

# HIV and Ageing

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# Outline

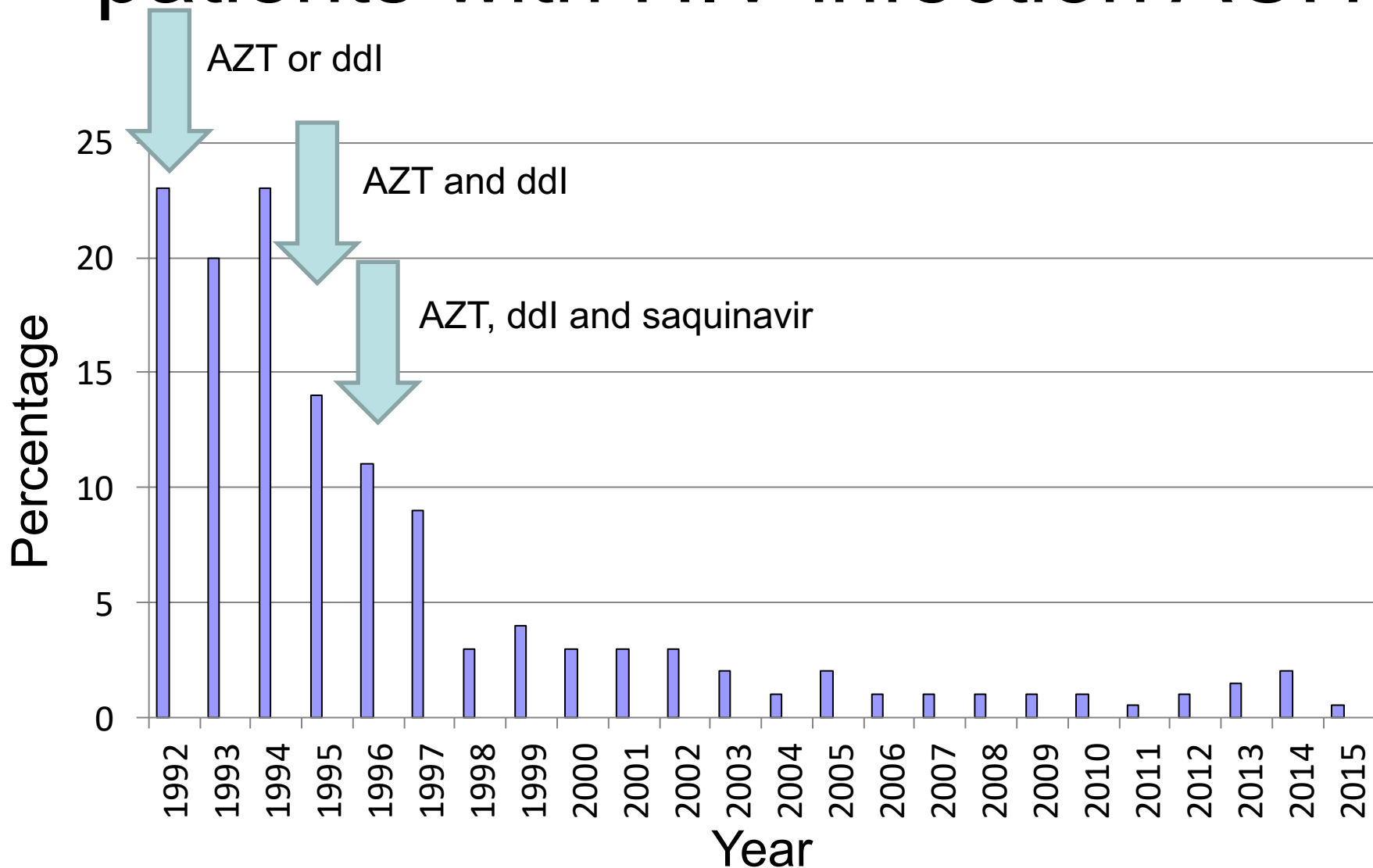
- Introduction
- HIV infection and premature ageing
- What may contribute to premature ageing?
- Reducing chronic inflammation related to HIV infection
- What we can do to slow the premature ageing process?

# Introduction

- The development of antiretroviral treatment (ART) is one of the greatest advances in modern medicine
- ART has changed HIV infection from a lethal disease to a chronic manageable illness



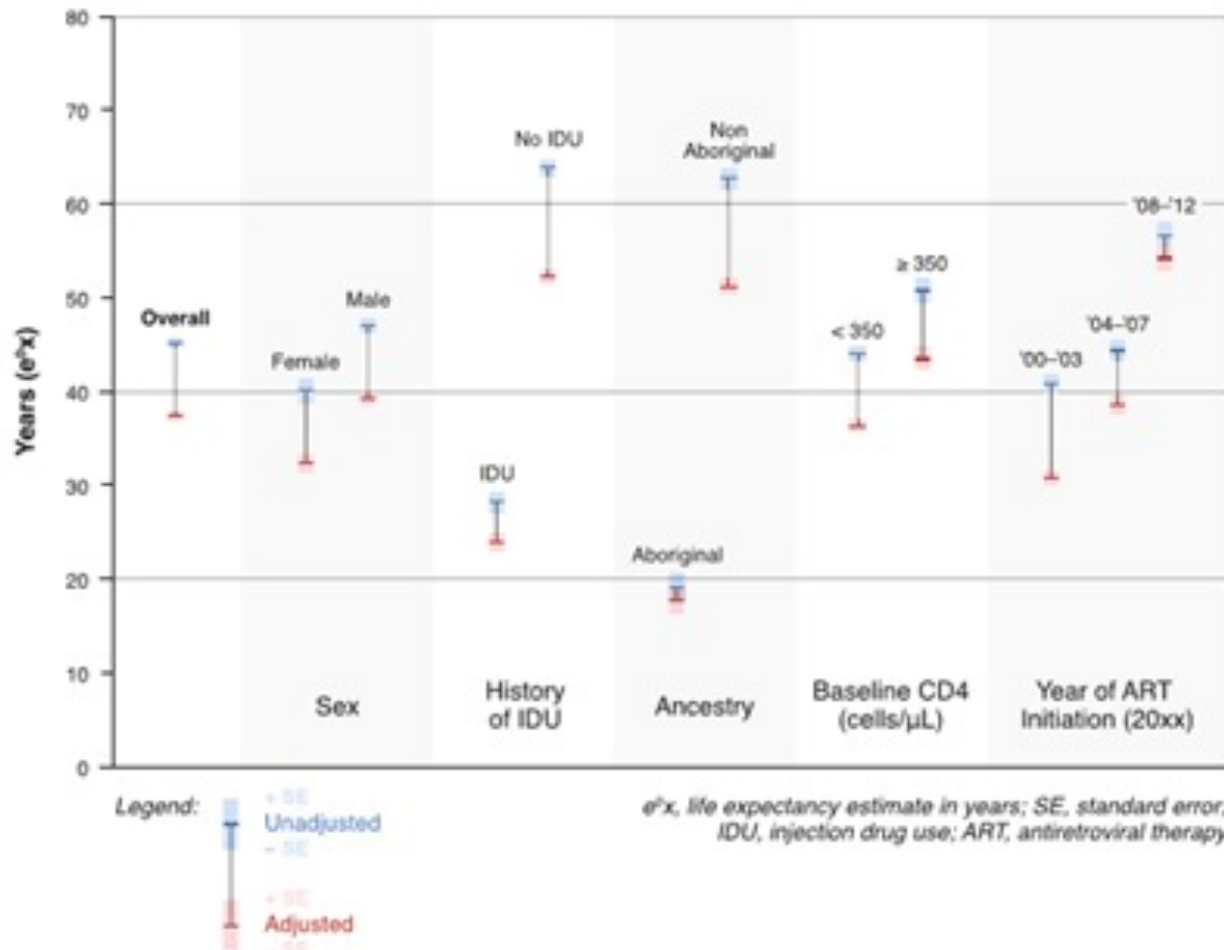
# Percentage yearly mortality for patients with HIV infection ACH



- Current estimates are that someone diagnosed with HIV infection today should live for almost as long as someone without HIV infection

# Life expectancy estimates at age 20 years

BMC Infect Dis 2015;15:274



**Fig. 1** Life expectancy estimates at age 20 years, showing unadjusted and adjusted values, by clinical and sociodemographic characteristics at baseline

- Despite the remarkable success of ART, it does not fully restore health
- Many people living with HIV infection seem to age more quickly than those without HIV infection

# HIV infection and premature ageing

- The slightly shorter lifespan is largely due to an increased risk of “non-AIDS” complications
  - heart disease
  - liver disease
  - kidney disease
  - neurological conditions
  - some cancers
  - frailty
- Many of these complications are similar to those experienced by the elderly or those with other chronic diseases such as diabetes



# Rates of acute myocardial infarction by HIV status and age

JAMA Intern Med 2013;173:614

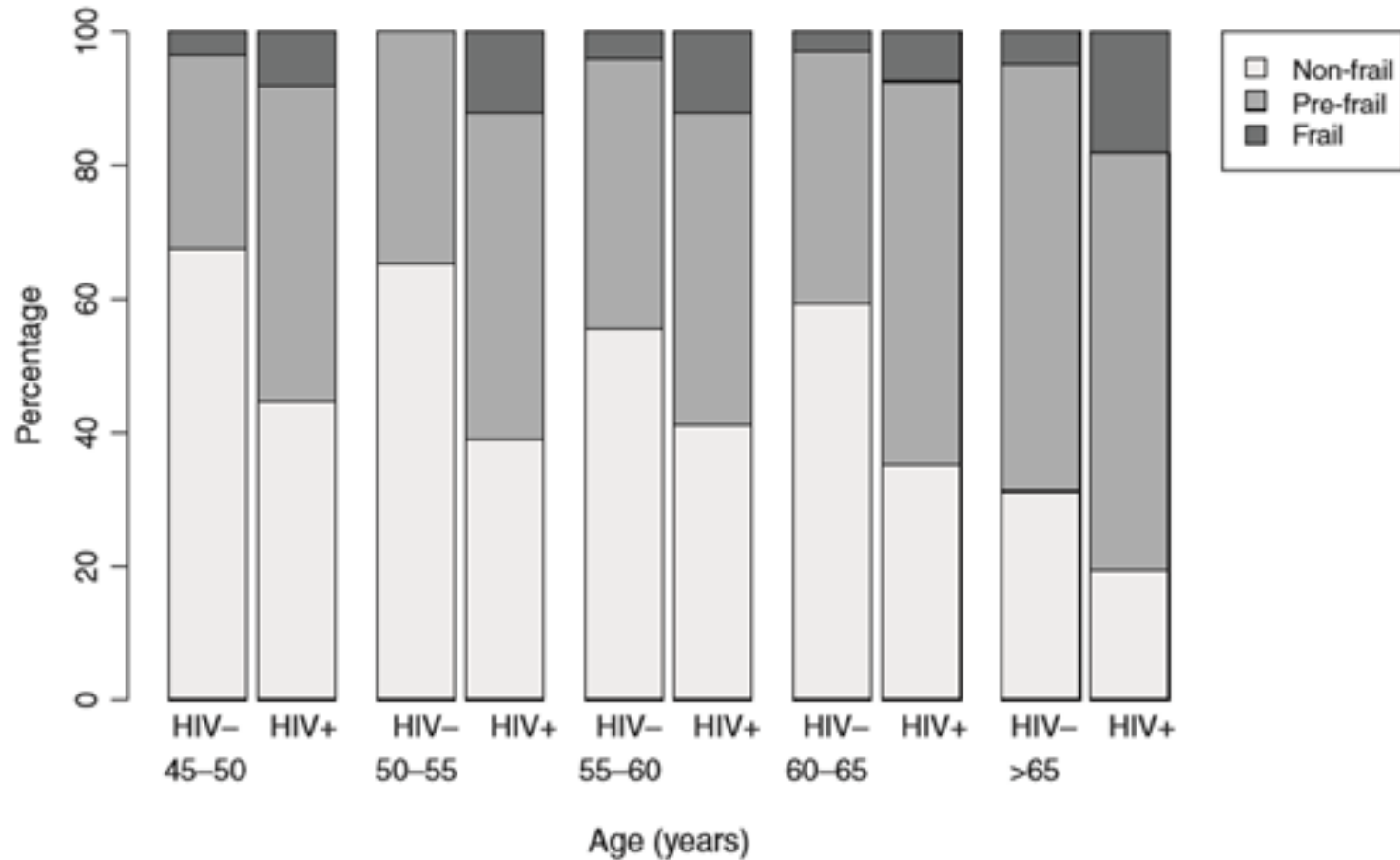
Status	Age Group,y							
	<30	30-39	40-49	50-59	60-69	70-79	80-89	>89
<b>Uninfected</b>								
No. of participants	1175	6783	21 866	19 805	4209	1120	148	3
No. of AMI events	0	10	164	218	66	36	14	0
AMI rates per 1000 person-years (95% CI)	...	0.3 (0.2-0.6)	1.5 (1.3-1.7)	2.2 (1.9-2.5)	3.3 (2.6-4.2)	6.7 (4.8-9.2)	21.5 (12.7-36.4)	...
<b>HIV Infected</b>								
No. of participants	725	3848	10 575	9342	2065	557	56	0
No. of AMI events	0	13	105	171	46	25	3	0
AMI rates per 1000 person-years (95% CI)	...	0.7 (0.4-1.2)	2.0 (1.6-2.4)	3.9 (3.3-4.5)	5.0 (3.8-6.7)	10.0 (6.7-14.7)	13.5 (4.3-42.0)	...
Incidence rate ratio (95% CI)	...	2.19 (0.89-5.58)	1.34 (1.04-1.72)	1.80 (1.47-1.21)	1.53 (1.03- 2.26)	1.50 (0.86-2.57)	0.63 (0.12-2.25)	...

# Association between HIV status and frailty

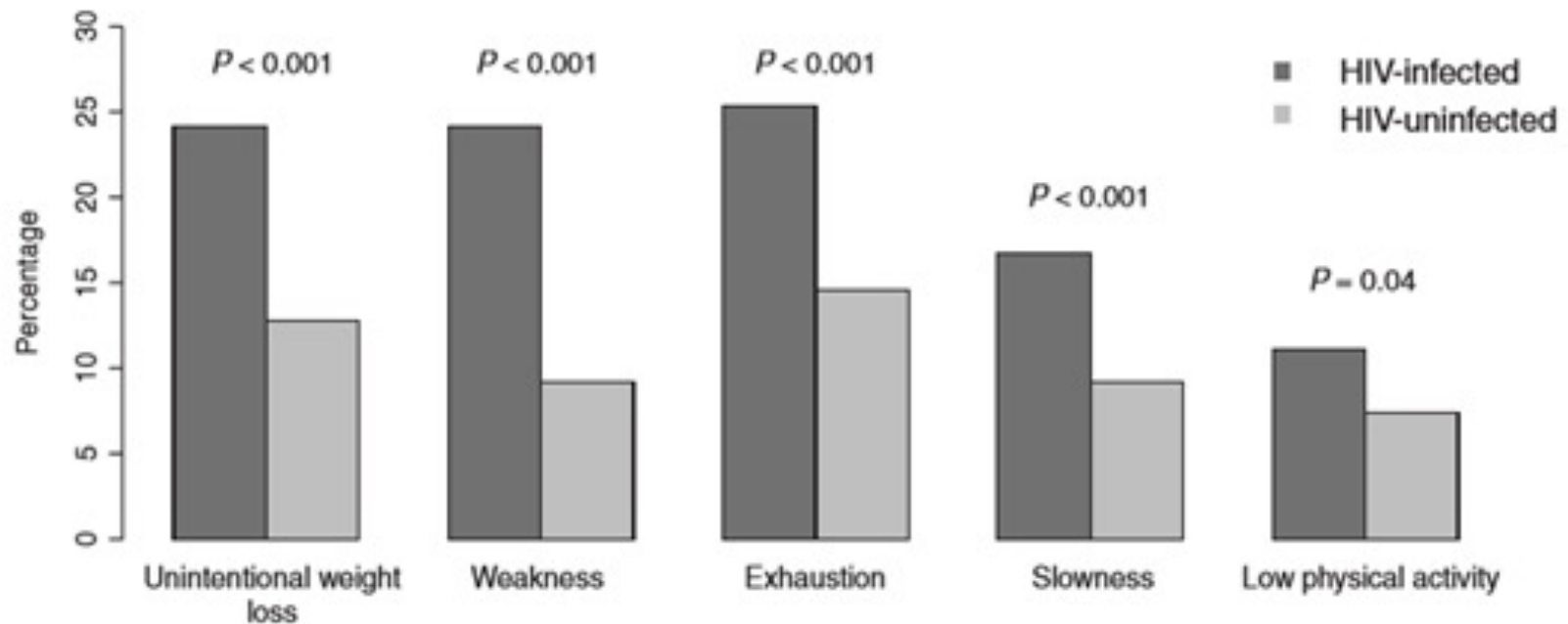
AIDS 2016;30:241

- Dutch study of 521 patients with HIV infection and 513 controls
- Median age 52 years, mean current CD4 count 563 cells/mm<sup>3</sup>, median nadir CD4 count 180 cells/mm<sup>3</sup>, 70% had a previous AIDS defining illness, 23% nadir BMI < 20 kg/m<sup>2</sup>
- HIV infection was an independent risk factor for frailty (after adjusting for age, gender, ethnicity, smoking and hepatitis C infection) (OR 2.39 p < 0.0001)
- This may in part be related to historic weight loss due to participants advanced HIV infection

# Prevalence of frailty by age and HIV infection status



# Prevalence of frailty criteria





# What contributes to this premature ageing?

- Chronic inflammation from HIV infection
- Higher prevalence of risk factors
- Higher prevalence of other illnesses
- ART Toxicity

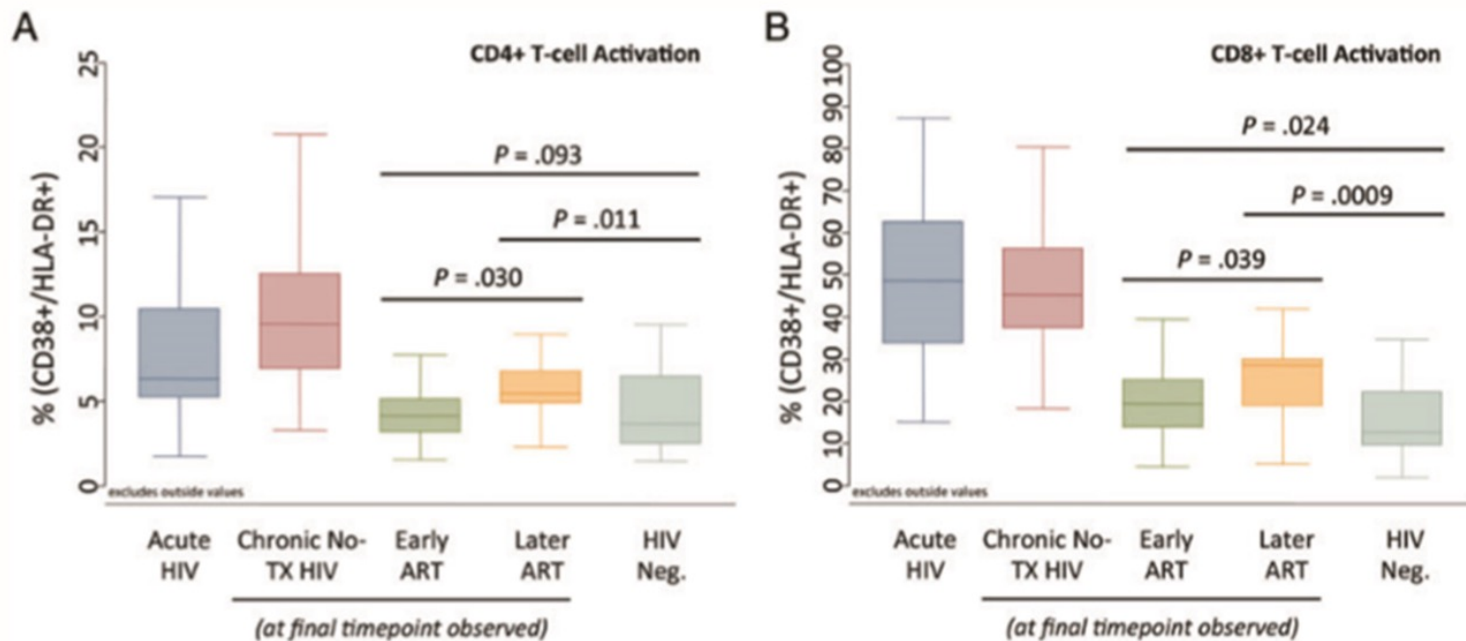
# Chronic inflammation from HIV infection

- Even people with well controlled HIV infection have a persistent low level inflammatory state
  - chronic immune activation due to ongoing HIV viral replication
  - inflammation due to other viruses (CMV, hepatitis B and C)
  - chronically leaky gut (microbial translocation)
  - increased incidence of skin and sinus disease

# Persistent inflammation due to HIV infection

J Infect Dis 2013;208:1202

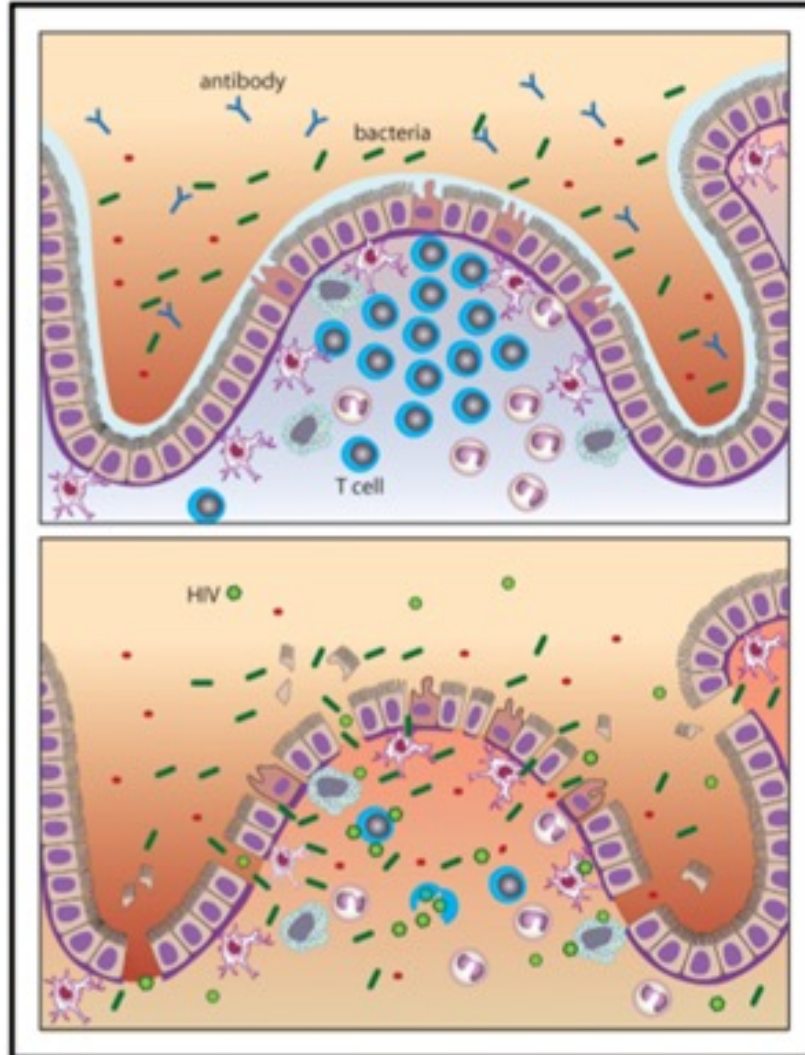
- Higher levels of T cell activation have been linked to cardiovascular disease and increased mortality





# Impact of HIV infection on gut mucosa

Immunity 2013;39:633



# Higher prevalence of risk factors

- Smoking AIDS 2015;29:221
  - in a North American and Western European cohort of people living with HIV infection 46.5% were currently smokers
  - the general population current smoking rate for the same regions ranges from 17 to 30%



© Reuters

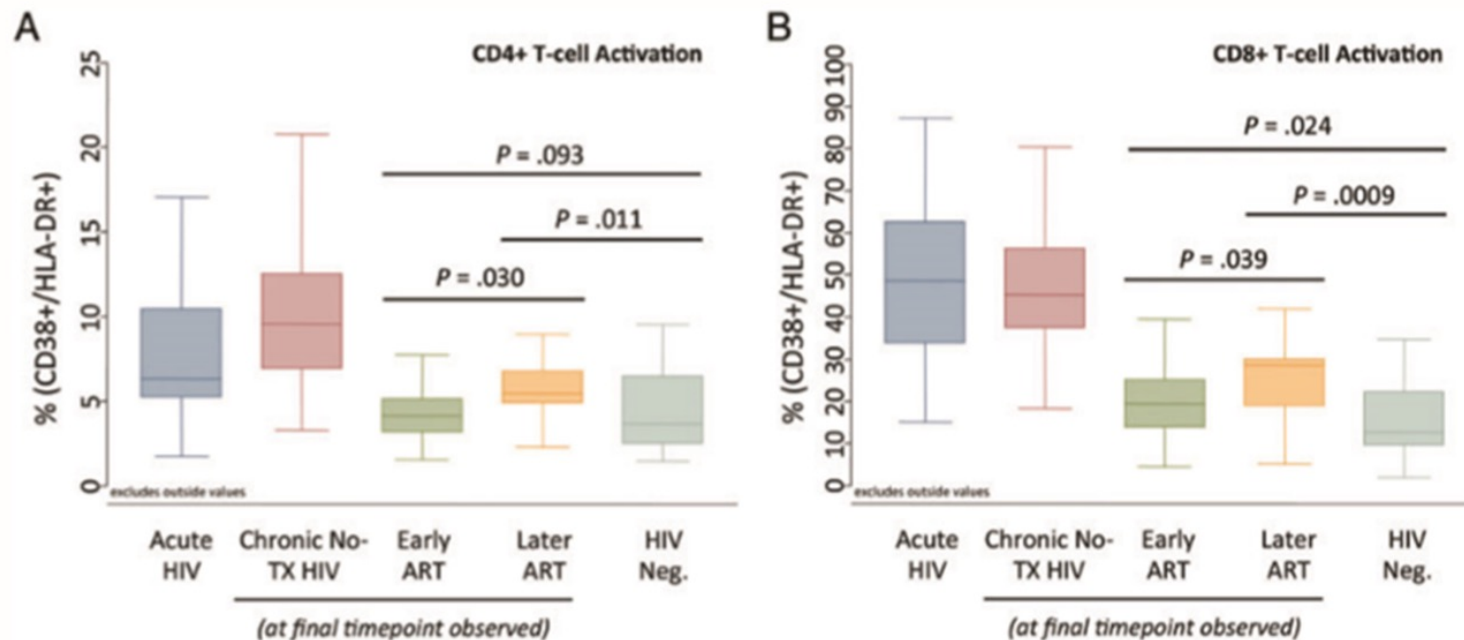
# What can reduce chronic inflammation related to HIV infection?

- Earlier treatment of HIV infection
- Rosuvastatin

# Early treatment of HIV infection results in reduced T cell activation

J Infect Dis 2013;208:1202

- T cell activation have been linked to cardiovascular disease and increased mortality

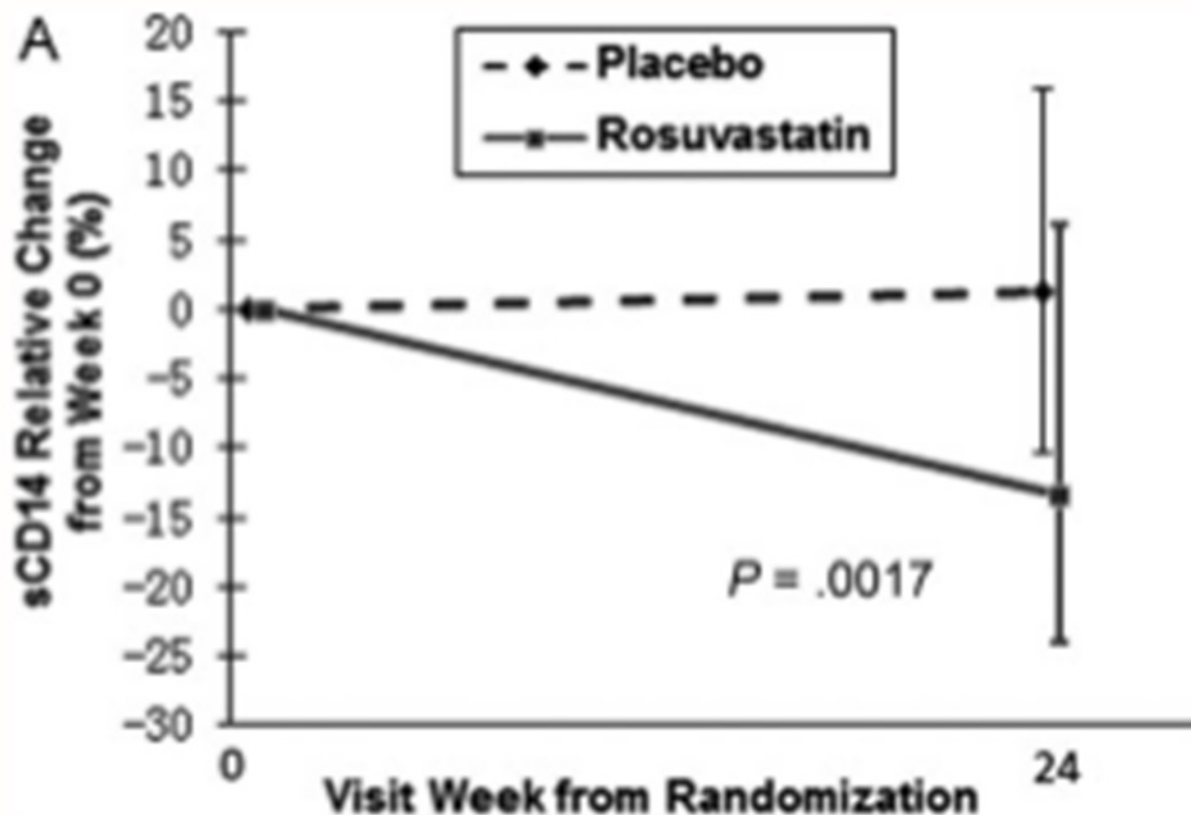


# Rosuvastatin

Clin Infect Dis 2014;58:588

- Activated monocytes may contribute to inflammation and cardiovascular disease
- Soluble CD14
  - marker of monocyte activation
  - independent predictor of mortality in people with HIV infection
  - linked to faster vascular disease progression
- People with HIV infection receiving ART were randomised to receive rosuvastatin or placebo

# Change in sCD14 with rosuvastatin







# What can we all do to slow the premature ageing process associated with HIV infection?

- Diagnose HIV infection early
- Start ART early
- Stay active
- Have a healthy diet
- Reduce substance abuse (smoking, alcohol, other recreational drugs)
- Screen for and treat hypertension, diabetes, kidney disease and liver disease



- Saffie: Look, mum. All you've got to do is eat less and take a bit of exercise.
- Eddie: Sweetie, if it was that easy, everyone would be doing it. Anyway, I don't know what you mean. I do take exercise!
- Saffie: You get out of bed, it ends there.

Thank you