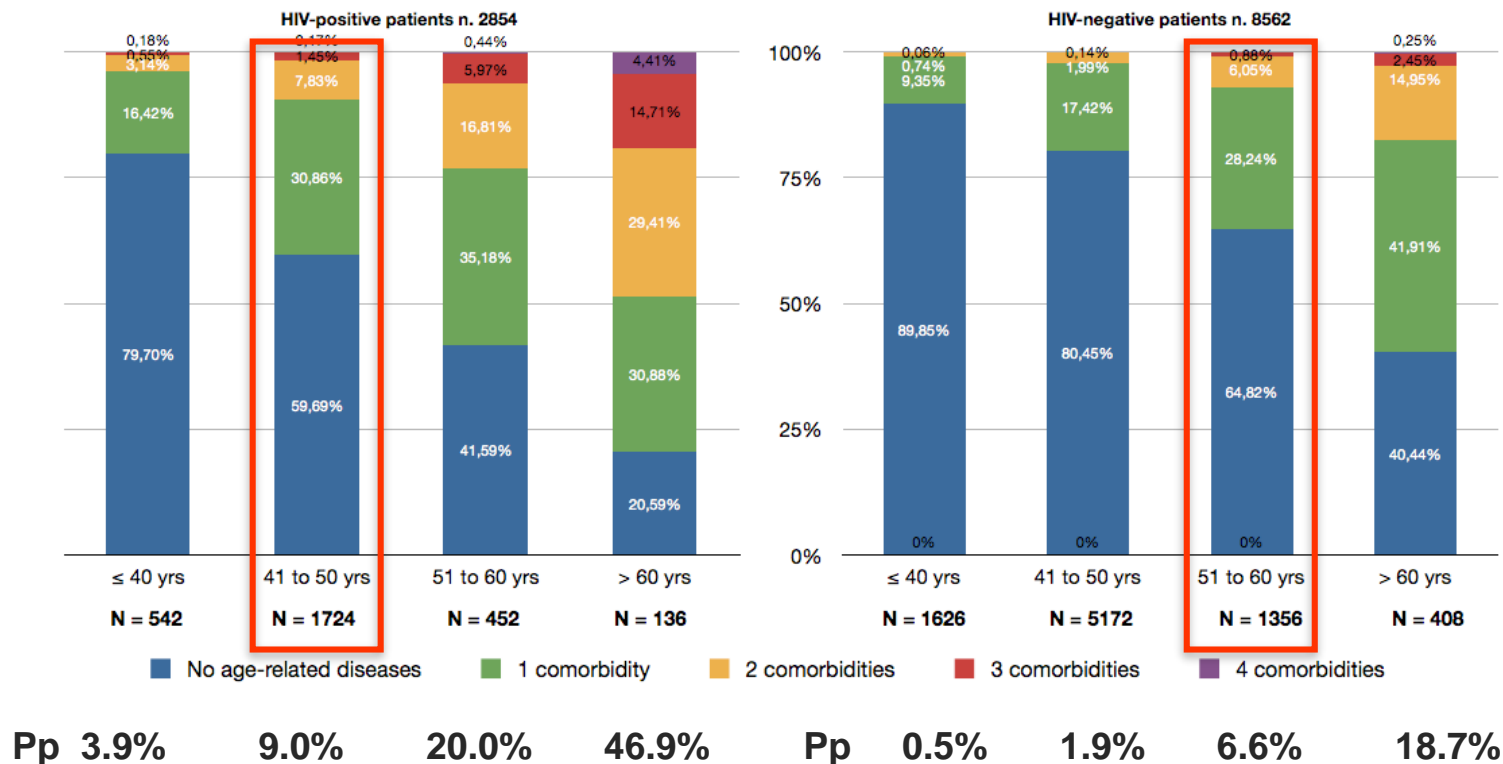
Accentuated:

condition occurs more
frequently because of
increased risks or exposure
(ex smoking)

Influence screening & management



Poly-pathology prevalence in cases and controls, stratified by age categories

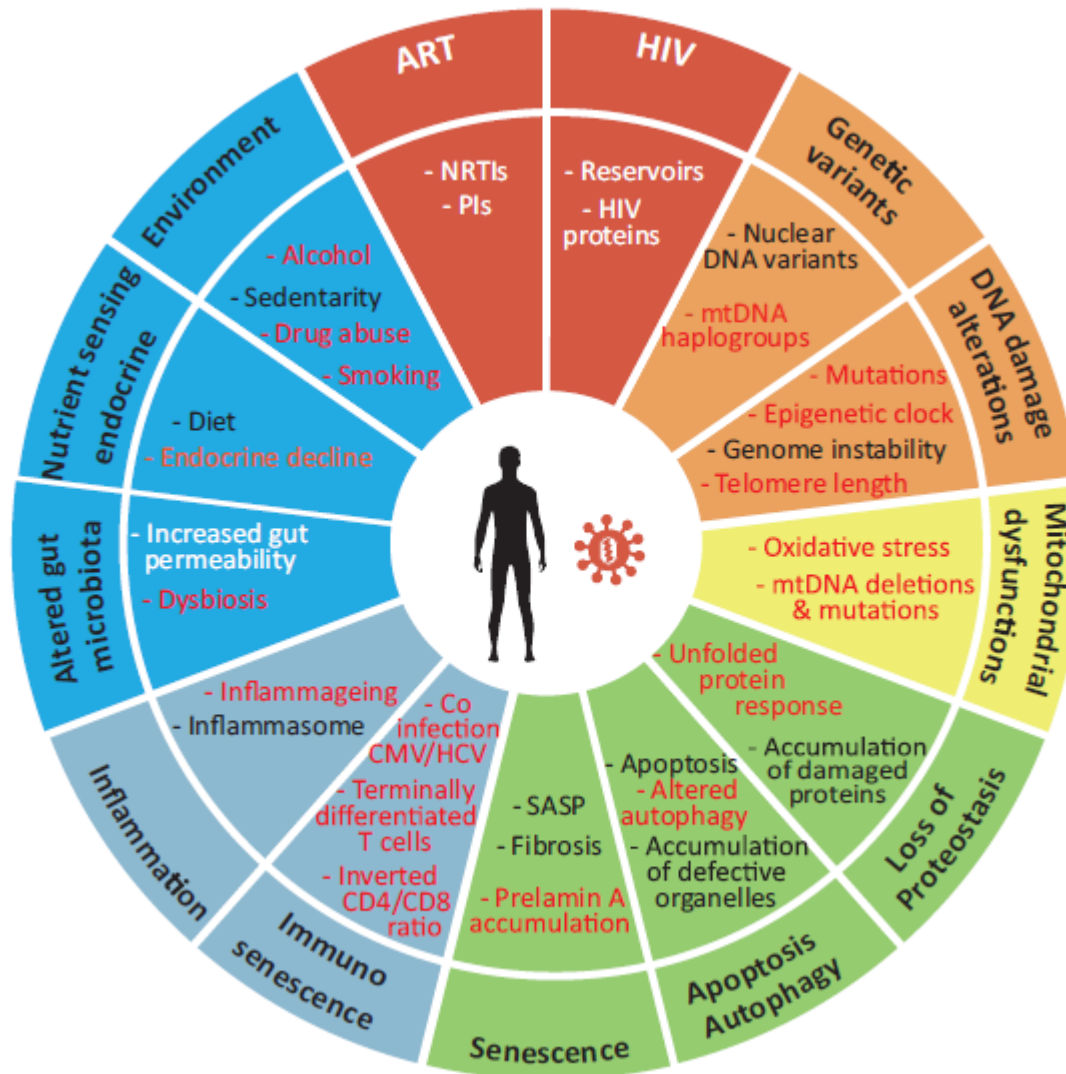


Pp prevalence was higher in cases than controls in all age strata (all p-values <0.001)

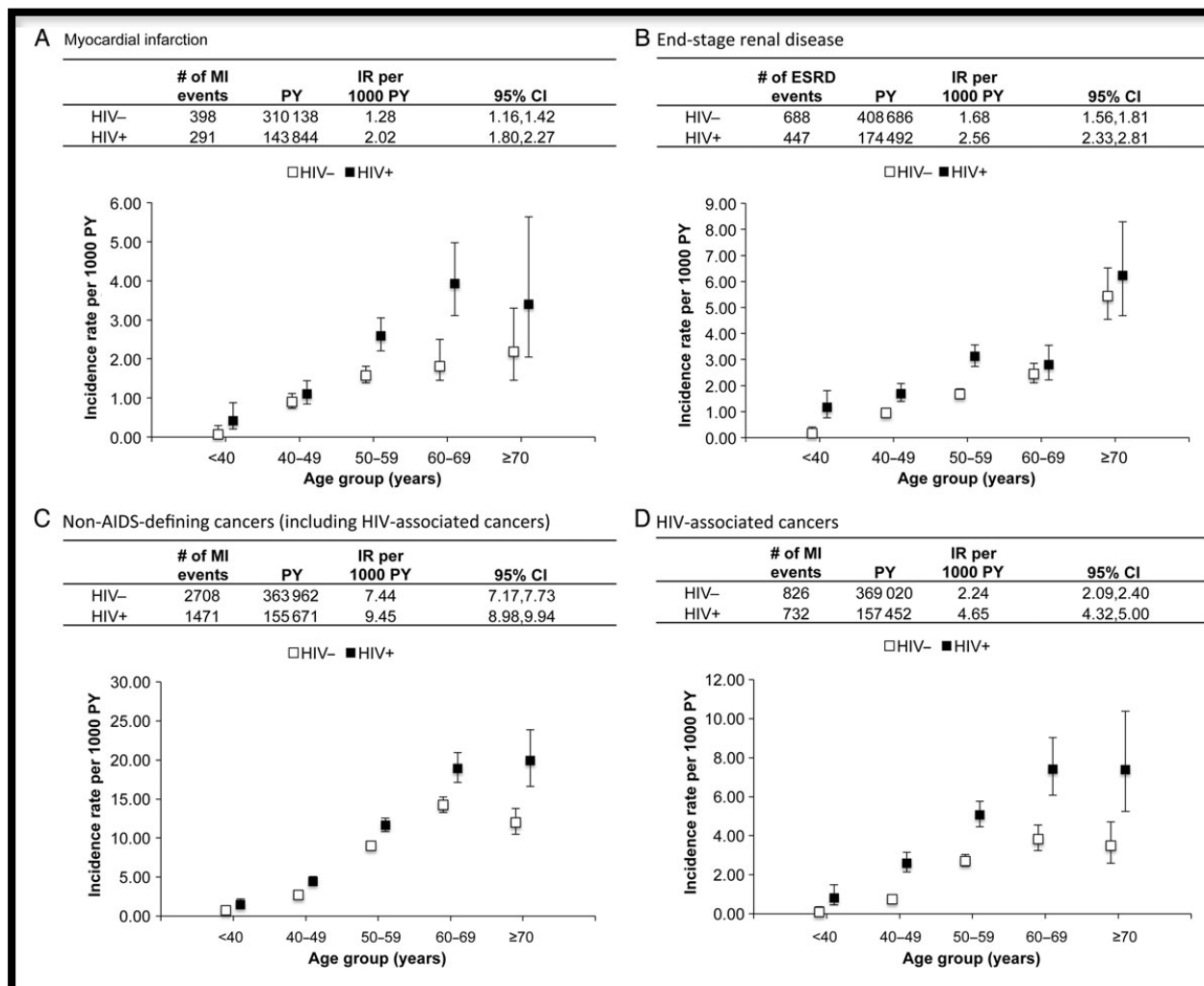
Pp prevalence seen cases aged 41-50 was similar to that observed among controls aged 51-60 controls (p=0.282)



General and HIV-specific mechanisms of ageing



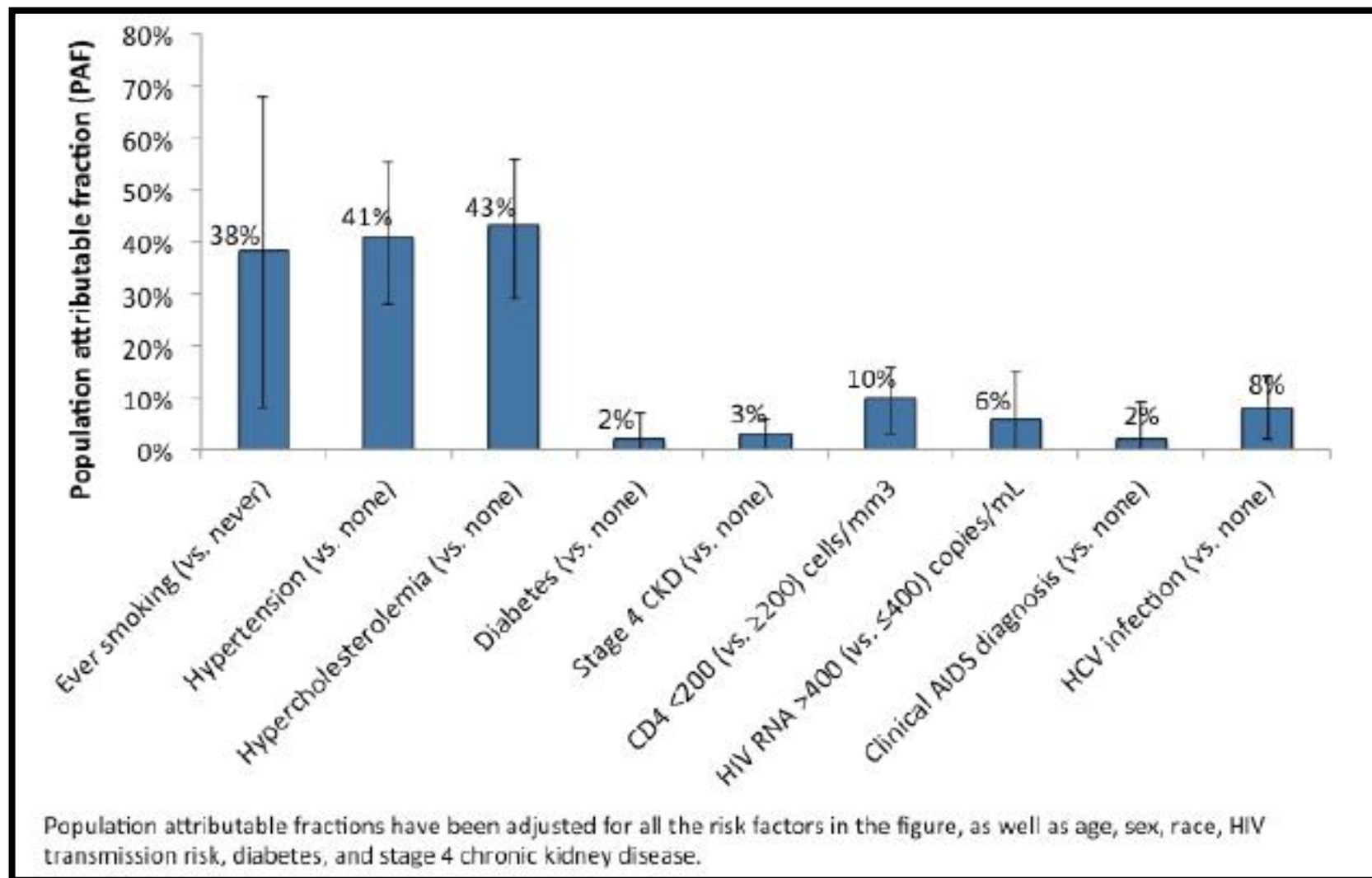
Events Are Not Happening Substantially Earlier, but Are More Frequent



Althoff KN, et al. *Clin Infect Dis* 2015;60:627-638.



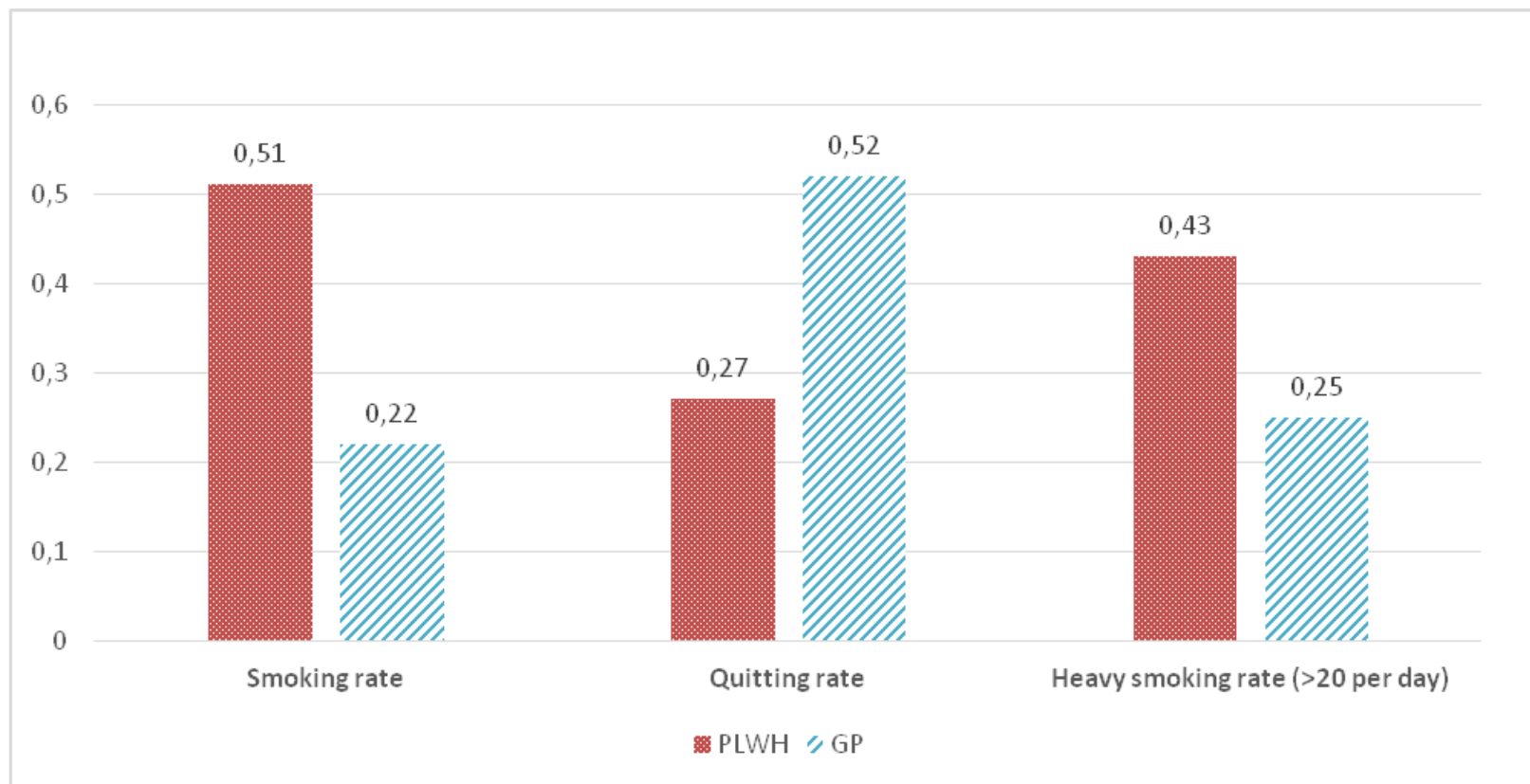
Adjusted Population Attributable Fractions for MI



Smoking habits in Italian HIV-infected people compared with general population

1087 HIV-positive
STOPSHIV Study

5420 HIV-Negative
ISTAT Database



De Socio GV et al, *submitted*



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

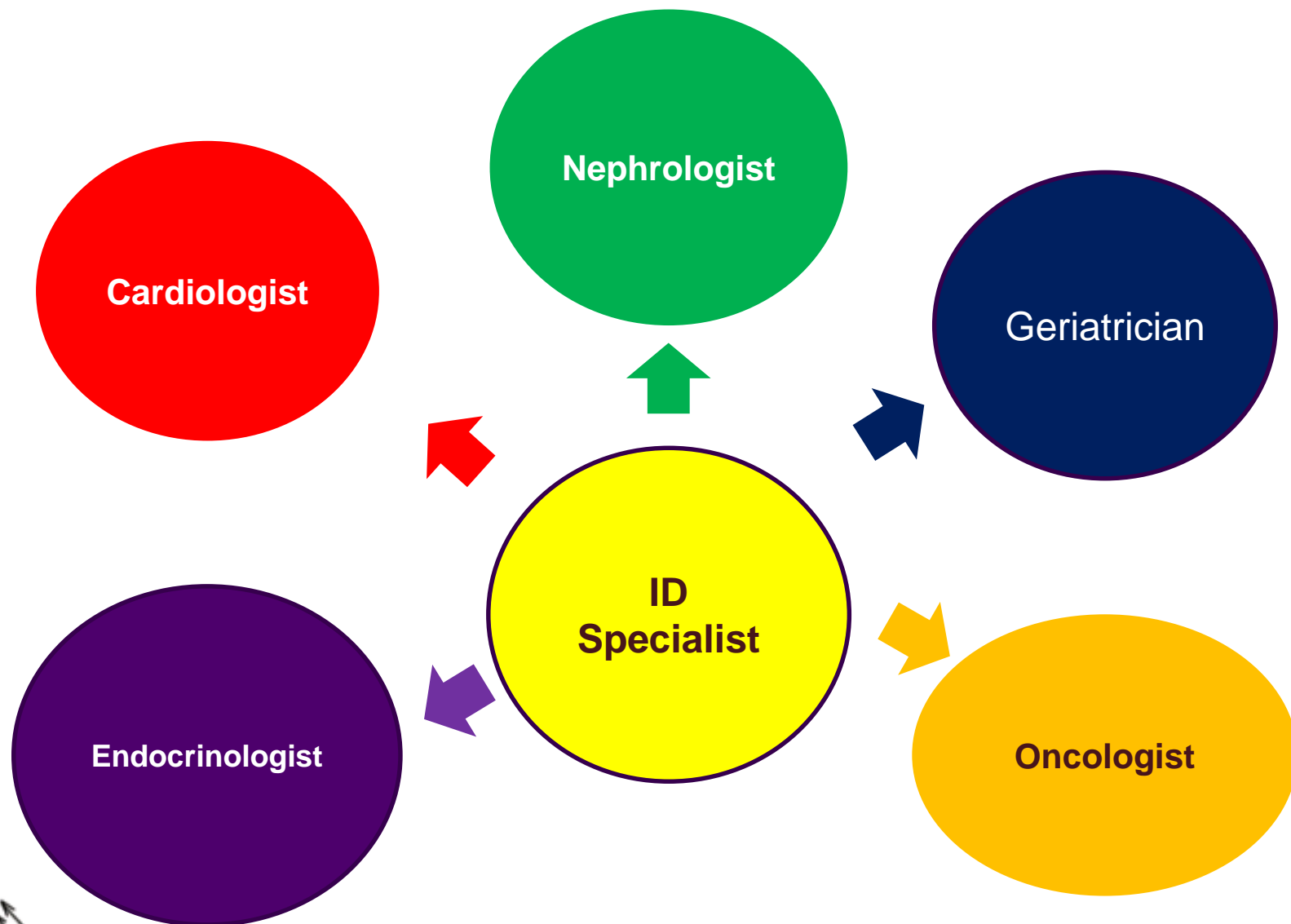


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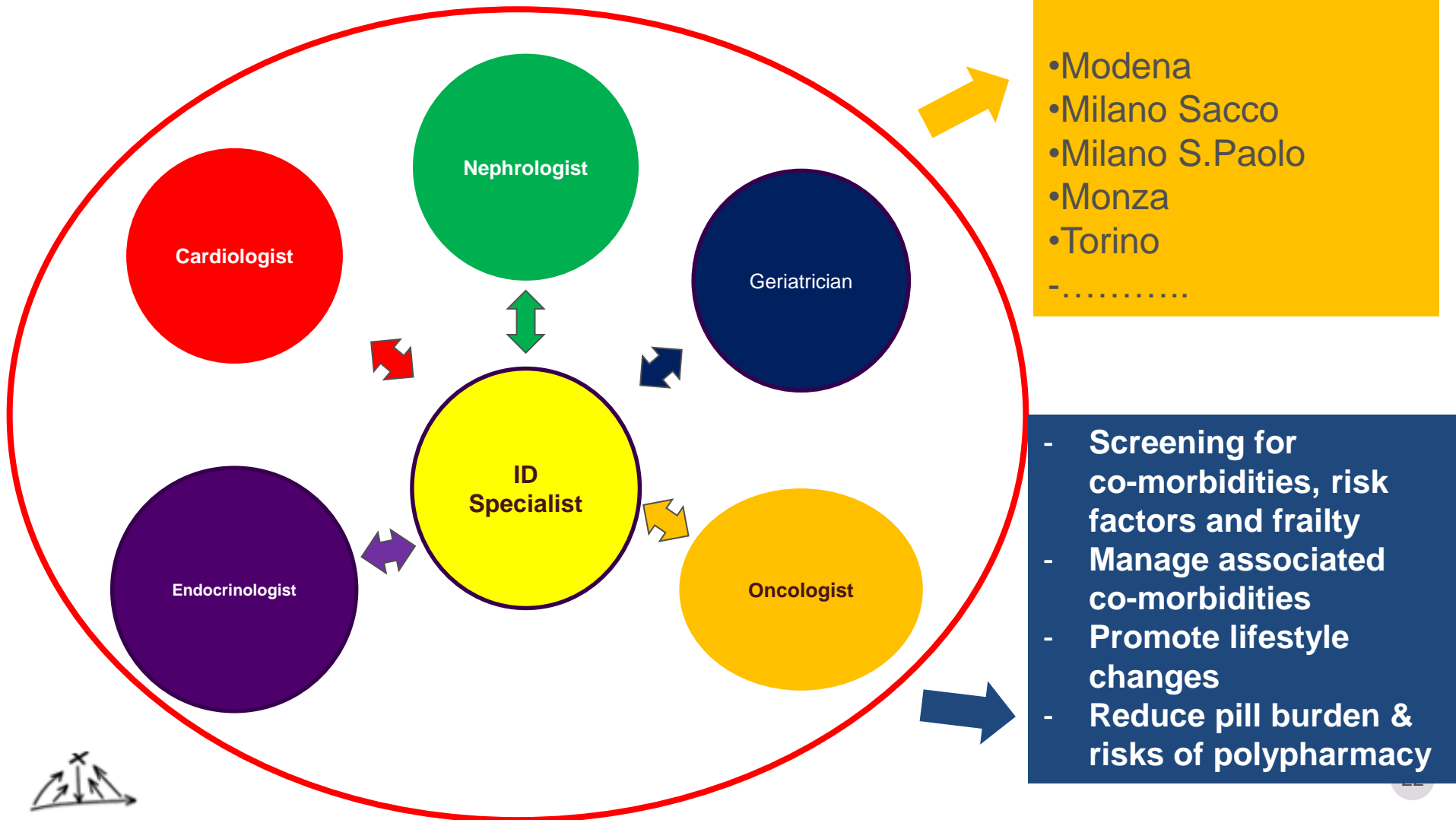


The traditional approach to co-morbidities

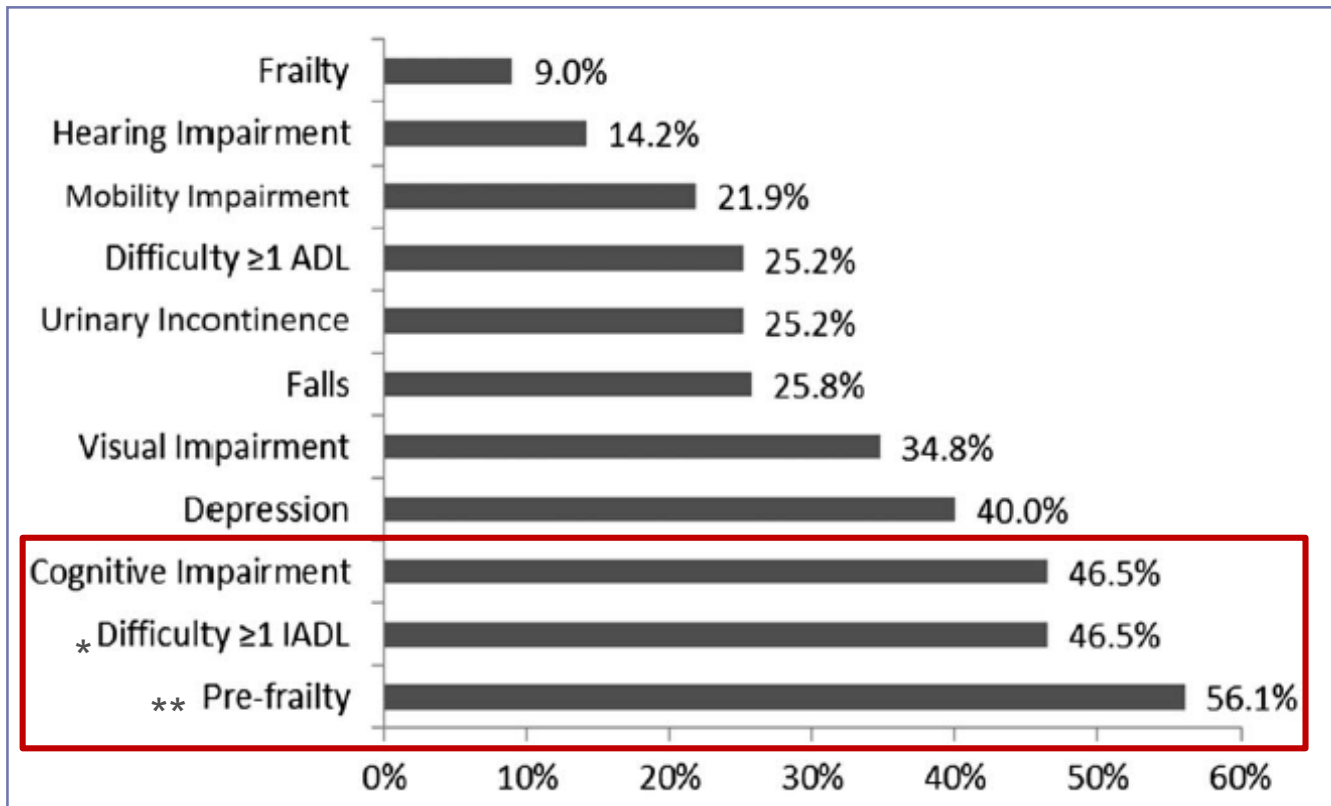


An integrated approach

Different specialists work together to find the best possible solutions to complex clinical problems.



Burden of geriatric syndromes

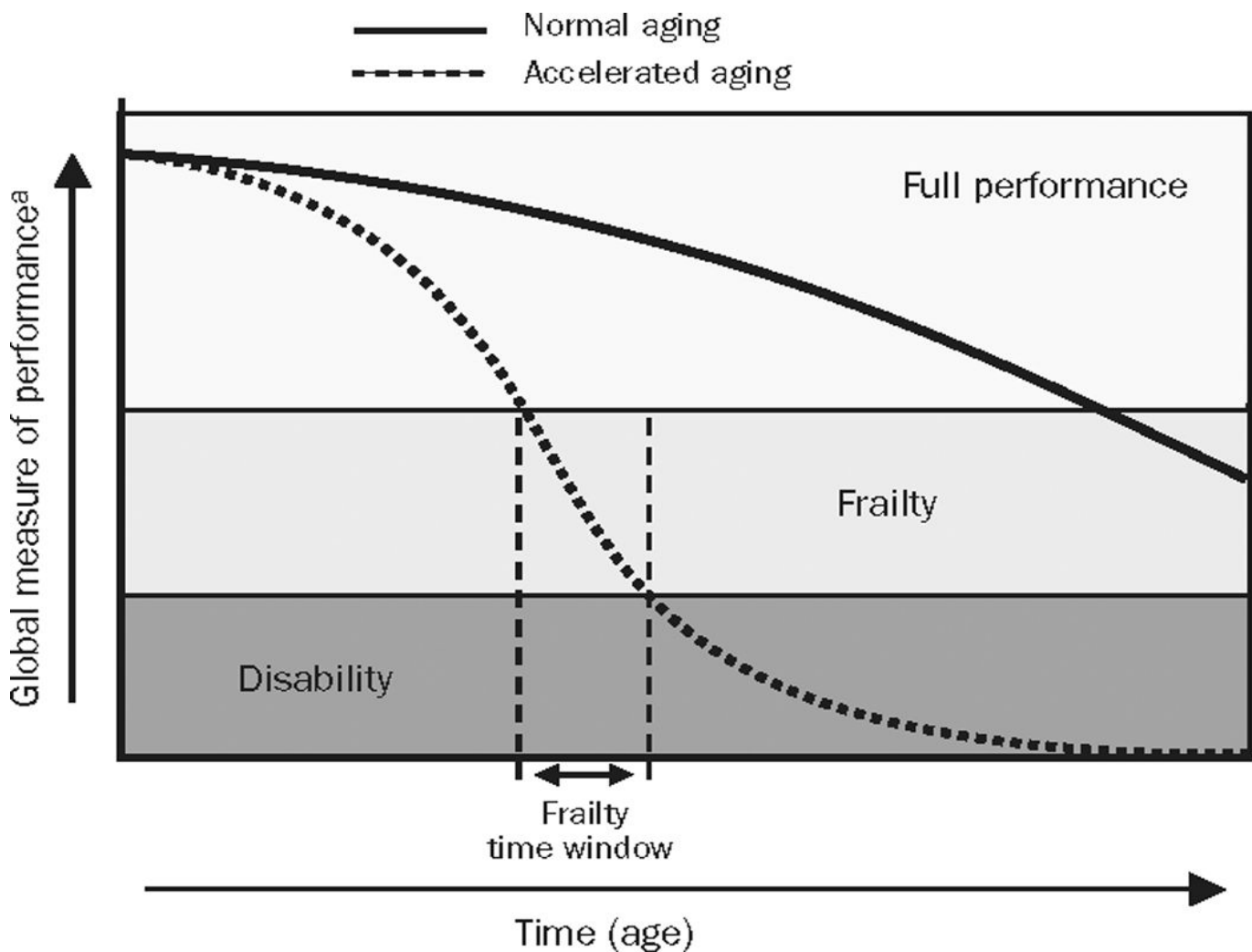


*difficulty with instrumental activities of daily living

** Participants were classified on *Fried criteria* as frail if they met 3 or more of the 5 criteria and were classified as prefrail if they met 1 or 2 of the criteria.



Trajectories of health and functioning.



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Things to Think About Before Starting Therapy in an Older Patient

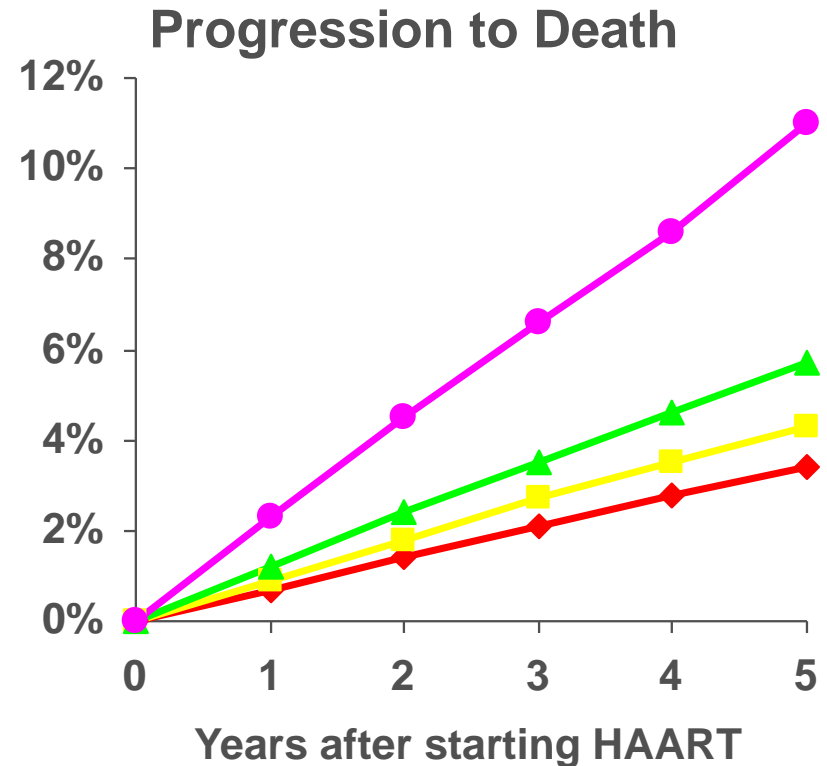
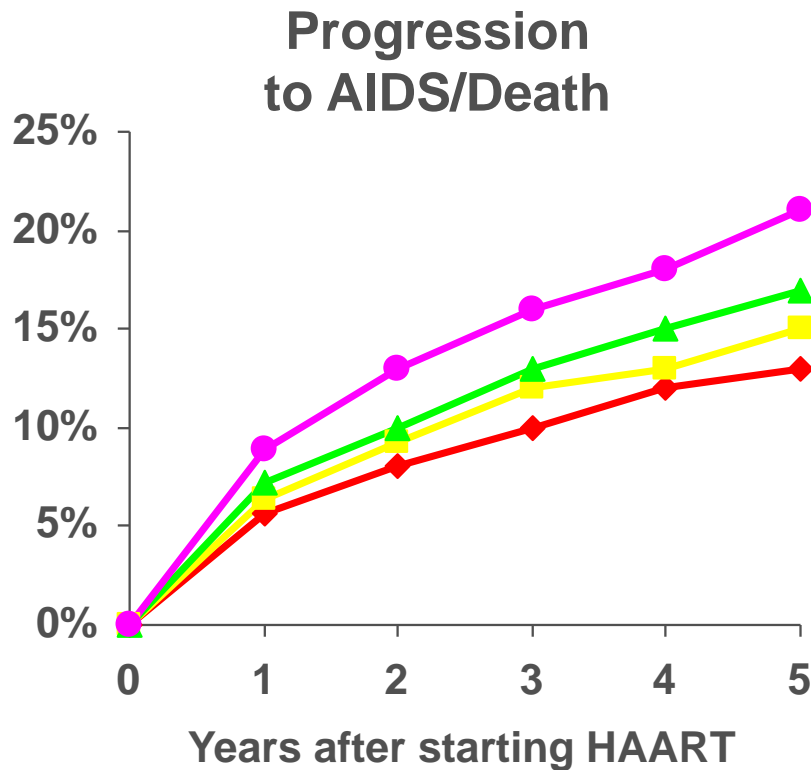
- ART recommended for all patients regardless of CD4+ cell count; especially important for older patients
 - Greater risk of serious AIDS and non-AIDS complications
 - Potentially a blunted immunologic response to ART

DHHS Guidelines. October 2018.



Disease Progression After HAART vs Age

No prior AIDS or IDU; baseline CD4 100 – 199, VL > 10⁵

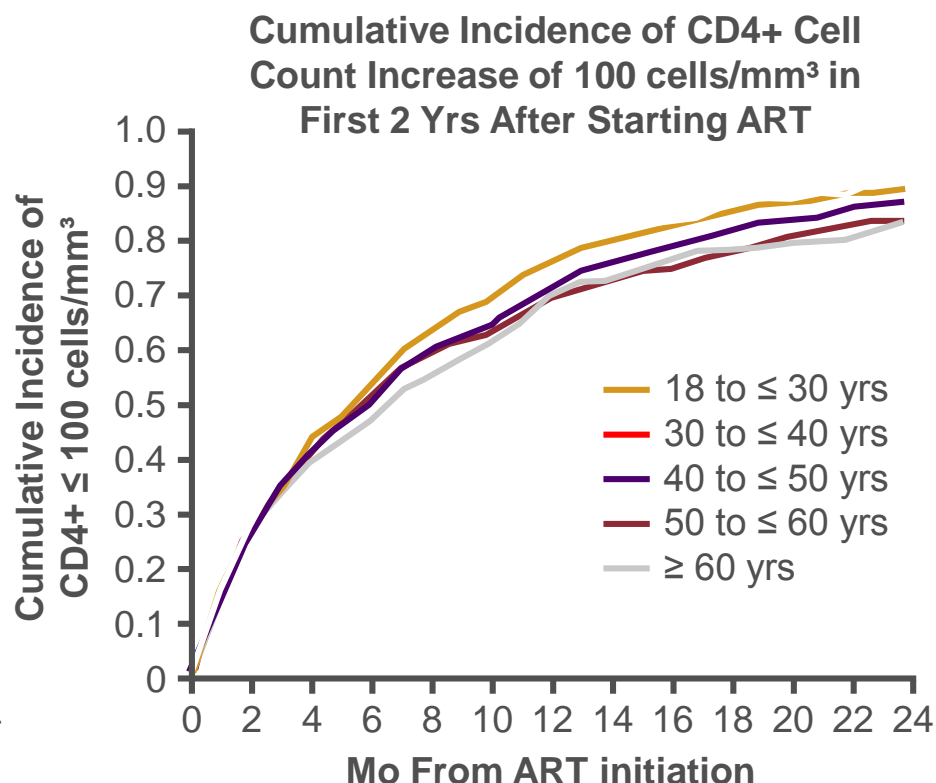
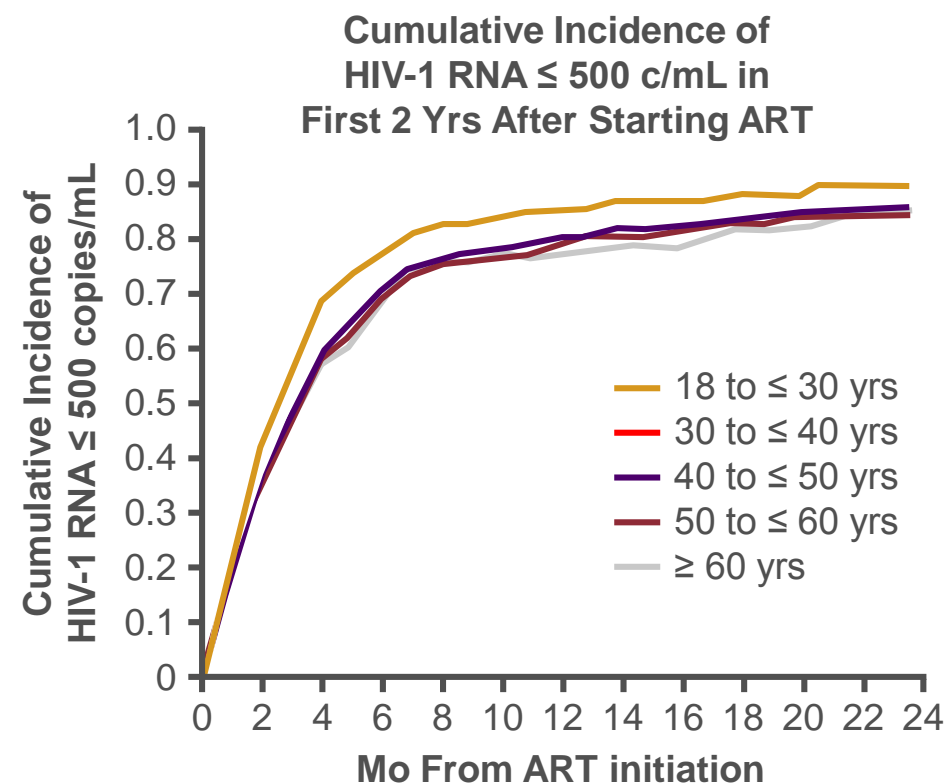


Age —◆— 16 - 29 —■— 30 - 39 —▲— 40 - 49 —●— ≥50



NA-ACCORD: Immunologic but Not Virologic Response Decreased in Older Pts

- Analysis of pts who received initial ART with a boosted PI or NNRTI-based regimen in 19 cohort studies (NA-ACCORD; N = 12,196)



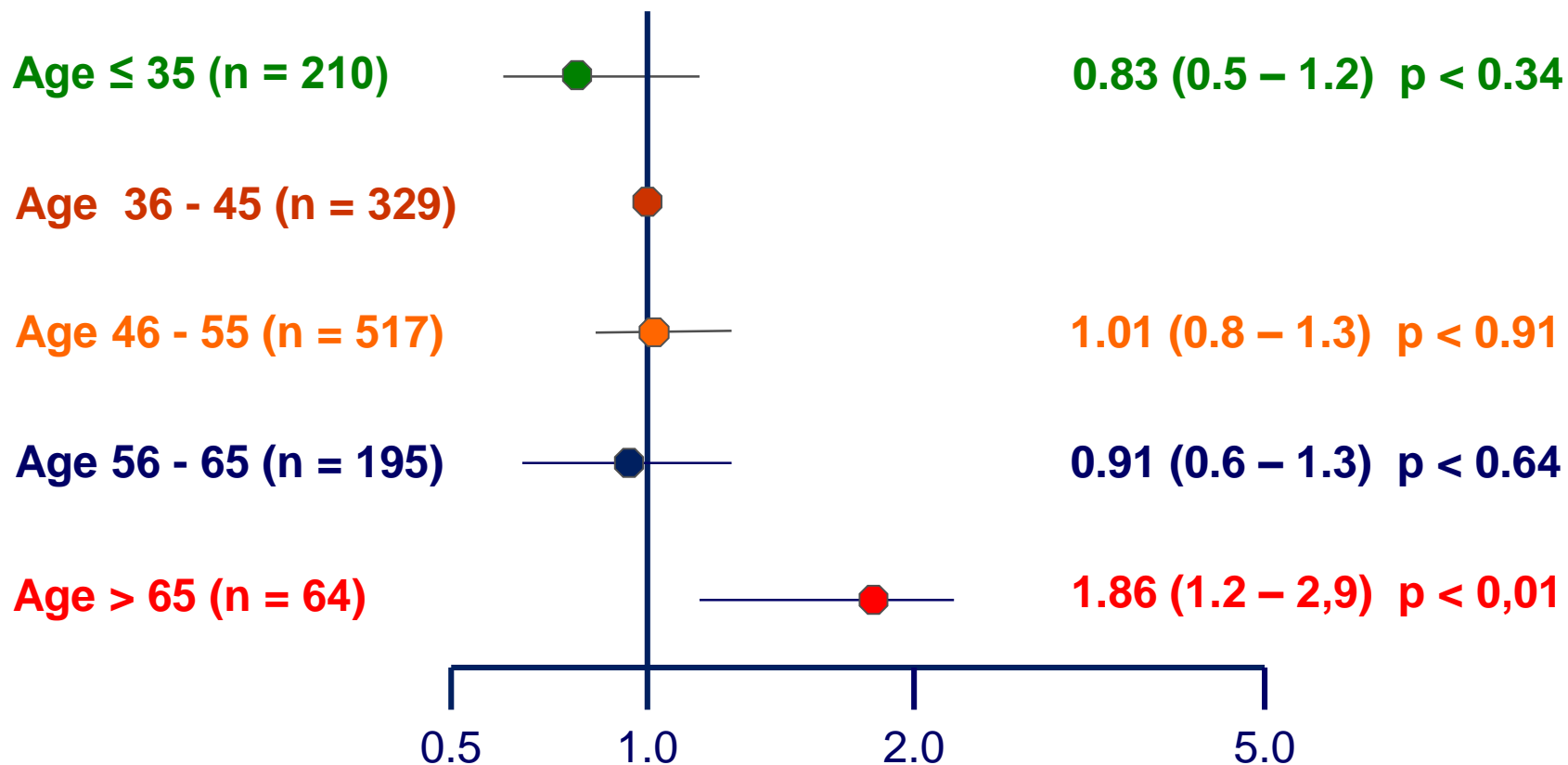
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 - Bone, kidney, metabolic, cardiovascular, and liver health should be monitored closely



SCOLTA Cohort

Risk of Treatment Discontinuation for Any Reason



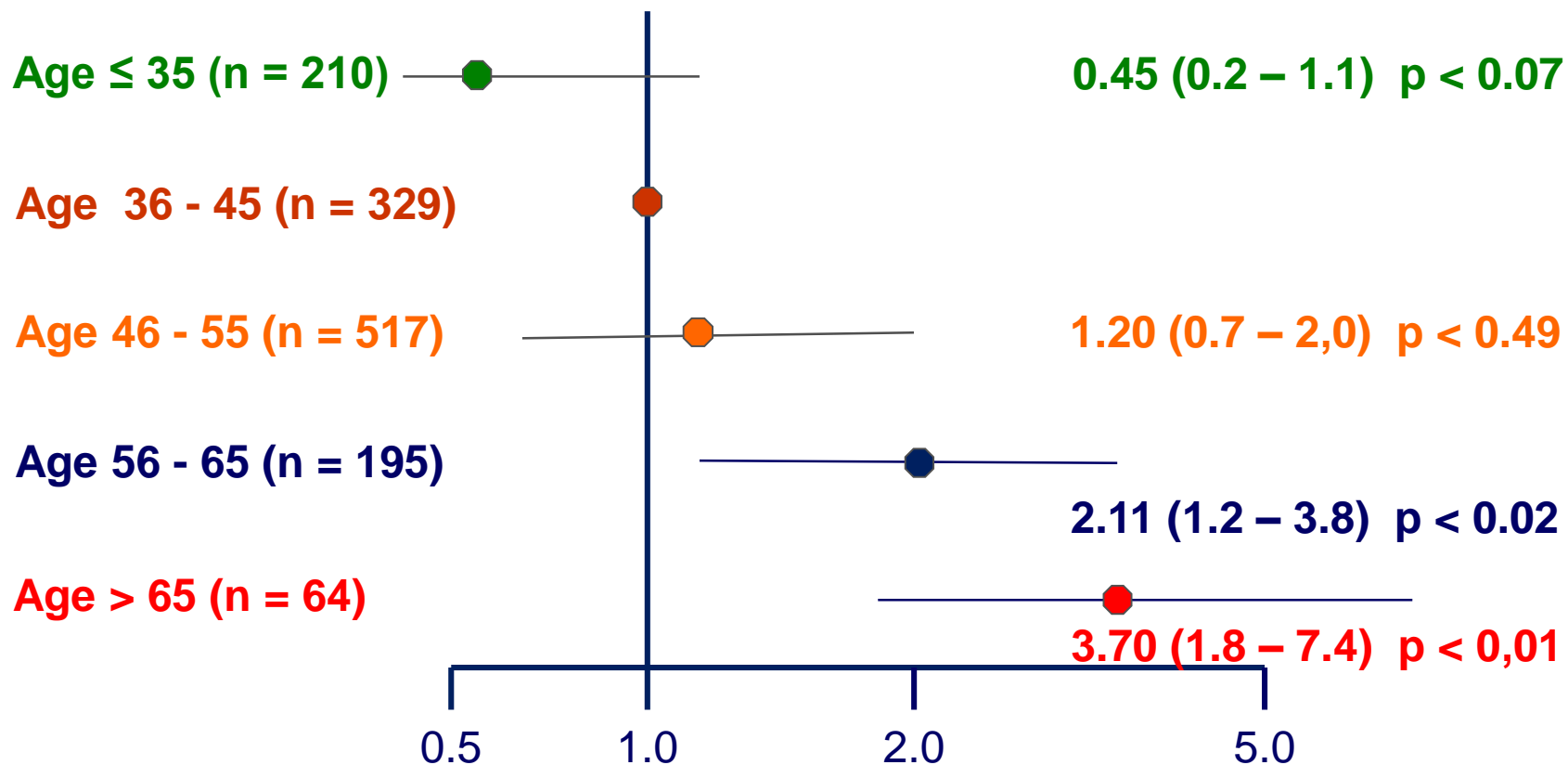
Corrected for: Gender, CDC Stage, ART-naïve status, ARV Regimen

SCOLTA Cohort, *unpublished data*



SCOLTA Cohort

Risk of Treatment Discontinuation for Adverse Events



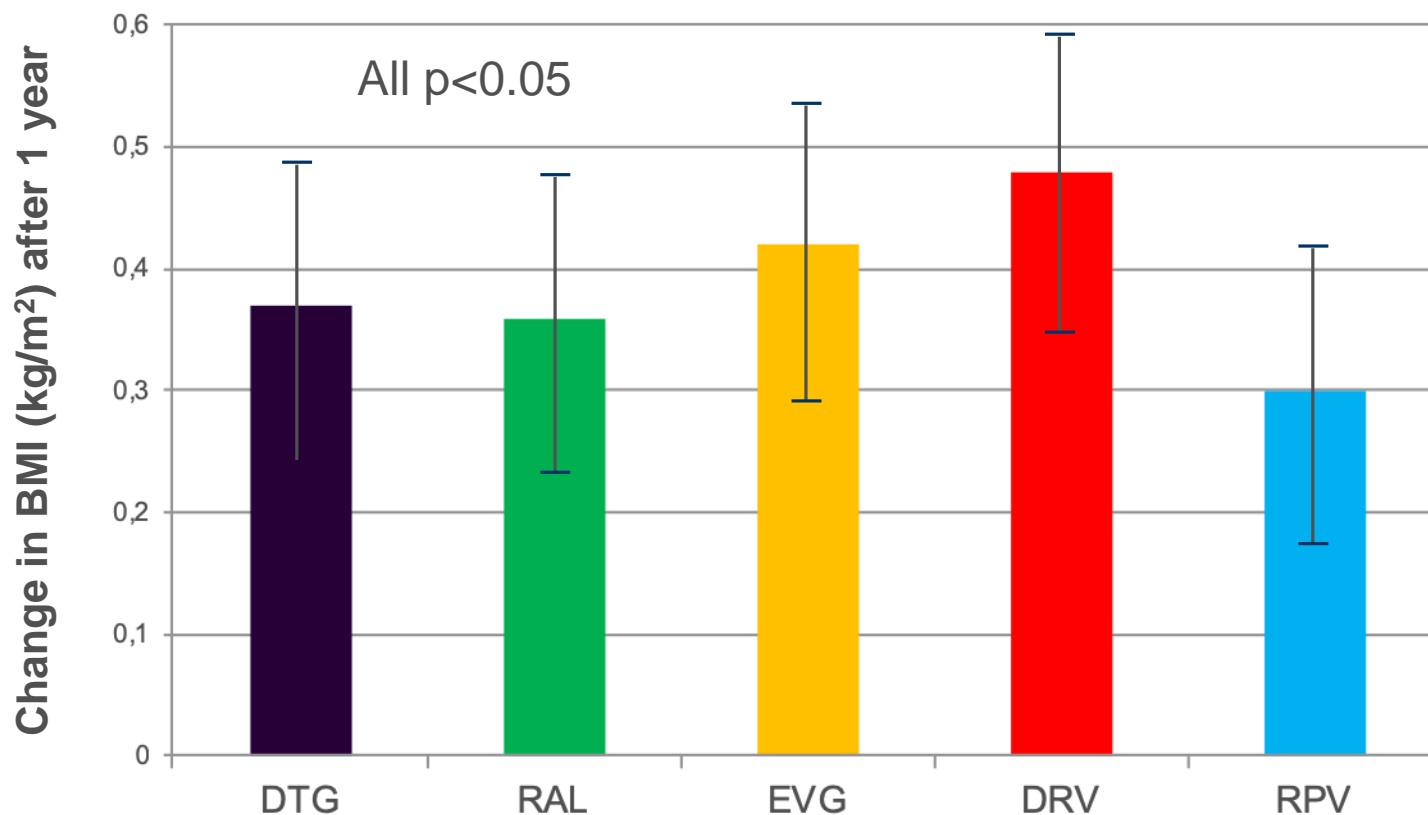
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SCOLTA Cohort, *unpublished data*



Weight Gain in SCOLTA Cohort

1118 cART experienced PLWH with at least 1 year of follow up



Adjusted for sex, age, CD4+, detectable VL, CDC Stage, duration of ART, lipodysytophy and BMI at study entry
BMI gain correlated with low baseline BMI ($P = .002$) and **older age ($P = .0007$)**.



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- Adverse drug events from ART and concomitant drugs may occur more frequently in older patients with HIV
 - Bone, kidney, metabolic, cardiovascular, and liver health should be monitored closely
- Polypharmacy is common in older patients with HIV
 - Greater risk of drug–drug interactions

DHHS Guidelines. October 2018.



Additional Drug–Drug Interactions With ART

	ATV/ RTV	DRV/ RTV	EFV	RPV	DTG	EVG/ COBI	RAL	ABC	FTC	3TC	TDF
Antacids											
PPIs											
Alfuzosin											
Budesonide											
Fluticasone											
Sildenafil											
St John's wort											
Escitalopram											
Aspirin											
Ibuprofen											
Codeine											
Methadone											
Morphine											
Oxycodone											
Tramadol											
Diazepam											
Midazolam											
Pimozide											
Phenytoin											
Rifampicin											

- No clinically significant interaction expected
- These drugs should not be coadministered
- Potential interaction that may require a dosage adjustment
- Potential interaction predicted to be of weak intensity



Summary

- The majority of people with HIV are now or soon will be age 50 and older, and are facing an increasing burden of comorbidities and medications.
- Some health issues with aging occur at an accentuated rate, and others may occur at an accelerated rate (earlier than expected).
- Adhering to current recommendations for screening/treatment may be beneficial in well-functioning patients aging with HIV, while others may need a unique approach (Frail patients).
- Earlier initiation of antiretroviral therapy and correct choice of antiretroviral therapy.



GRAZIE PER L'ATTENZIONE!

Edouard Boubat – *Boulevard Saint-Germain, Paris, 1948*

