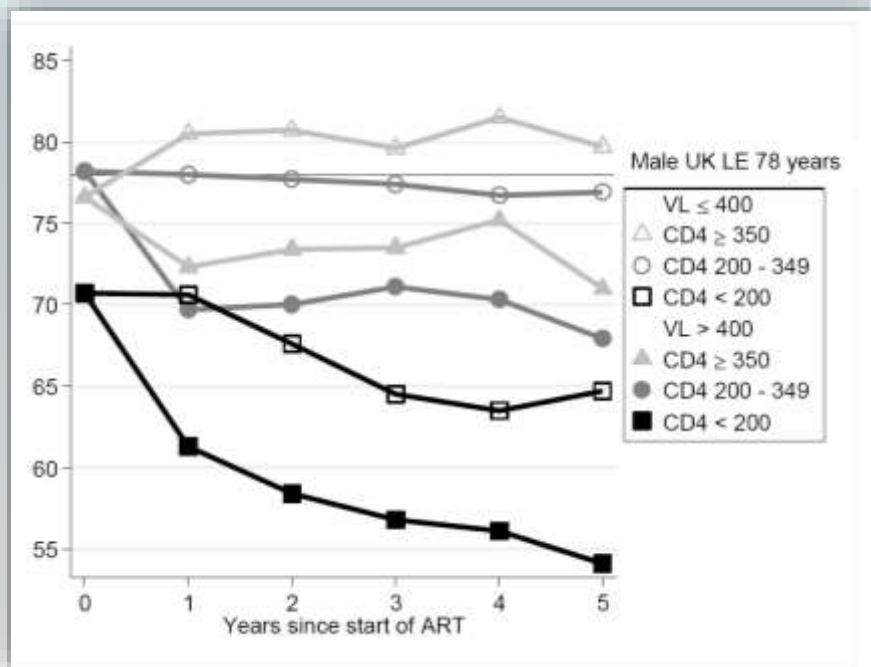


**Co-morbidities in the older HIV
population
- findings from the D:A:D study**

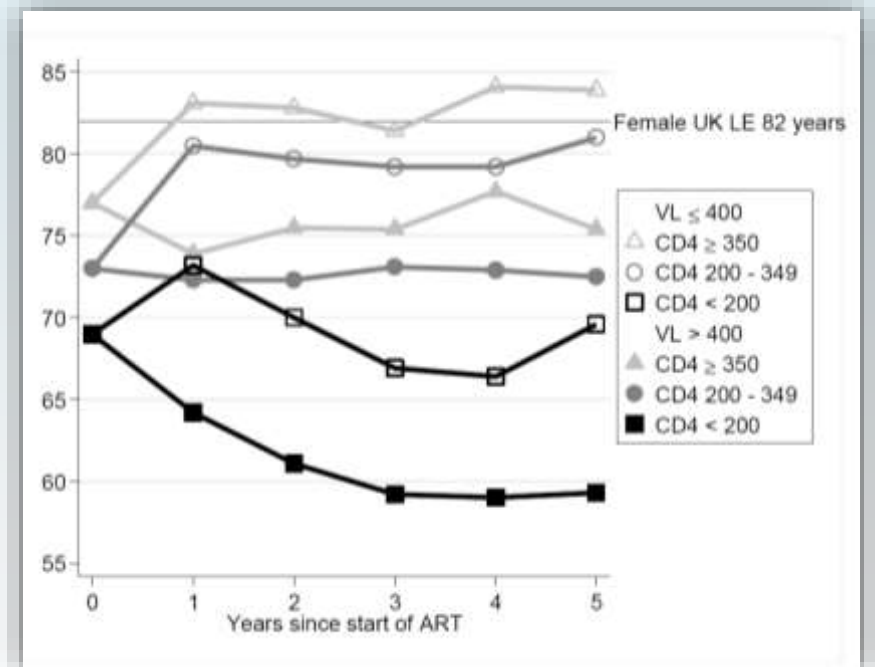
Caroline Sabin

Improvements in life expectancy in HIV

Expected age at death* - men

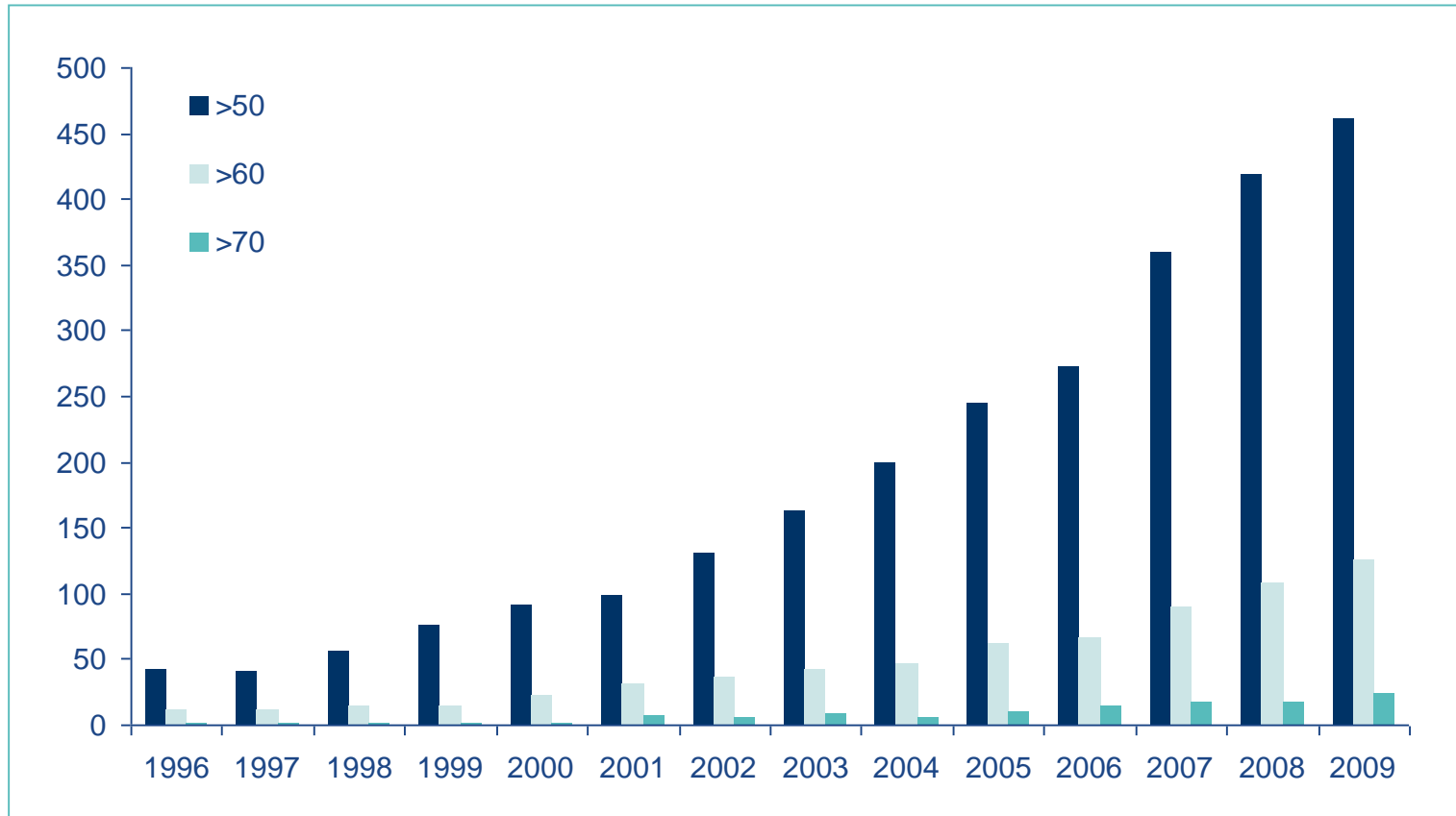


Expected age at death* - women



* Expected age at death for a person aged 35 years with different durations of antiretroviral therapy according to current CD4 count and viral load suppression

Patient age in Brighton cohort: 1996-2009



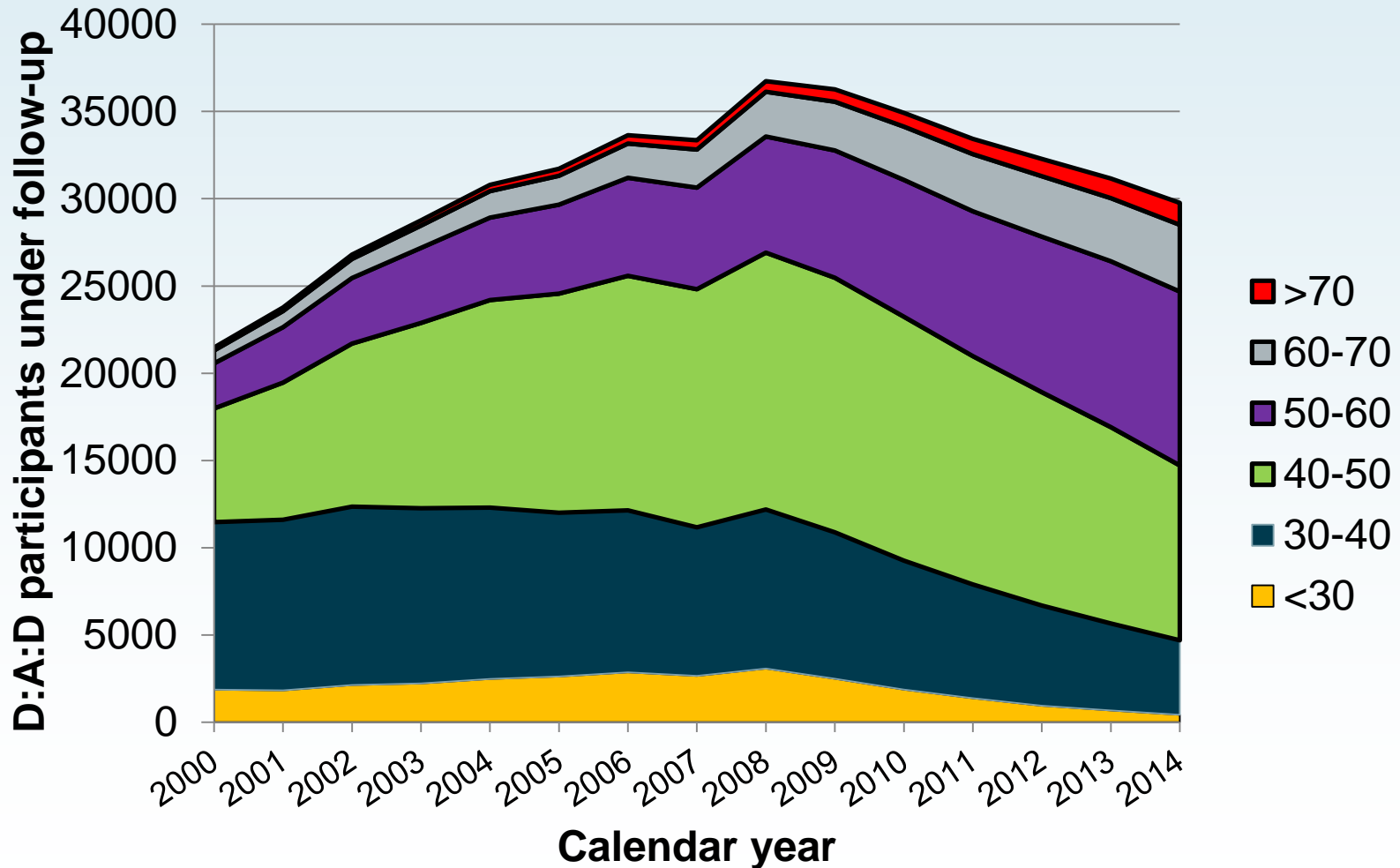
Topics

- The D:A:D population – how is it changing and what are the characteristics of the older D:A:D population?
- Associations with cardiovascular disease, cancer and liver-related outcomes
- Mortality and causes of death in D:A:D participants

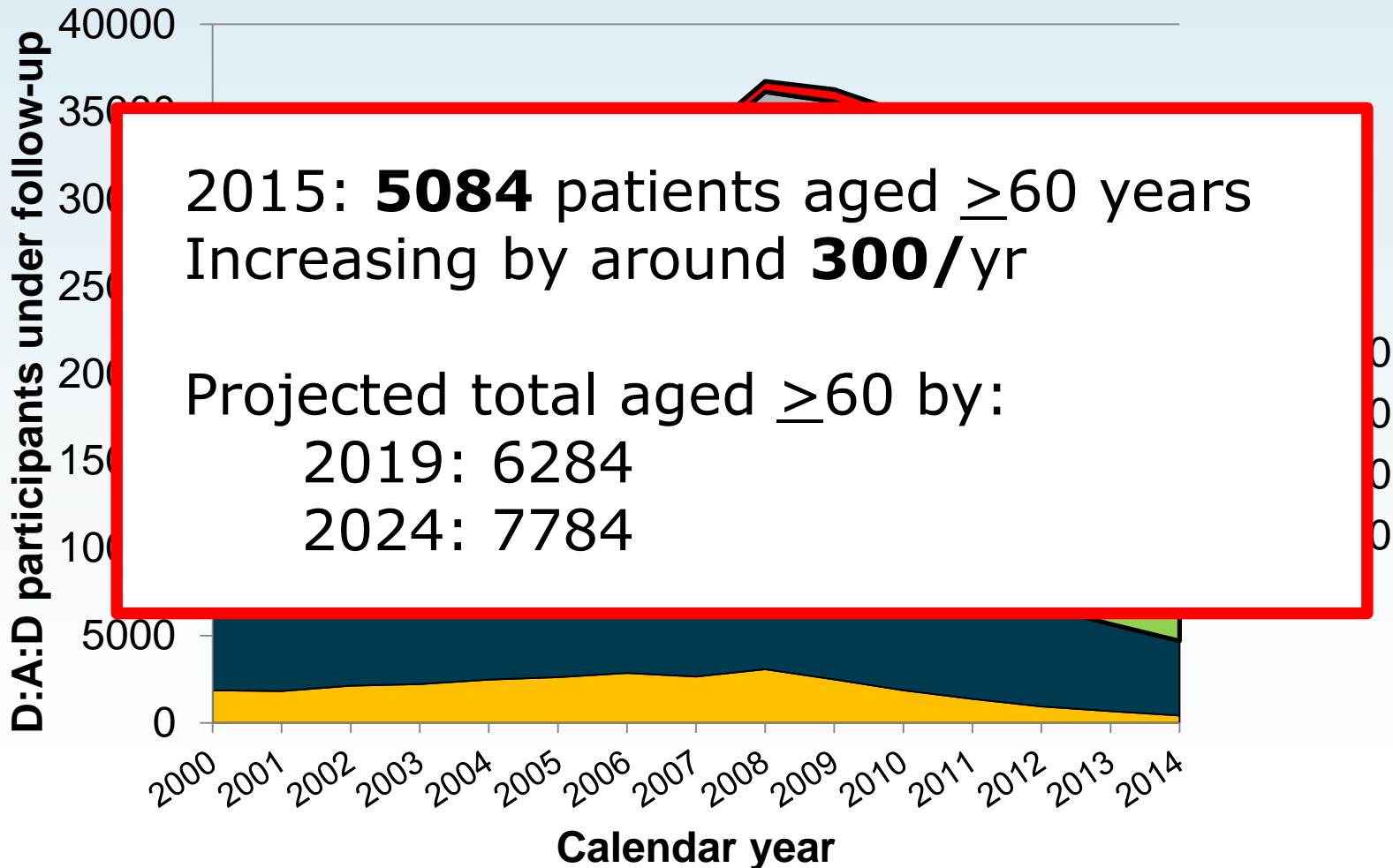
The D:A:D Study

- Collaboration of 11 cohort studies from Europe, USA and Australia set up to study association between ARV treatment and CVD
- Study currently follows >50,000 patients
- Information collected on socio-demographic, clinical, treatment and laboratory variables
- All incident outcomes validated and coded centrally at coordinating office
- Outcomes: MI, stroke, invasive CV procedures, diabetes mellitus, death, cancers, end-stage liver disease, end-stage renal disease

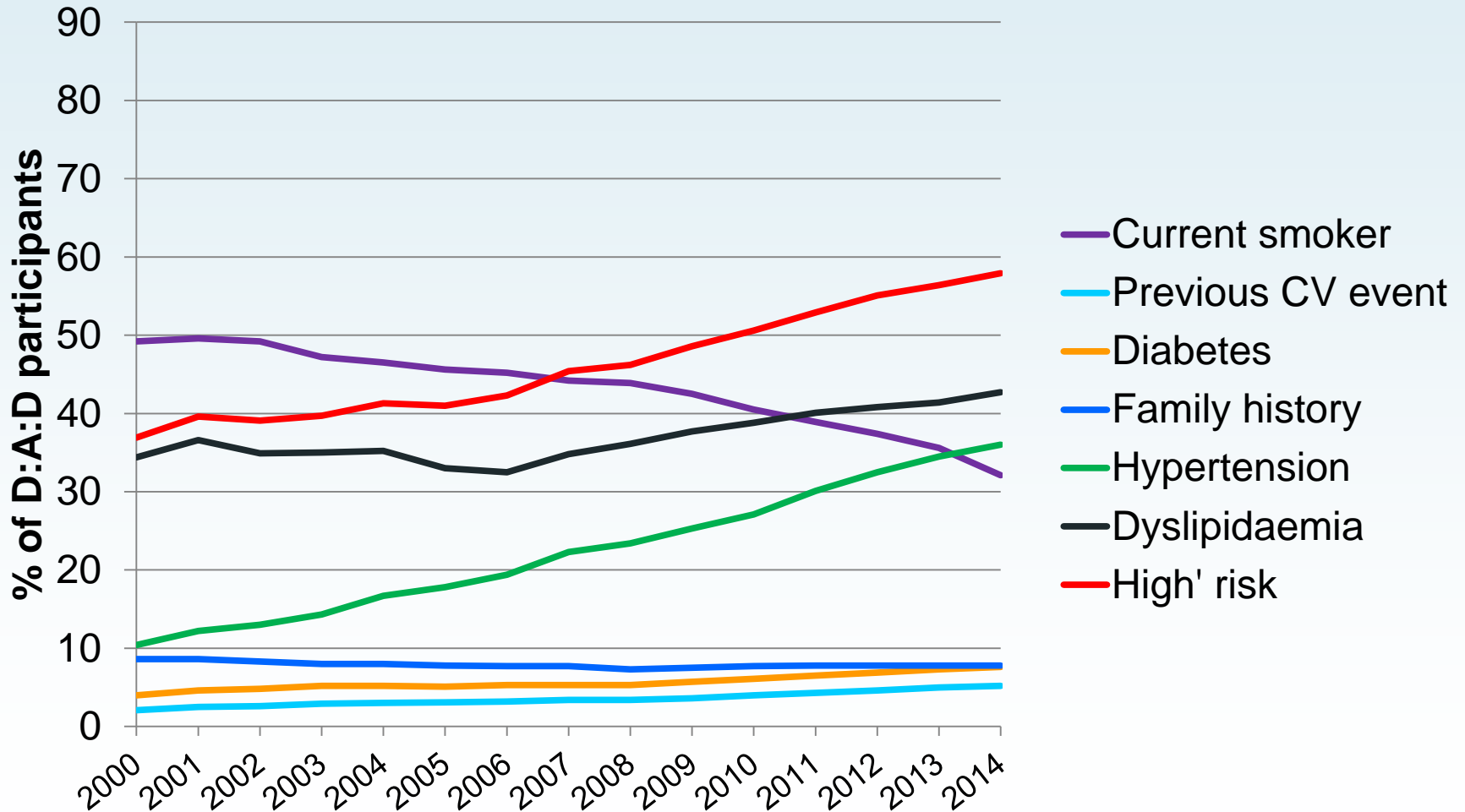
Age distribution of patients in D:A:D



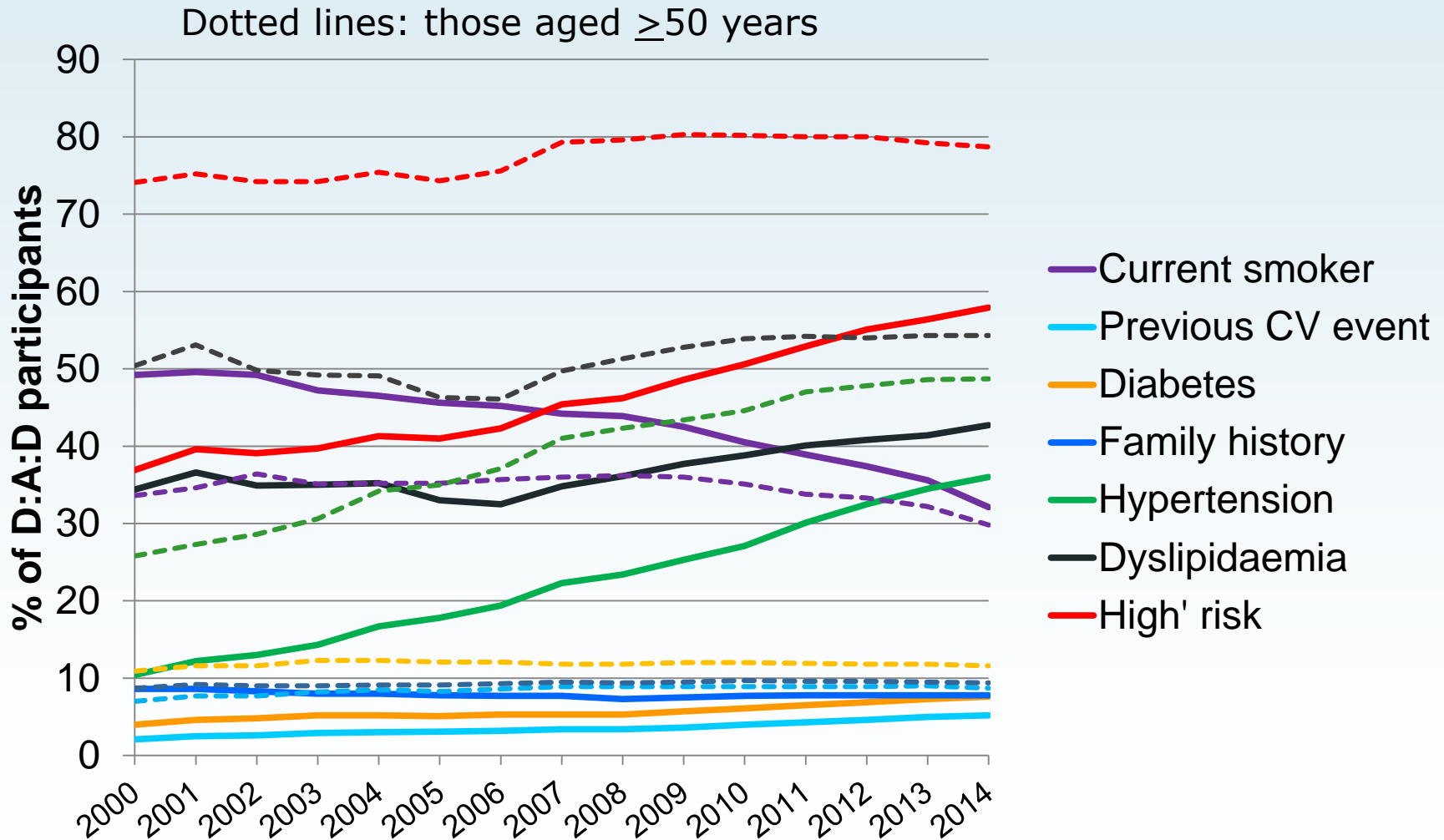
Age distribution of patients in D:A:D



Changing prevalence of CVD risk factors



Changing prevalence of CVD risk factors



Characteristics of those aged >50

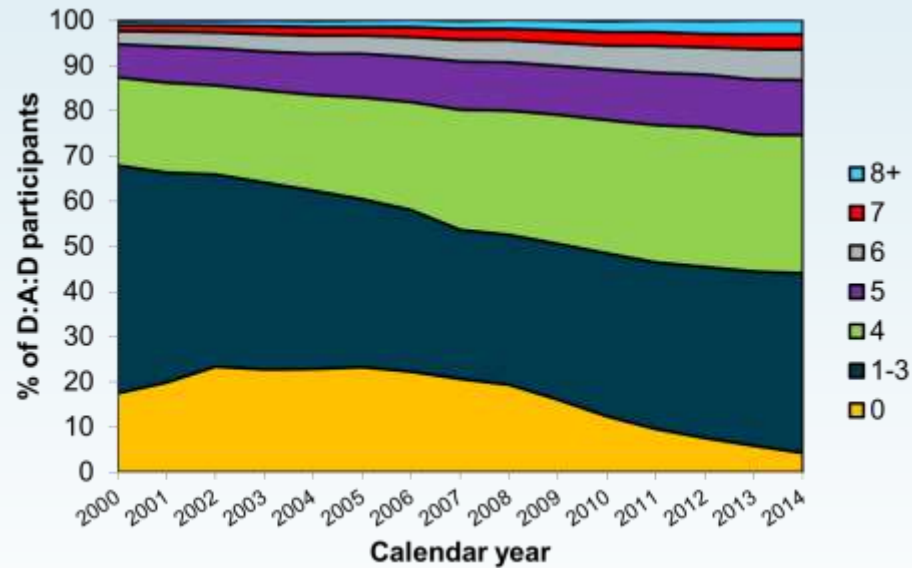
- 13,529 participants seen since 2014 aged ≥ 50 years (45.8% of population under follow-up)
- 81.4% male
- Median (IQR) CD4: 580 (404, 785) cells/mm³
- HIV RNA <50 copies/ml: 82.1%
- Median (IQR) ART drugs received: 8 (0, 24)
- Duration of ART exposure:
 - 62.2% >10 years
 - 34.4% >15 years
 - 0.2% >20 years

Characteristics of those aged >50

Previous CVD events	N (%)
Myocardial infarction	419 (3.1)
Stroke	376 (2.8)
Diabetes	1422 (10.5)
Angioplasty	626 (4.6)
Bypass	175 (1.3)
Endarterectomy	36 (0.3)

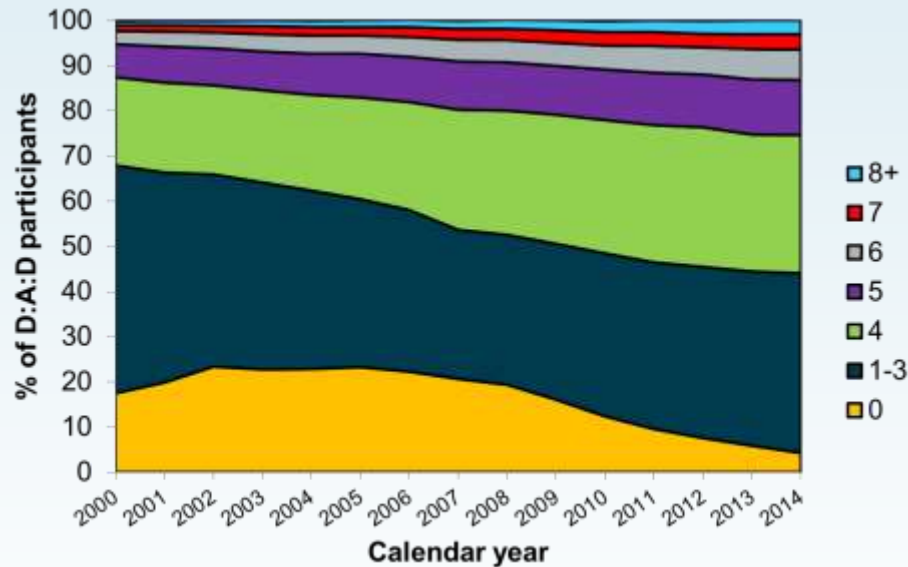
Polypharmacy (ART+other meds)

All D:A:D participants

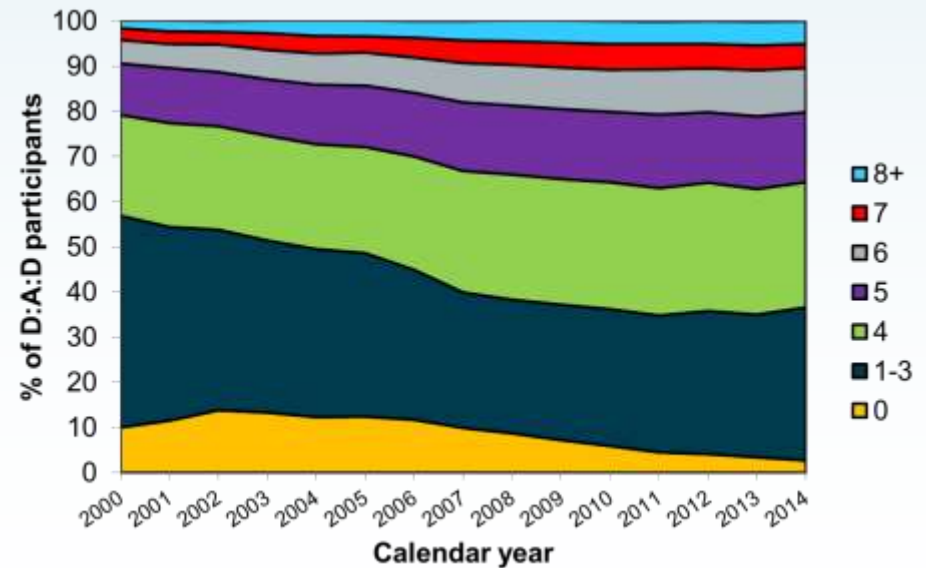


Polypharmacy (ART+other meds)

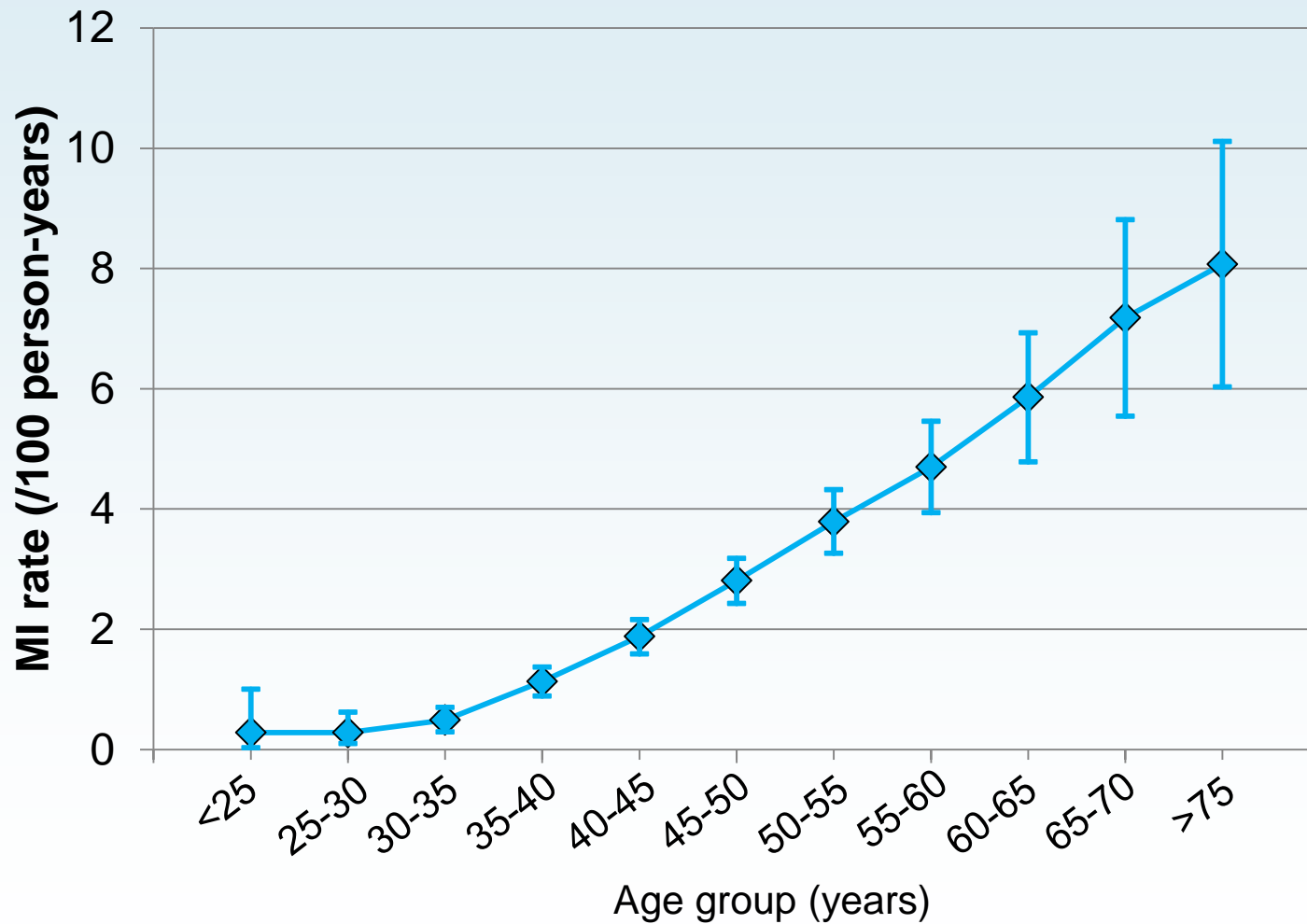
All D:A:D participants



Participants aged ≥ 50



MI rate, stratified by age group



CVD associations with age

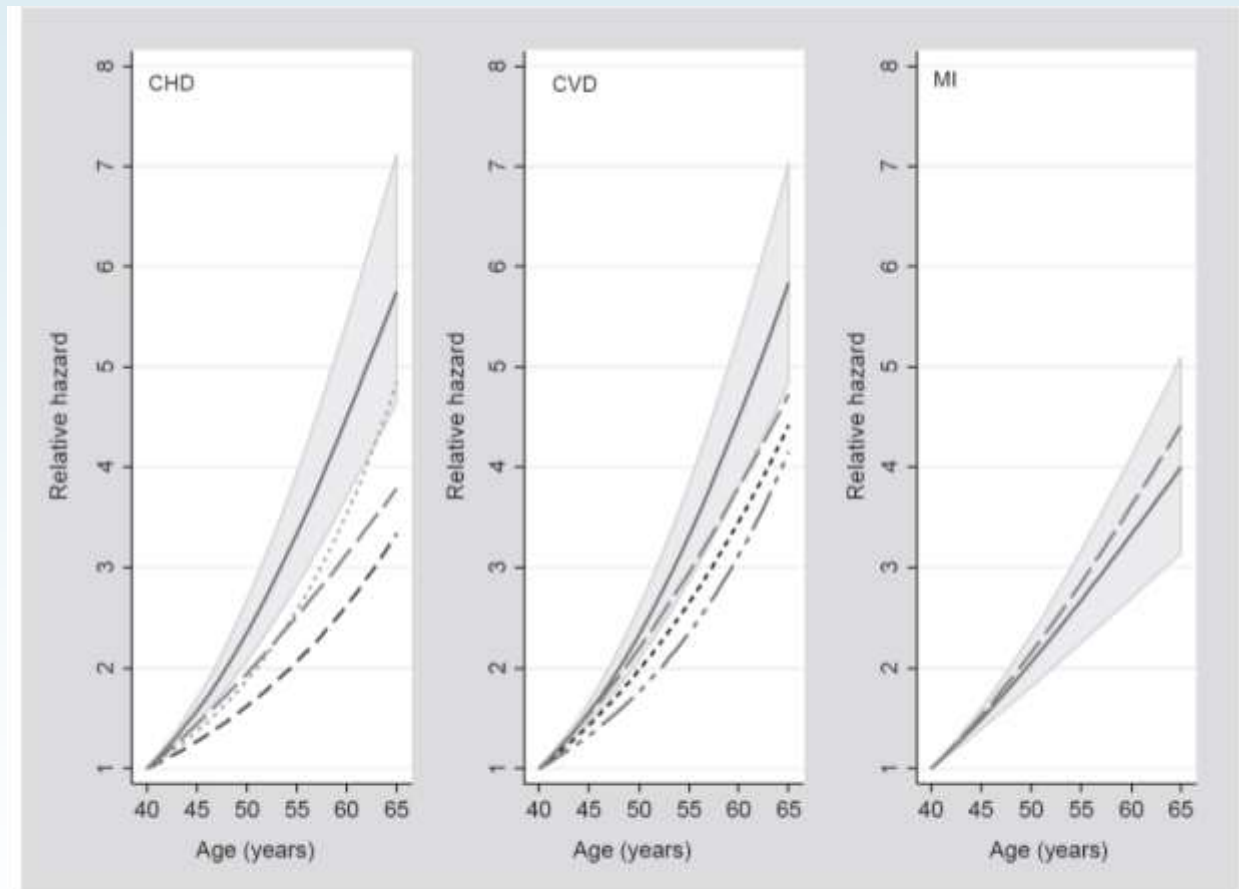


Fig. 2 Relative risk of coronary heart disease (CHD), cardiovascular disease (CVD) and myocardial infarction (MI) from age 40 years for D:A:D and respective general population equations: FHS_A (Framingham Heart Study, Anderson *et al.* [12]), FHS_W (Framingham Heart Study, Wilson *et al.* [13]), FHS_D (Framingham Heart Study, D'Agostino *et al.* [14]), CUORE and ASSIGN. Risk equations: D:A:D equation in all three panels, continuous line (95% confidence limits, blue shaded area); FHS_A, long-dashed line (all three endpoints); FHS_W, dashed line (CHD endpoint); FHS_D, short-dashed line (CVD endpoint); CUORE, very short-dashed line (CHD endpoint); ASSIGN, long-dashed–short-dashed line (CVD endpoint).

CVD associations with age

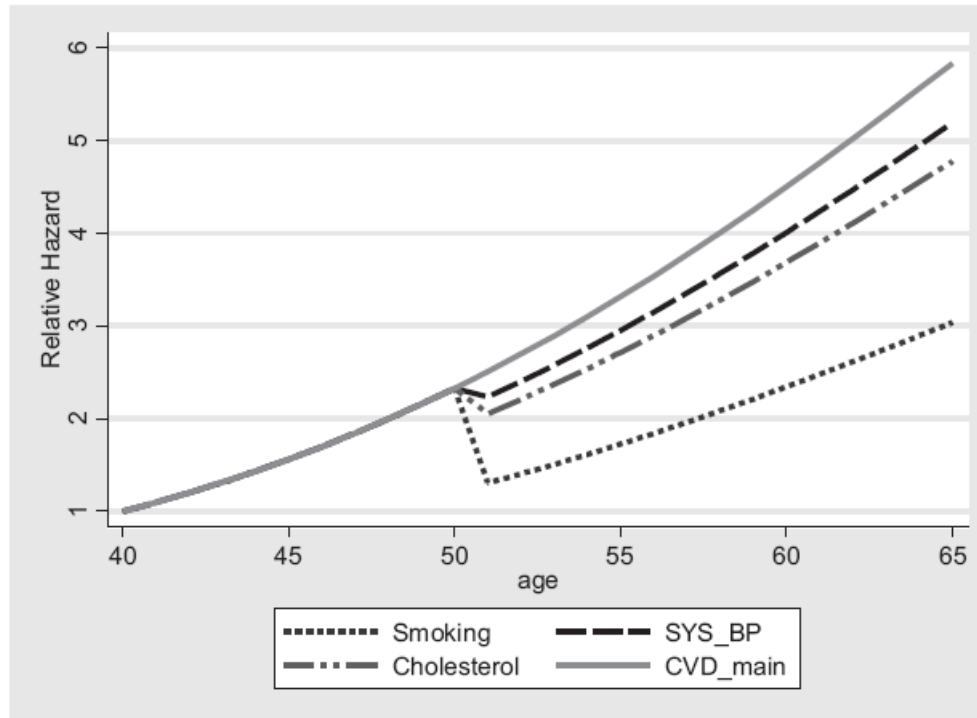
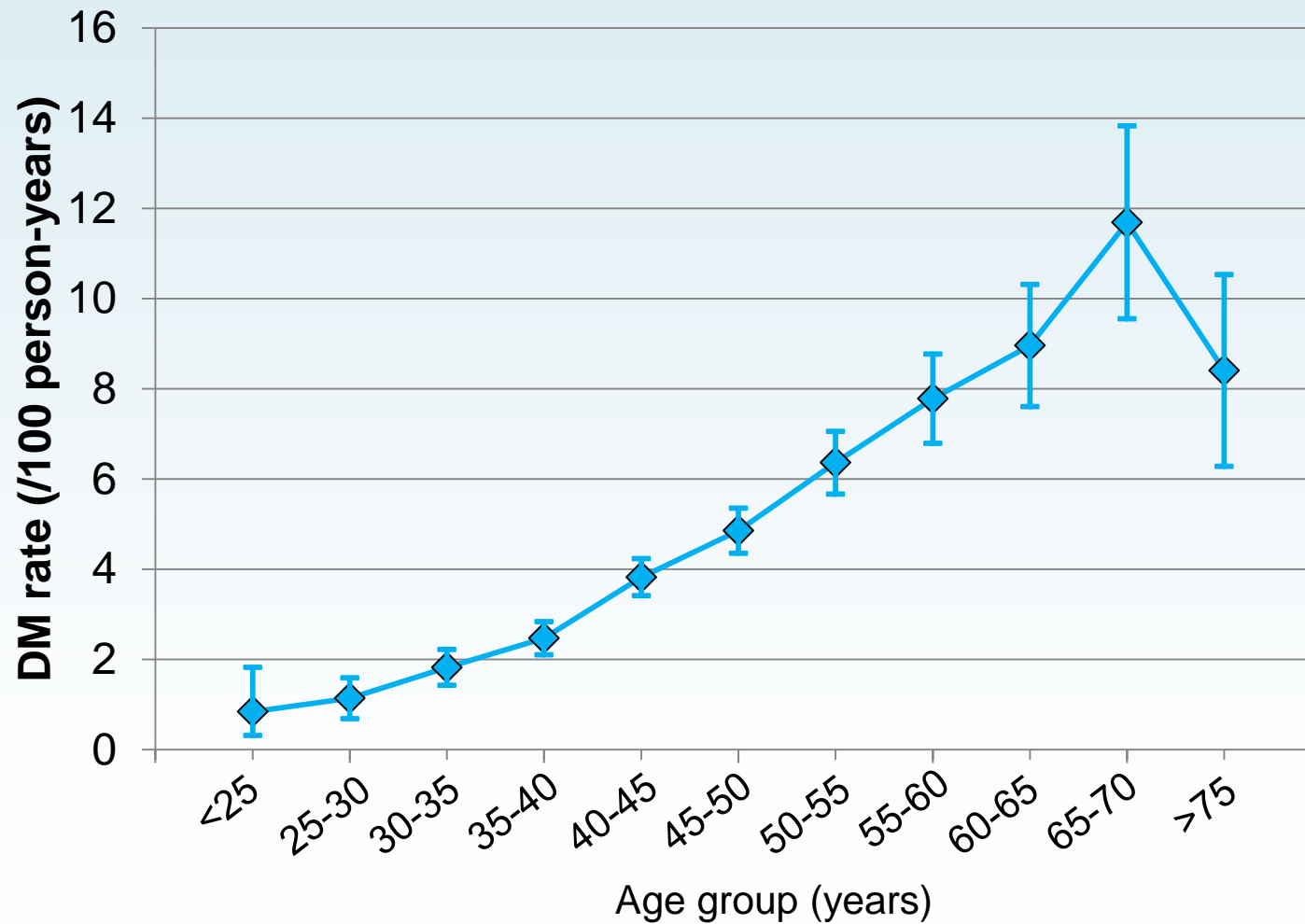
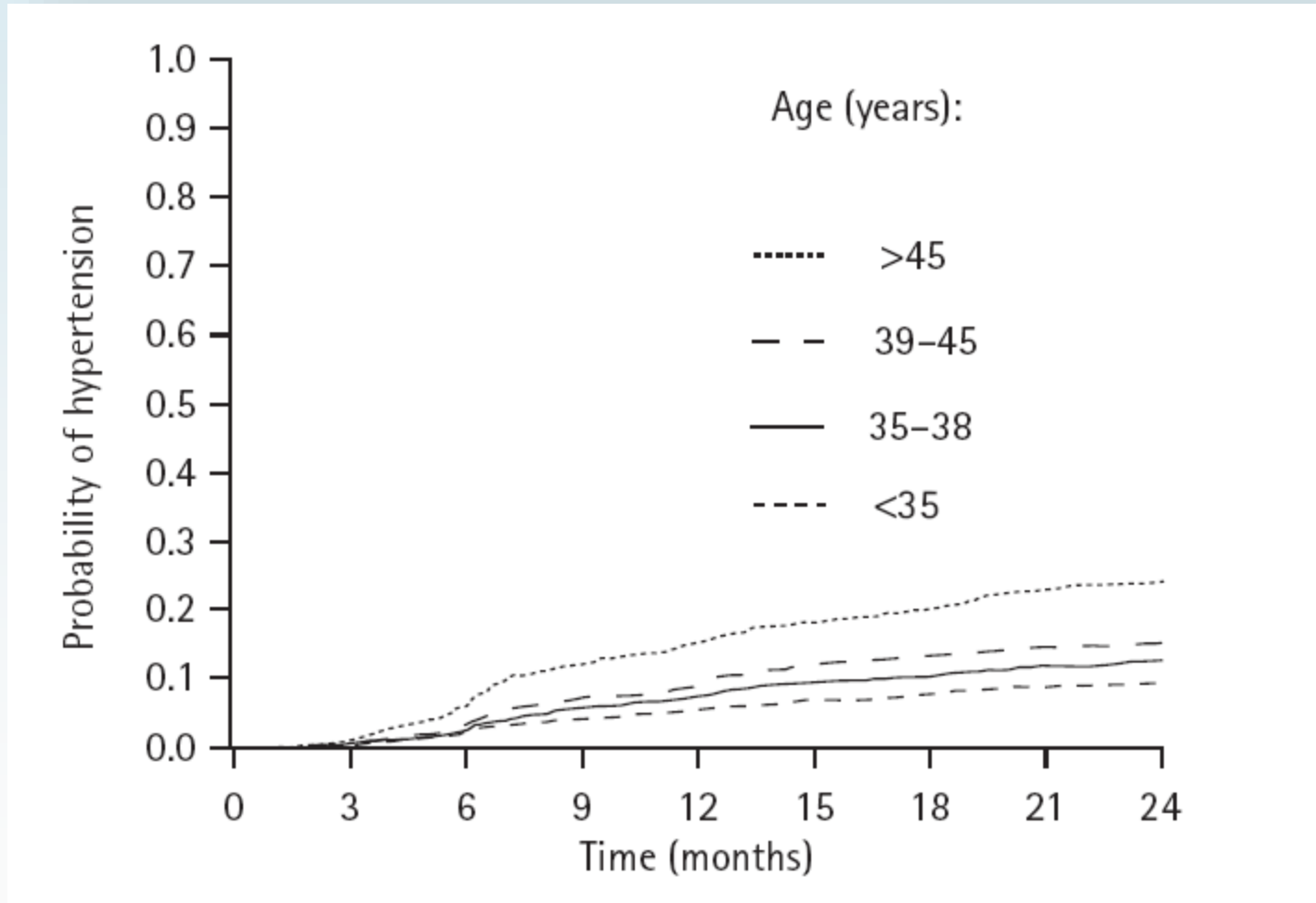


Fig. 3 Relative risk of cardiovascular disease (CVD) from age 40 years including stopping smoking, reducing cholesterol (by 1 mmol/L) or reducing systolic blood pressure (SYS_BP) (by 10 mmHg) at age 50 years.

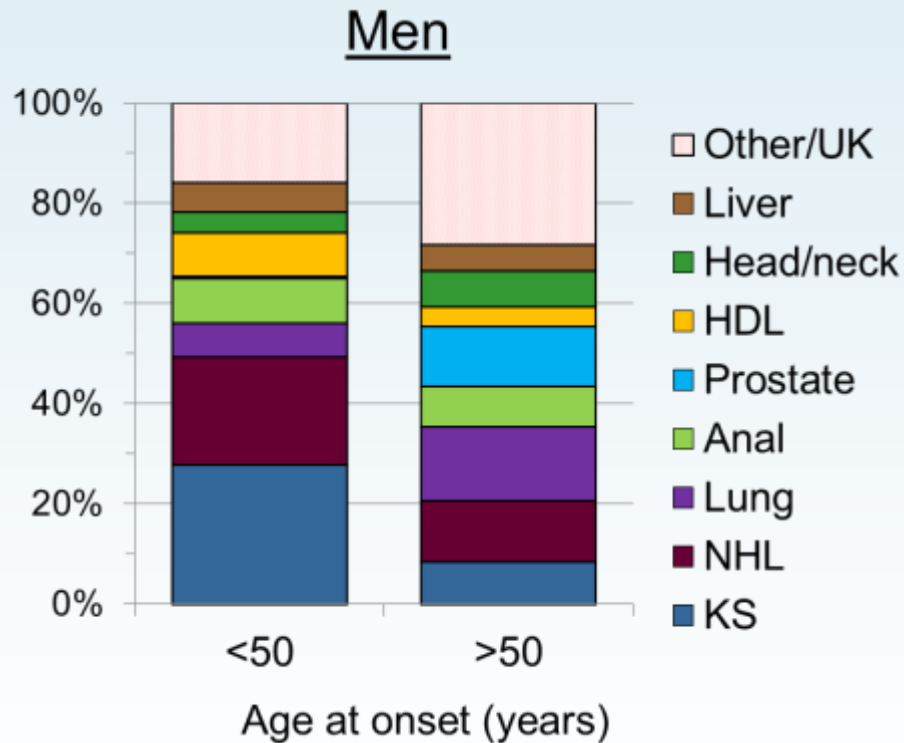
Diabetes rate, stratified by age group



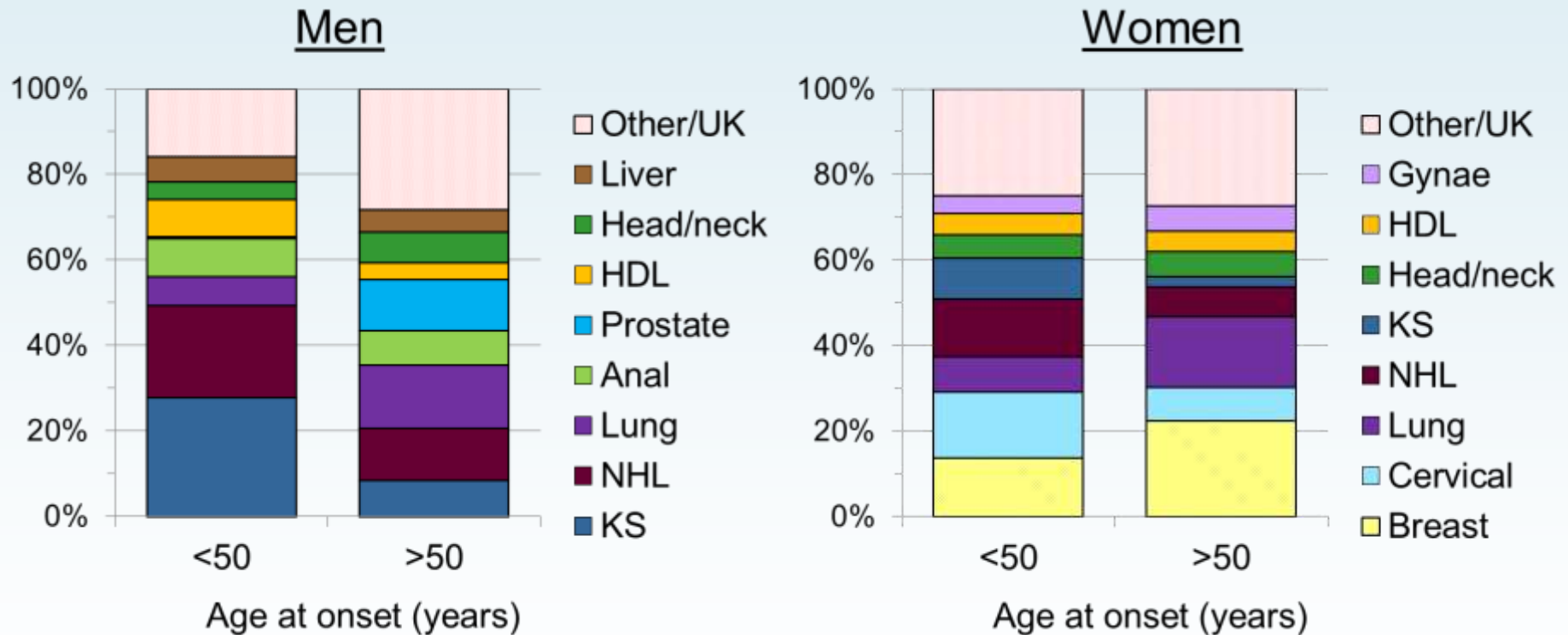
Hypertension



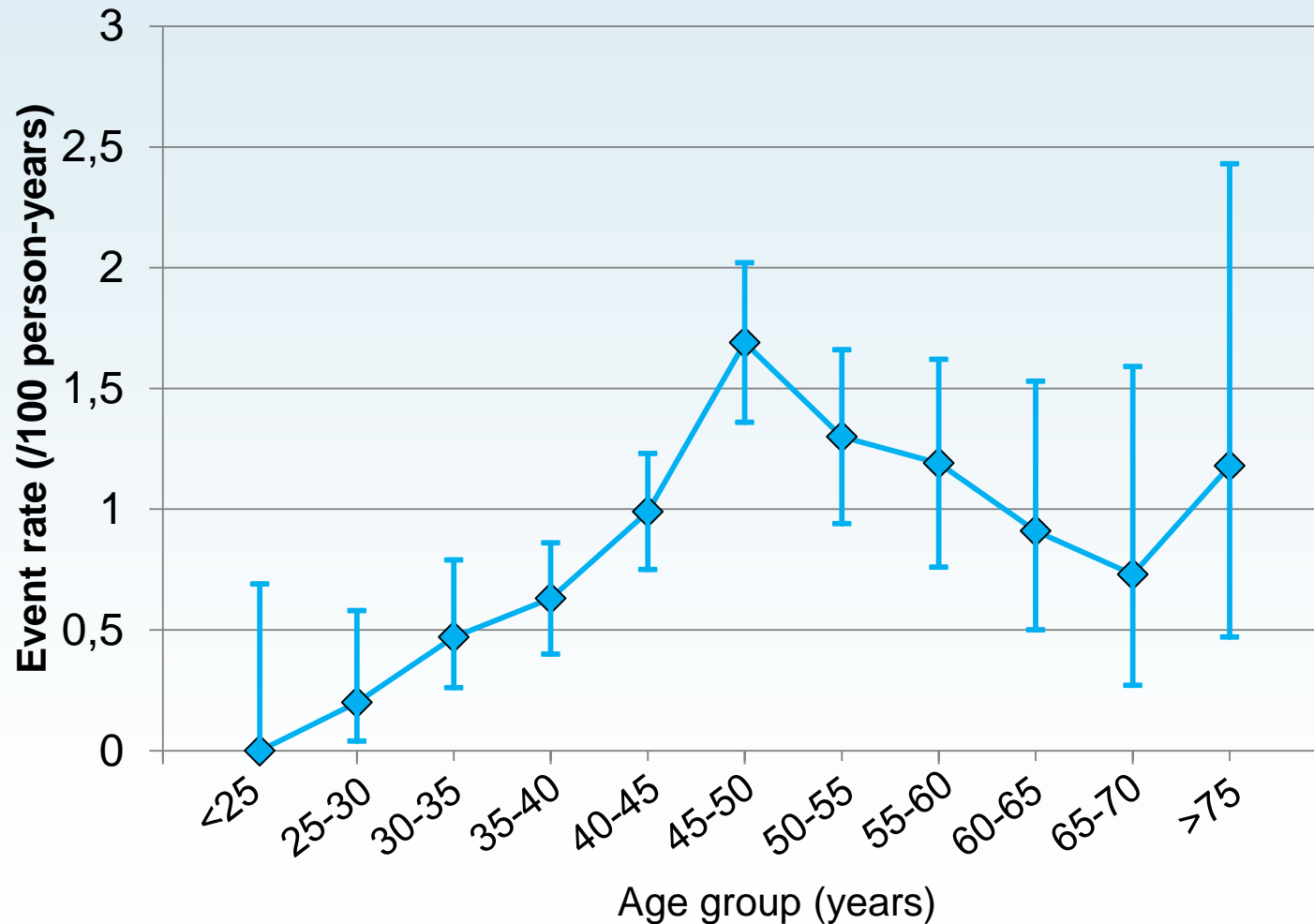
First cancer, stratified by age at onset



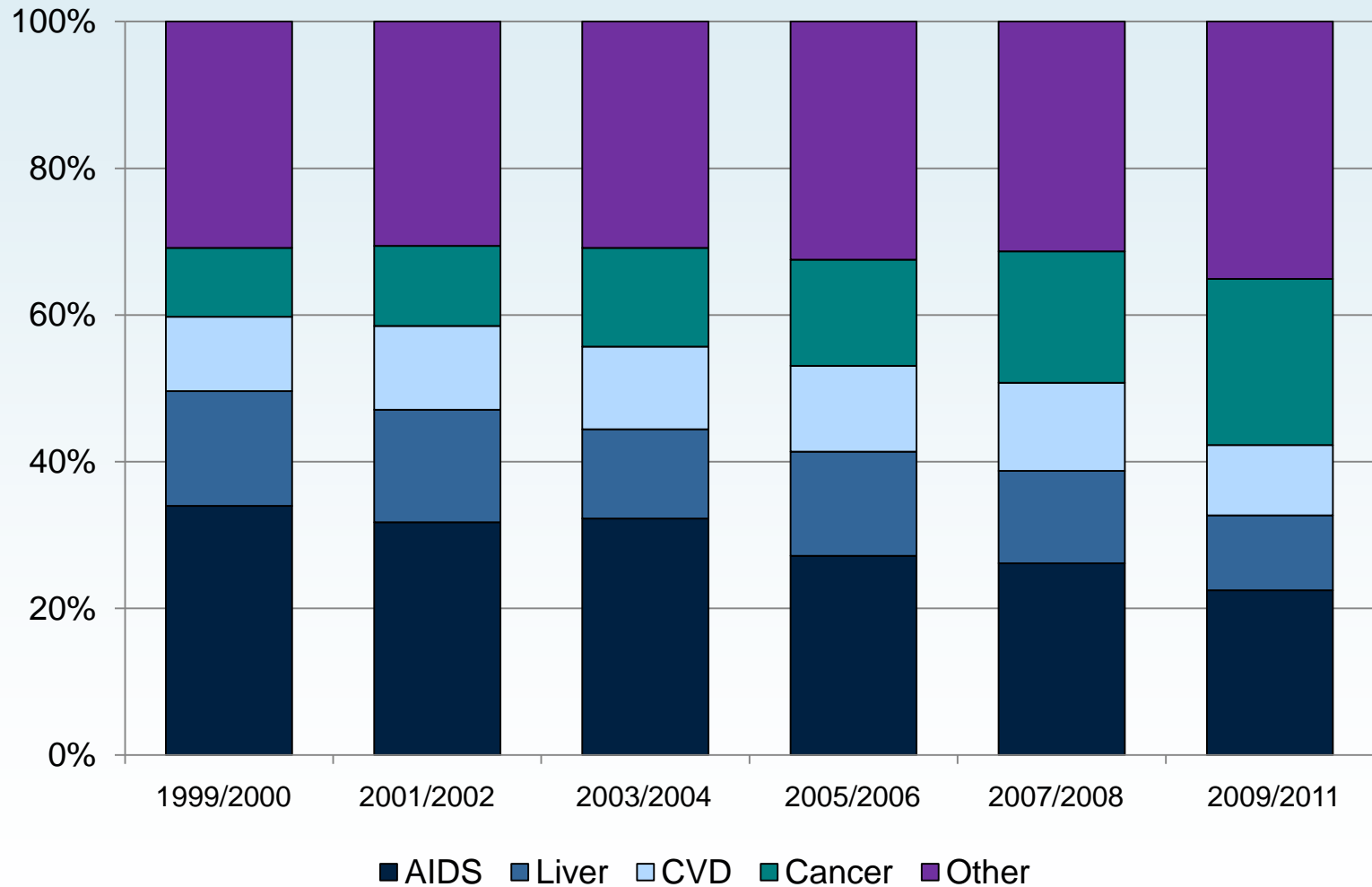
First cancer, stratified by age at onset



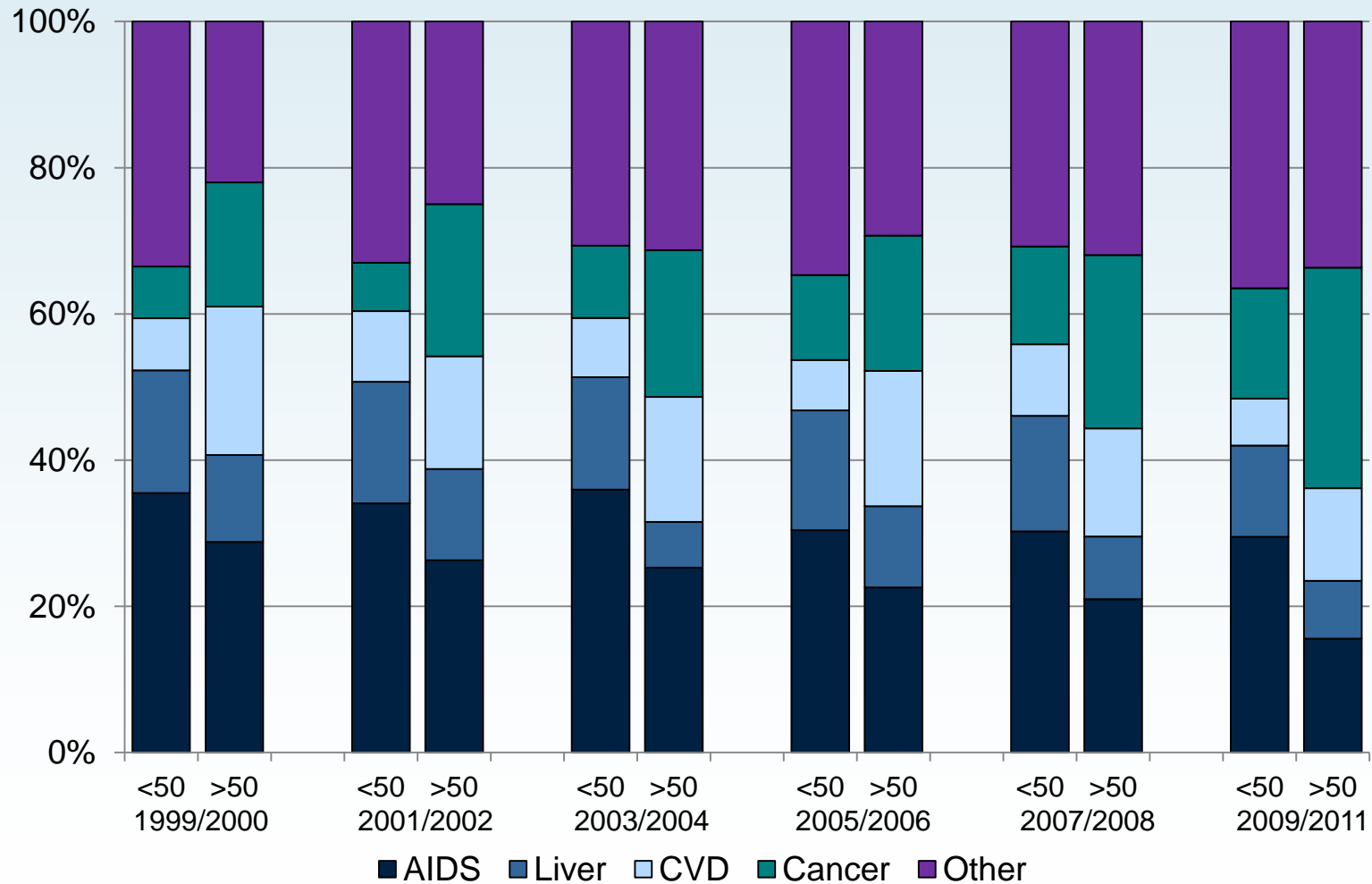
Liver outcomes*, stratified by age group



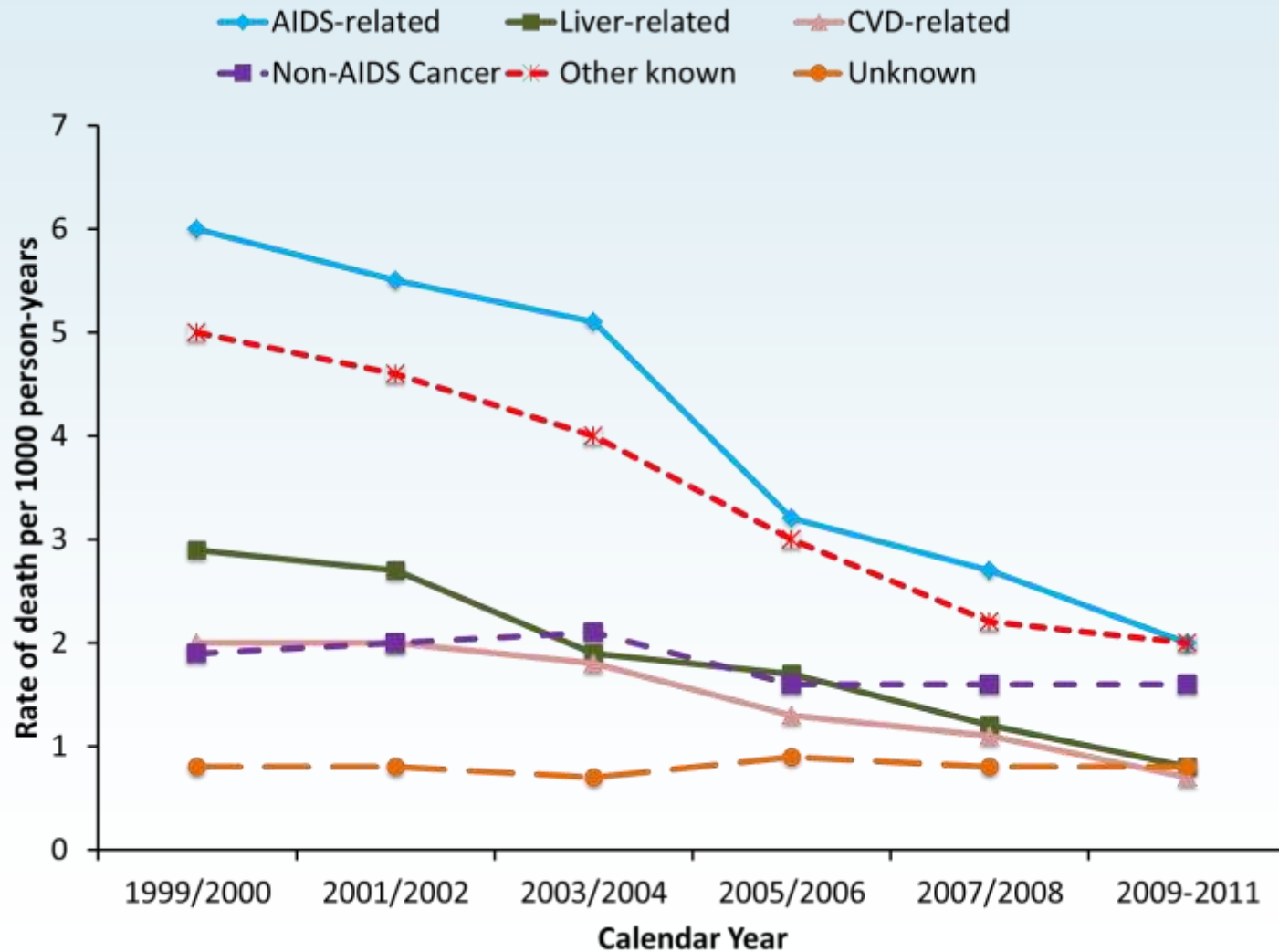
Causes of death



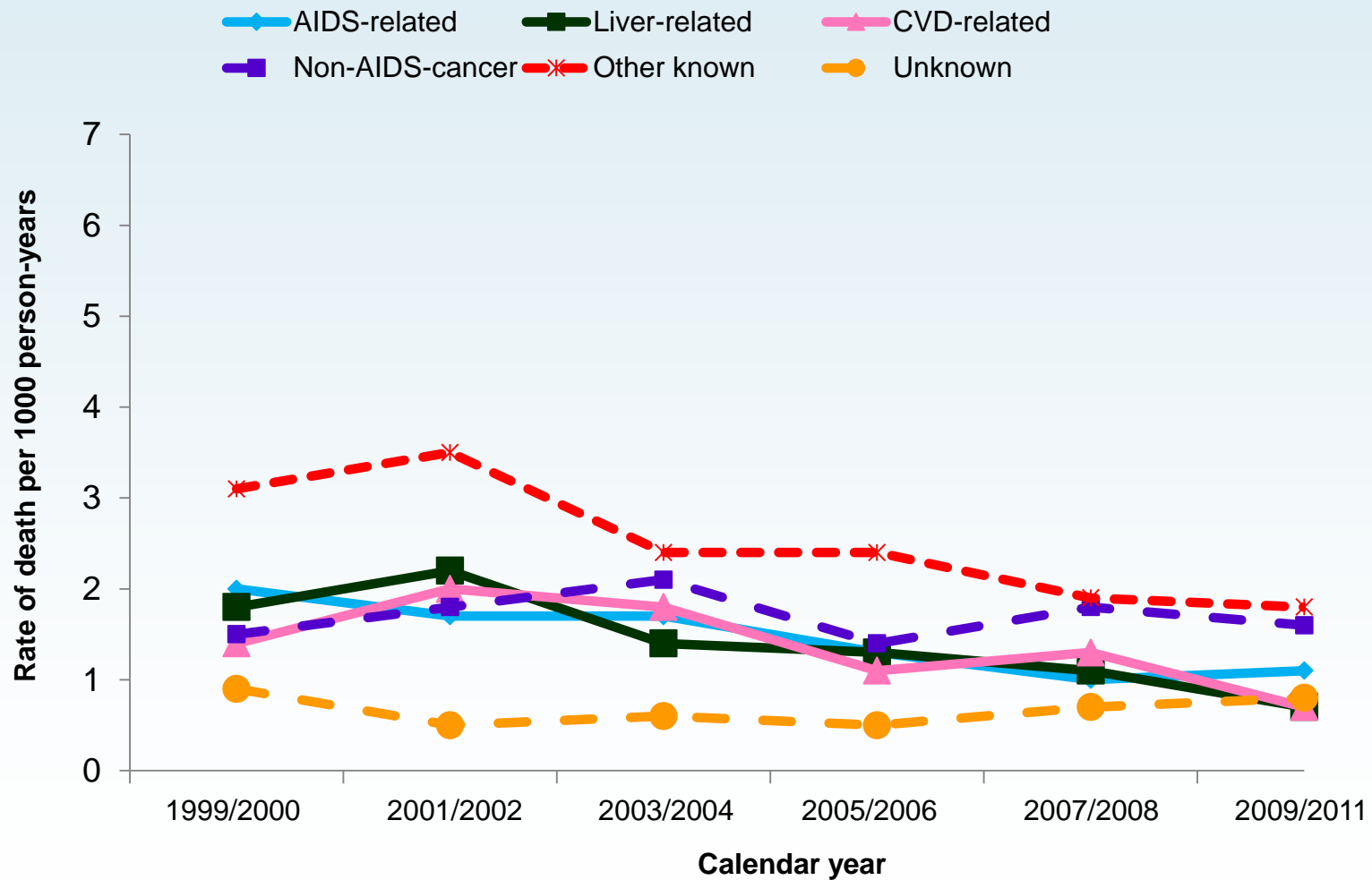
Causes of death



Age-standardised mortality rates



Age-standardised mortality rates (<400 cp/ml)



Short-term mortality after MI – D:A:D

	Year of MI				
	99-02	03-04	05-06	07-08	09-11
Number of MIs	212	194	157	171	110
Male gender (%)	91.0	92.8	90.5	89.5	92.7
Median age (years)	48	49	49	51	51
Median CD4 (cells/mm ³)	398	444	454	436	546
Current smoker (%)	49.5	46.9	55.4	57.3	58.2
Family history (%)	14.2	13.9	14.7	15.2	13.6
High Framingham risk (%)	28.8	23.2	22.3	26.9	32.7
Short-term mortality (%)	26.4	24.7	19.8	16.4	8.2

Improvements in mortality

- Later calendar year associated with decreased short-term mortality:
 - Hazard ratio 0.95 (95% CI 0.89-0.98) /later year
- There was, however, an increasing trend over time in the use of medical and surgical interventions post-MI
- After adjustment for these interventions, calendar year association was attenuated to 1:
 - Hazard ratio 0.98 (95% CI 0.92-1.04)

Summary

- The D:A:D population is aging
 - increasing proportion have CVD-related risk factors, including hypertension, dyslipidaemia and diabetes
 - Exposure to ART and other drugs is increasing
- Rates of diabetes, hypertension and MI increase with age, as do cancer rates
- However, no strong evidence to support a more rapidly increasing risk with older age than in the general population
- There are, however, expected differences in the types of cancer that occur and causes of death in younger and older people with HIV

Discussion

- Limited information with which to assess whether any previously reported associations (CVD, cancers, liver-endpoints) with cART are similar in younger/older people
 - Reported association between ABC and MI is similar in those with low, moderate and high CVD risk
- Comparisons with the general population are extremely difficult due to a lack of well-matched HIV-negative controls
 - Studies such as AgeHIV, POPPY and COBRA will provide helpful information
 - Do we really have any evidence of ‘premature’ ageing?
- Unclear whether older HIV-positive people are offered and/or initiate appropriate interventions for the prevention of CVD

D:A:D acknowledgements

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