D:A:D

Increased risk of cardiovascular disease (CVD) with age in men: a comparison of D:A:D with HIV negative CVD risk equations

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Background

- Risk of CVD in HIV positive (HIV+) persons compared to HIV negative (HIV-) populations is difficult to determine
  - Matched controls needed
    - Some studies estimate a 1.5 to 2 fold increased risk
    - Triant et al 2007 – demonstrated an increased risk of CVD in HIV+ compared to HIV- populations that also increased with age *Triant VA et al, 2007 J Clin Endocrinol Metab, pg 2506-12*
- Hypothesis:
  - if the risk of CVD increases faster with age in HIV+ persons, then we would expect the risk of CVD events per year older to be higher in D:A:D relative to the general population

Objectives

- To statistically model the relative increased risk of CVD per year older in D:A:D
- To compare to the relative risk of CVD per year older from conventional CVD risk equations from the general population

Methods (1)

- *Inclusion*: men without prior CVD and with conventional CVD risk factors available
  - age, family history of CVD, smoking, diabetes, cholesterol, HDL and systolic blood pressure
- *Endpoints*:
  - myocardial infarction (MI)
  - coronary heart disease (CHD): MI or invasive coronary procedure or CVD death
  - CVD: CHD or stroke.

Methods (2)

- Poisson regression analyses
  - Fitted a number of age effects adjusted for CVD risk factors in D:A:D risk equation
    - family history of CVD, smoking, cumulative (per year) lopinavir and indinavir use, recent (within 6 months) abacavir use, diabetes, cholesterol, HDL and systolic blood pressure
  - Sensitivity analyses
    - adjusting for calendar year, participating cohort
    - restricting the analysis to age less than 65 years
    - including all men regardless whether CVD risk factors were available

Methods (3)

CVD risk equations general population

- Framingham Heart Study
  - Anderson 1991 (FHS_A)
  - Wilson 1998 (FHS_W)
  - D'Agostino 2008 (FHS_D)
    - n>5500, age 30-74, baseline 1968-1975
- CUORE (Ferrario 2005)
  - Italian male cohort
    - n>6800, age 35-69, baseline 1986-1995
- ASSIGN (Woodward 2006)
  - Scottish Heart Health Extended cohort
    - n>12,000, baseline 1984-1989, age 30-74

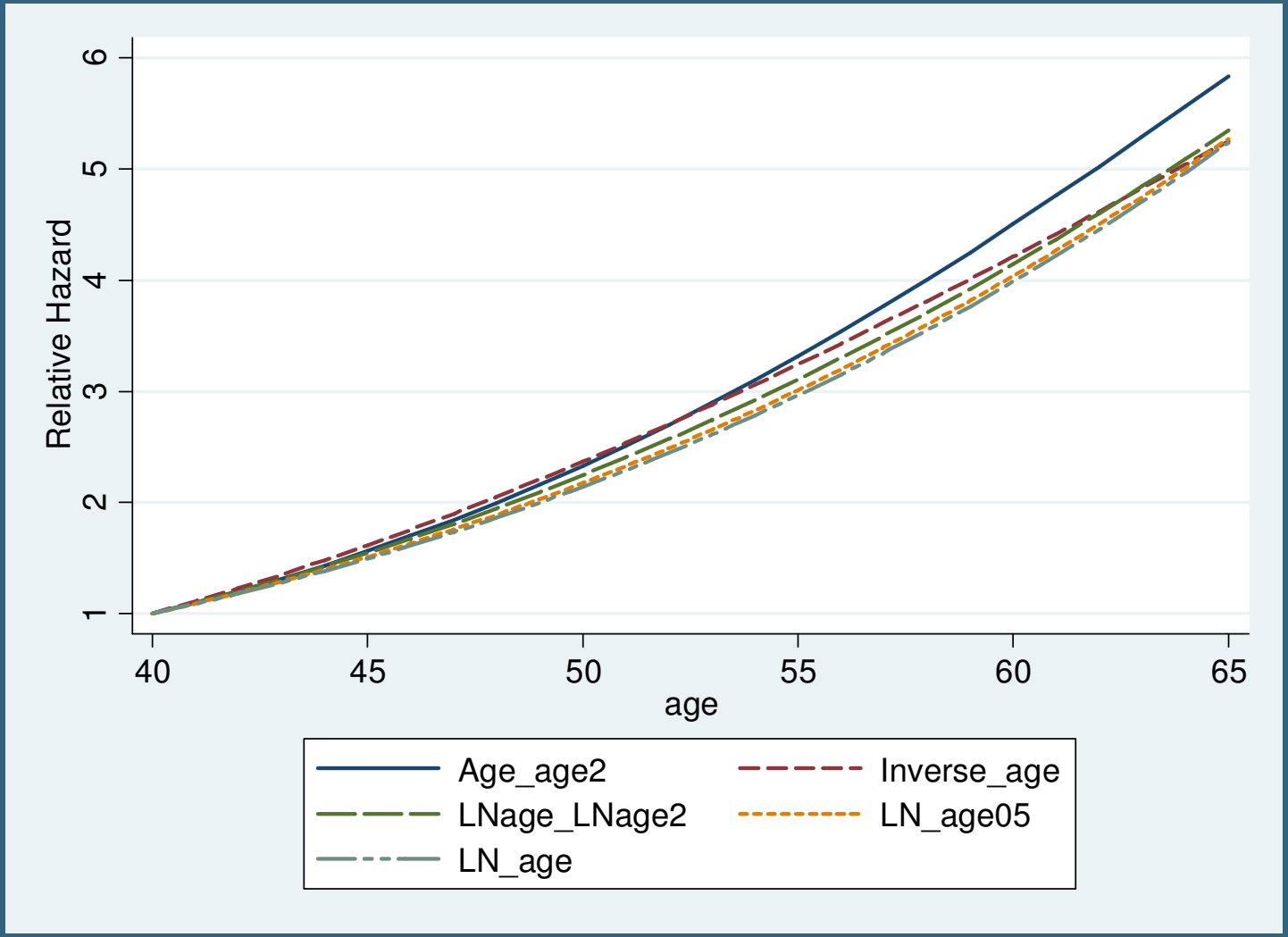
Methods (4)

- Graphically compared relative risk increase from age 40 years to age 65 years using the age effect in D:A:D and the age effects in the general population equations
- Unable to statistically compare D:A:D to the general equations due to different age effects
  - 95% confidence intervals for the D:A:D models
- Risk modification at age 50
  - stop smoking, cholesterol reduced by 1 mmol/mL, systolic blood pressure reduced by 10mmHg

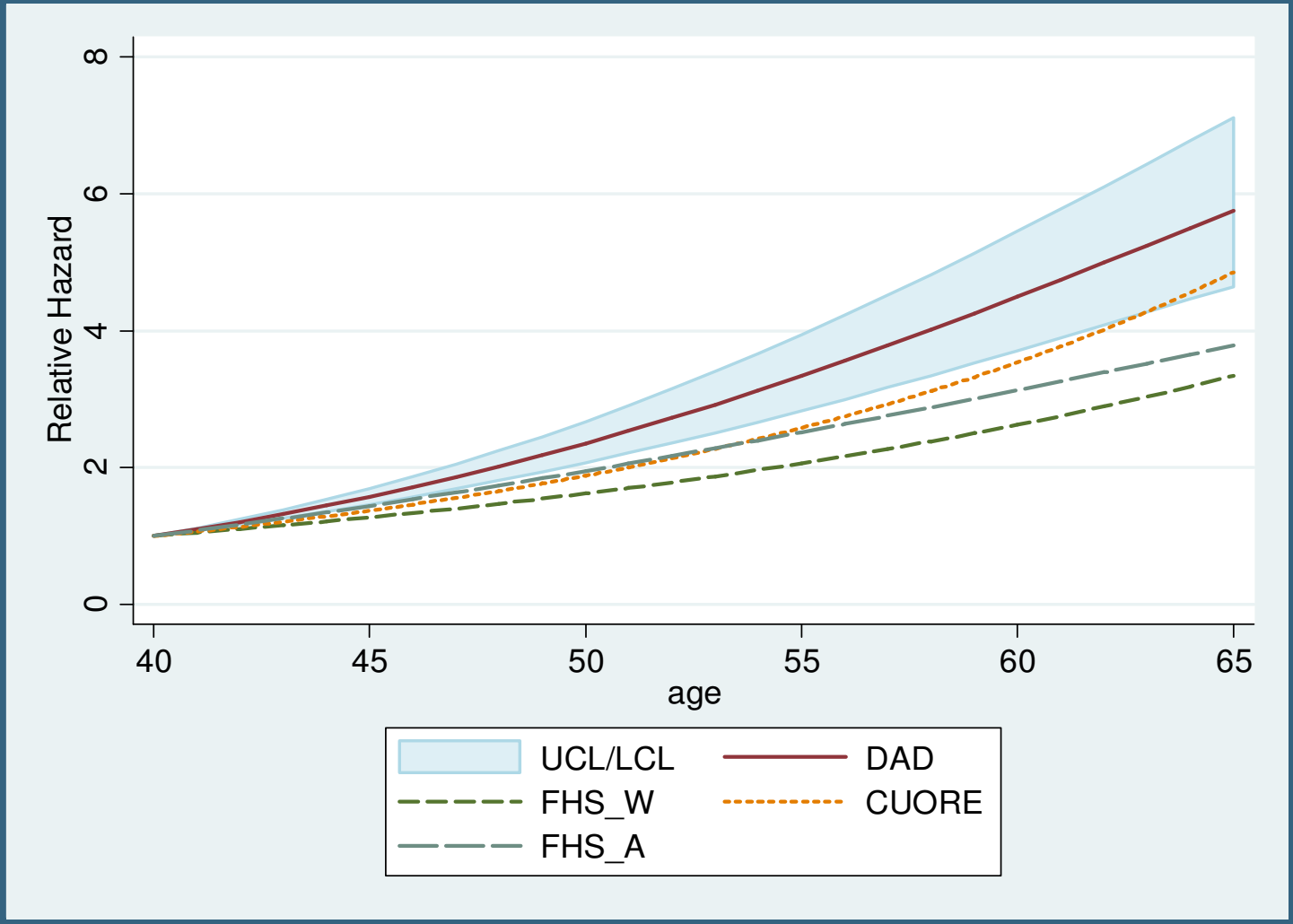
Results (1)

- 24,323 men with complete CVD risk factors were included in analyses
  - 139,115 person years (pyrs)
- 474 MI, 683 CHD and 884 CVD incident events
- Crude event rates (MI, CHD, CVD respectively):
  - 40-45 years: 2.29, 3.11 and 3.65 /1000 pyrs
  - 60-65 years: 6.53, 11.91 and 15.89/1000 pyrs

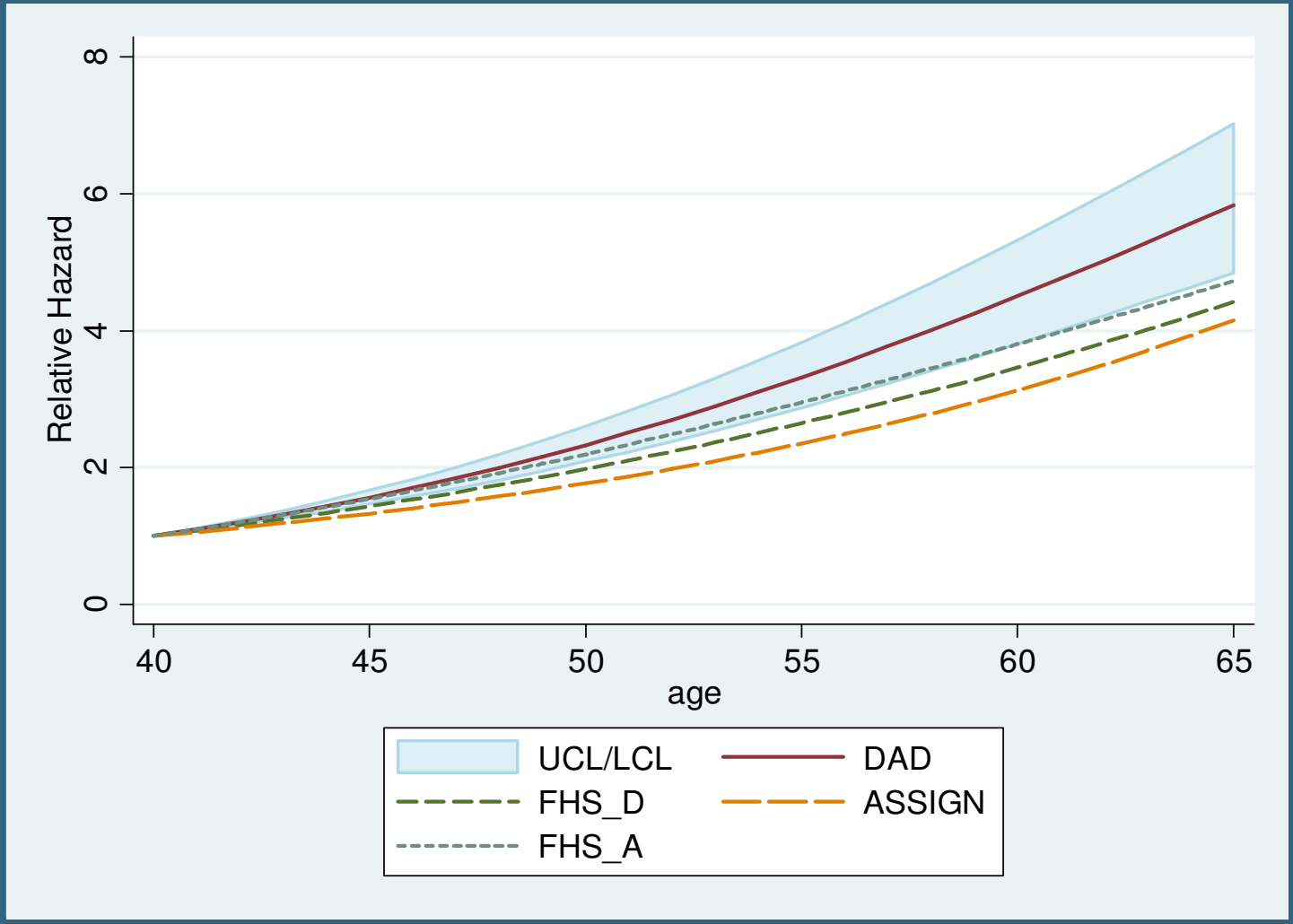
Comparison of different modelled age effects in D:A:D - CVD



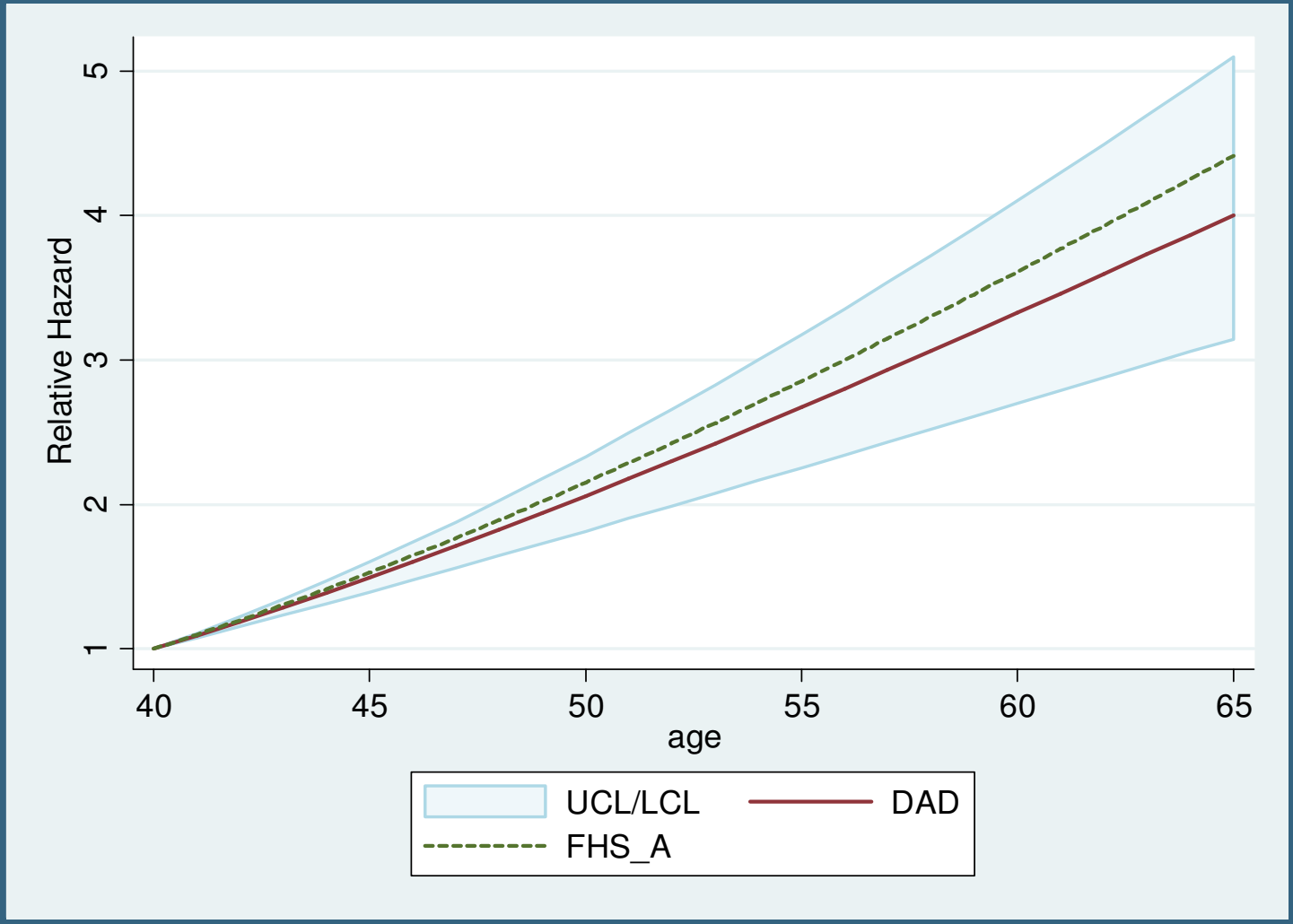
Relative risk of CHD from age 40 years



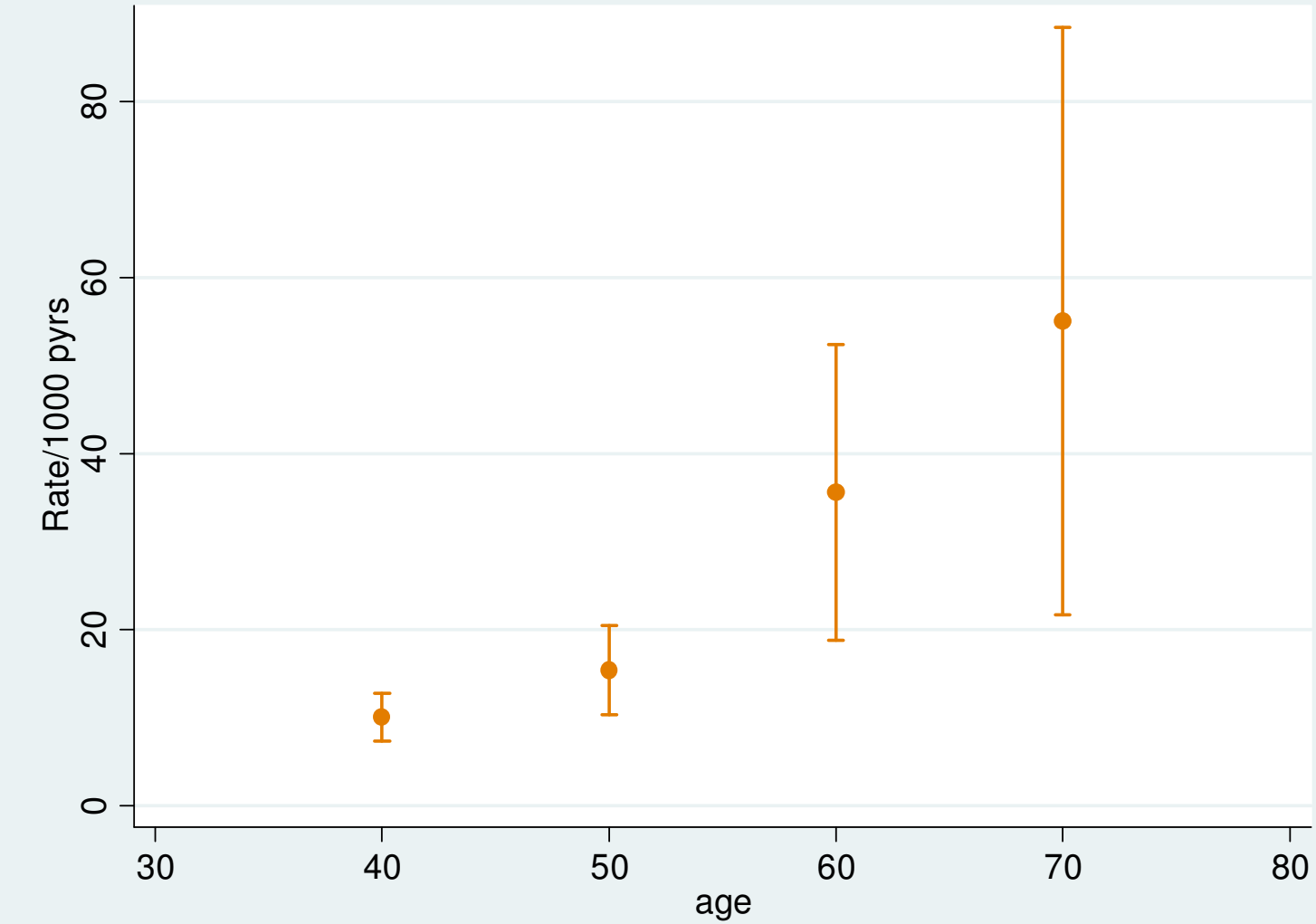
Relative risk of CVD from age 40 years



Relative risk of MI from age 40 years



Comparison with Triant et al, 2007



D:A:D

Triant VA et al, 2007 J Clin Endocrinol Metab, pg 2506-12

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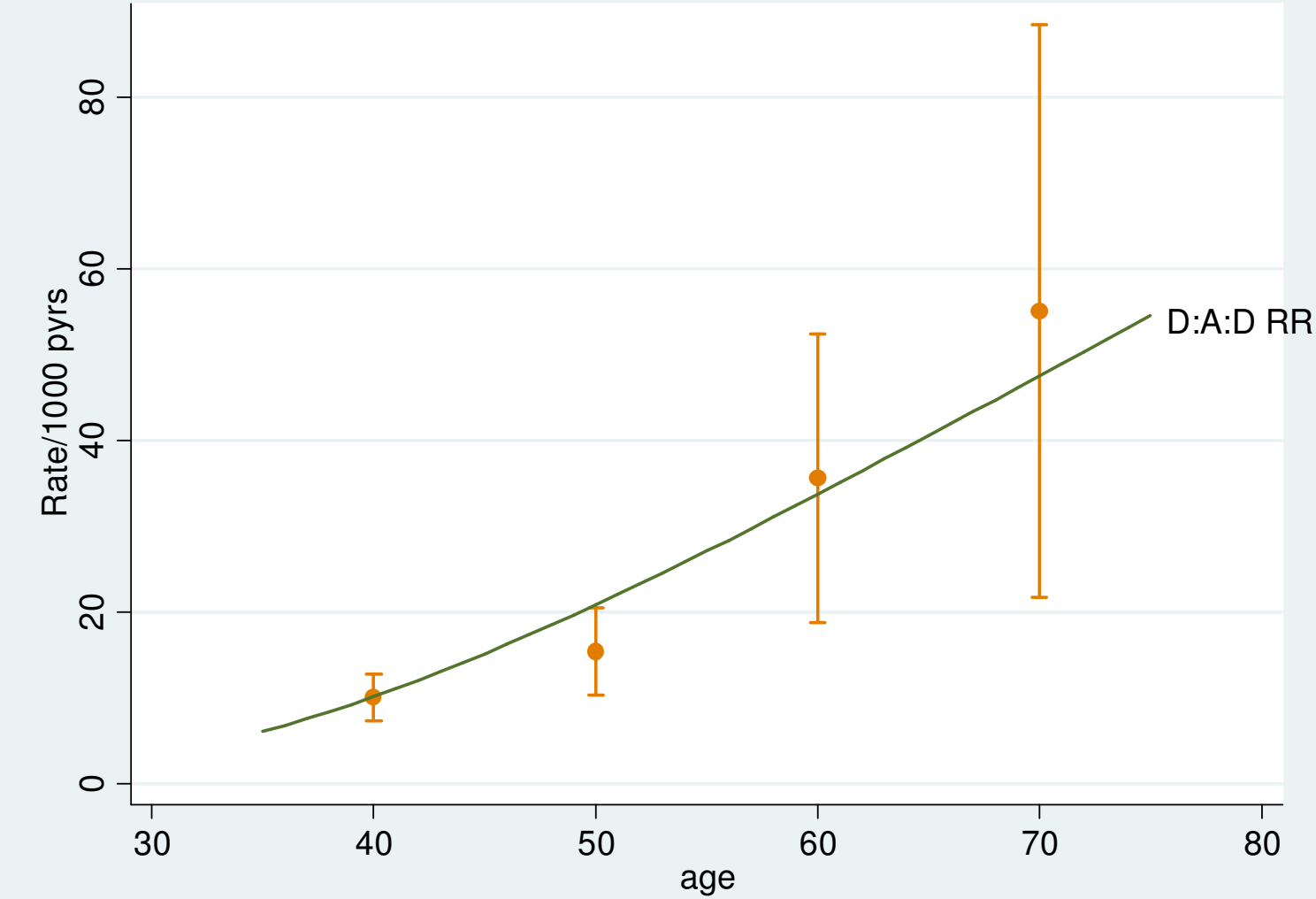

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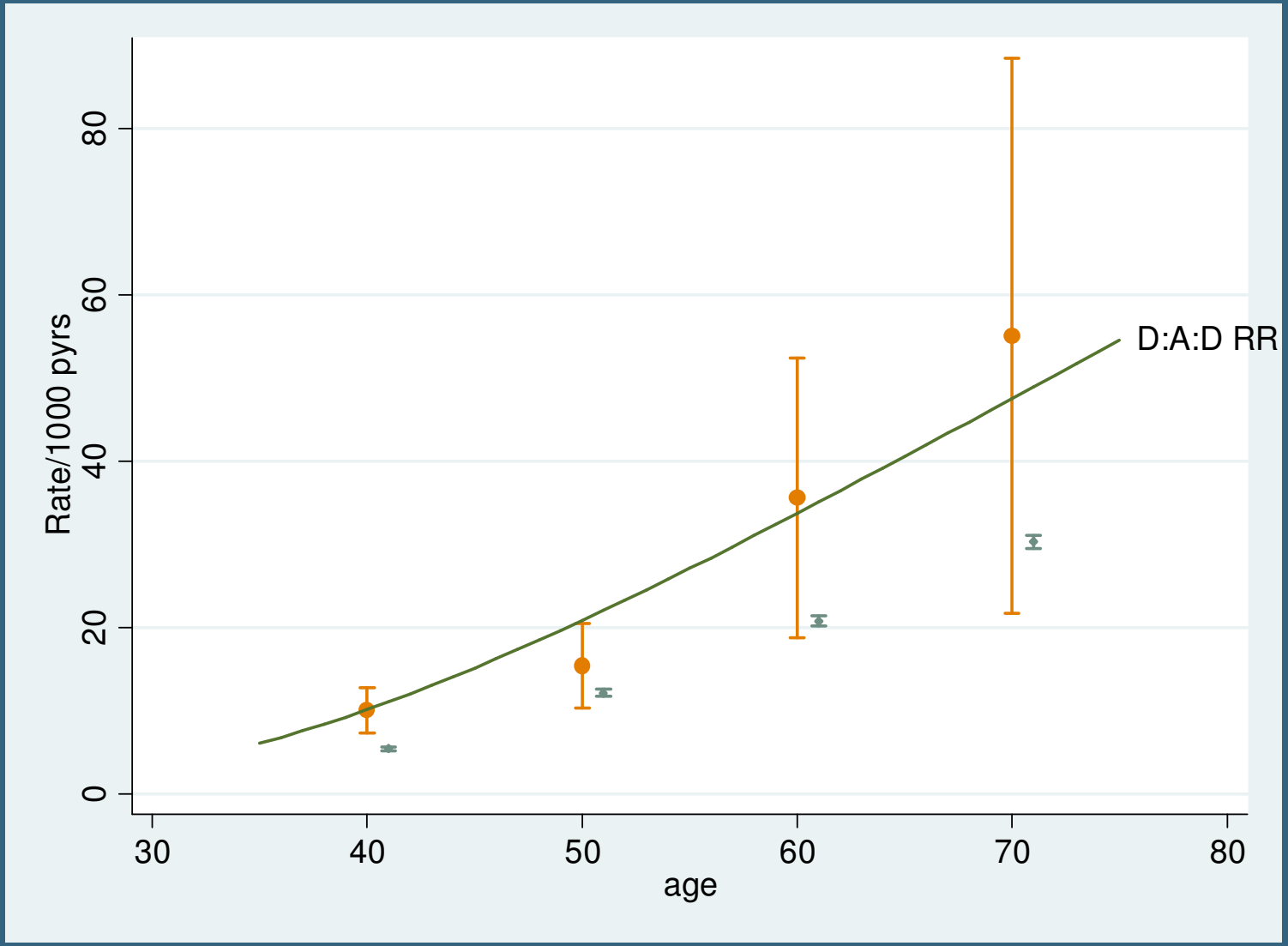

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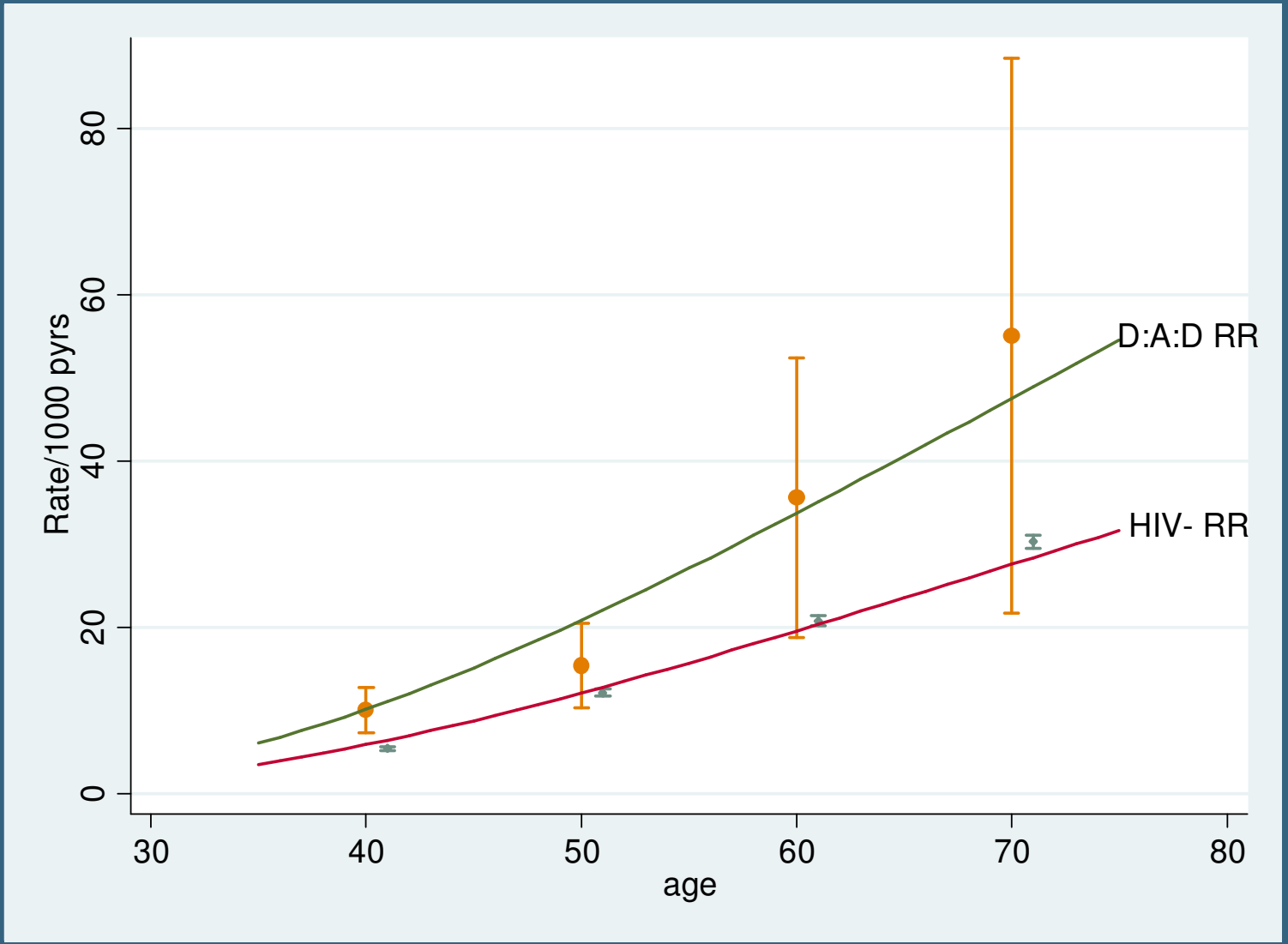
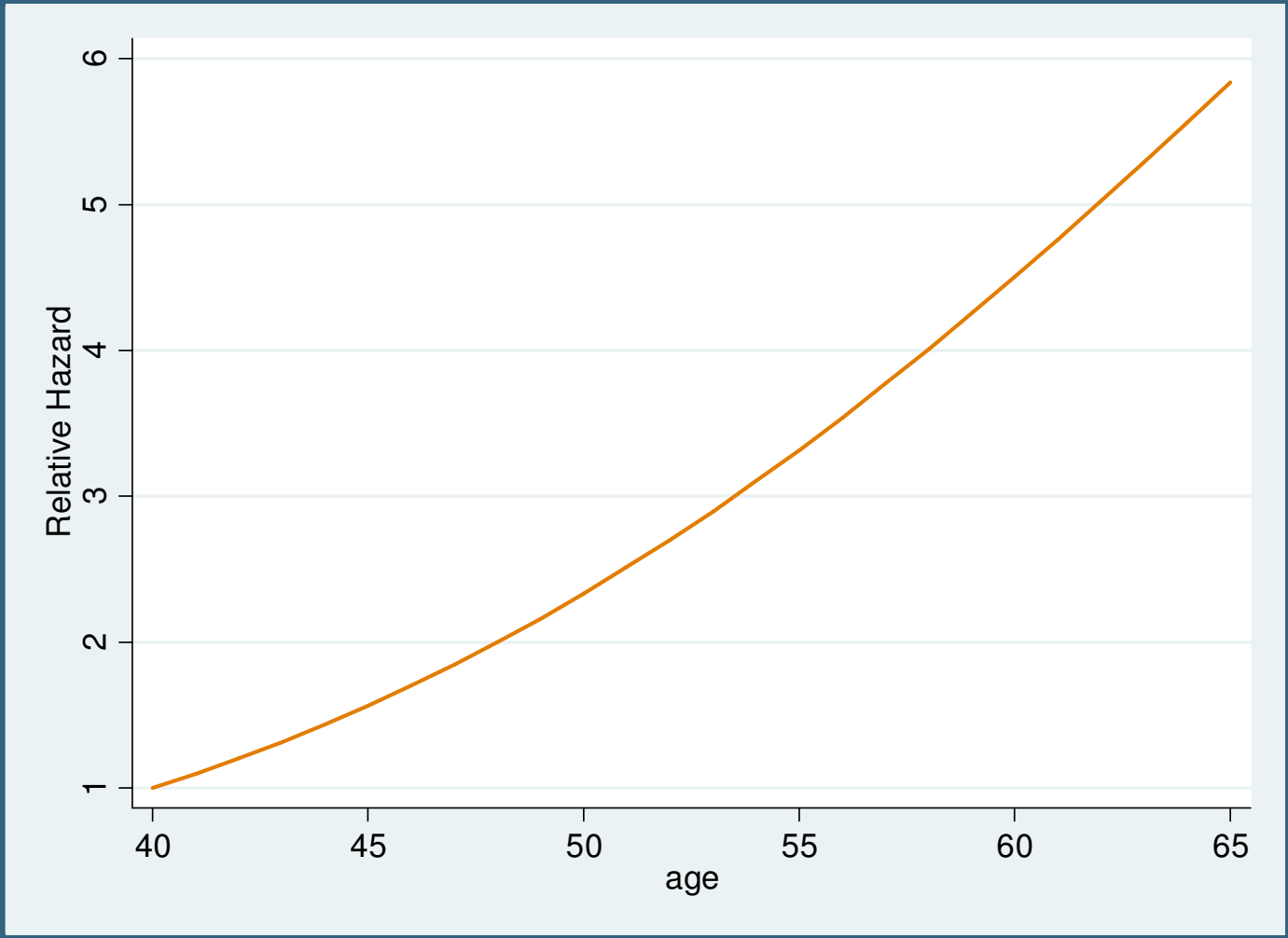


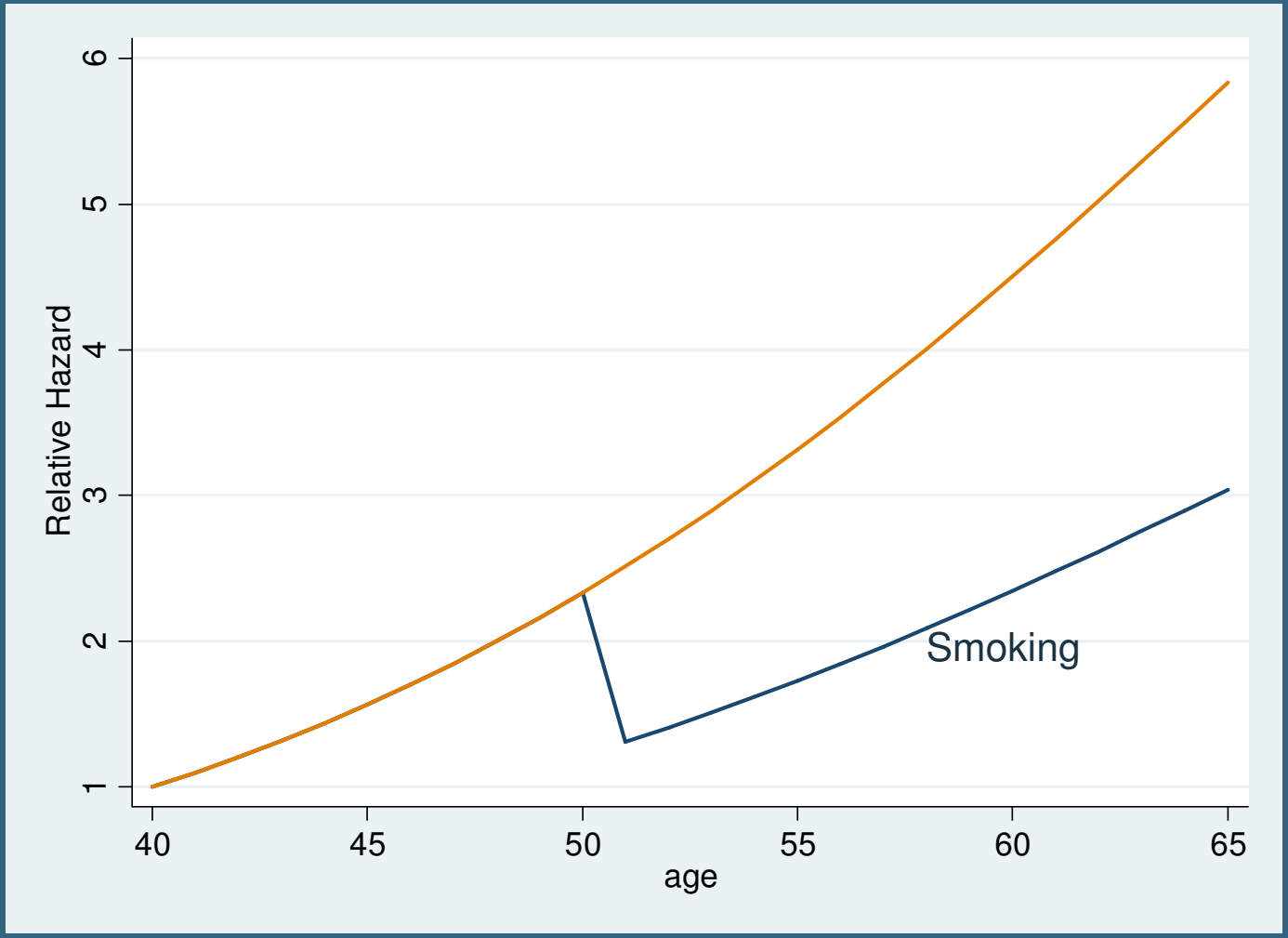
D:A:D

Triant VA et al, 2007 J Clin Endocrinol Metab, pg 2506-12

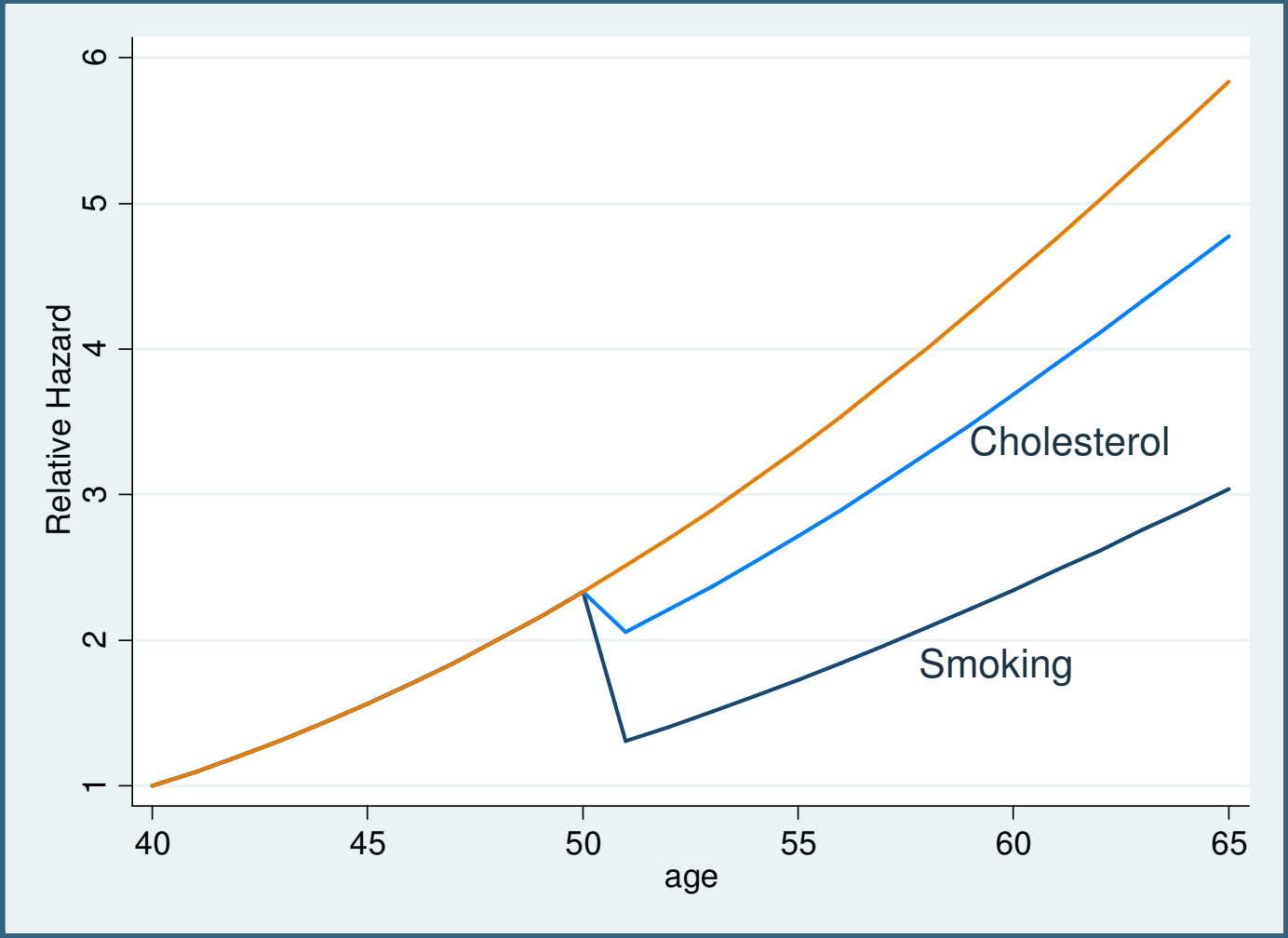
Relative risk of CVD with age – D:A:D



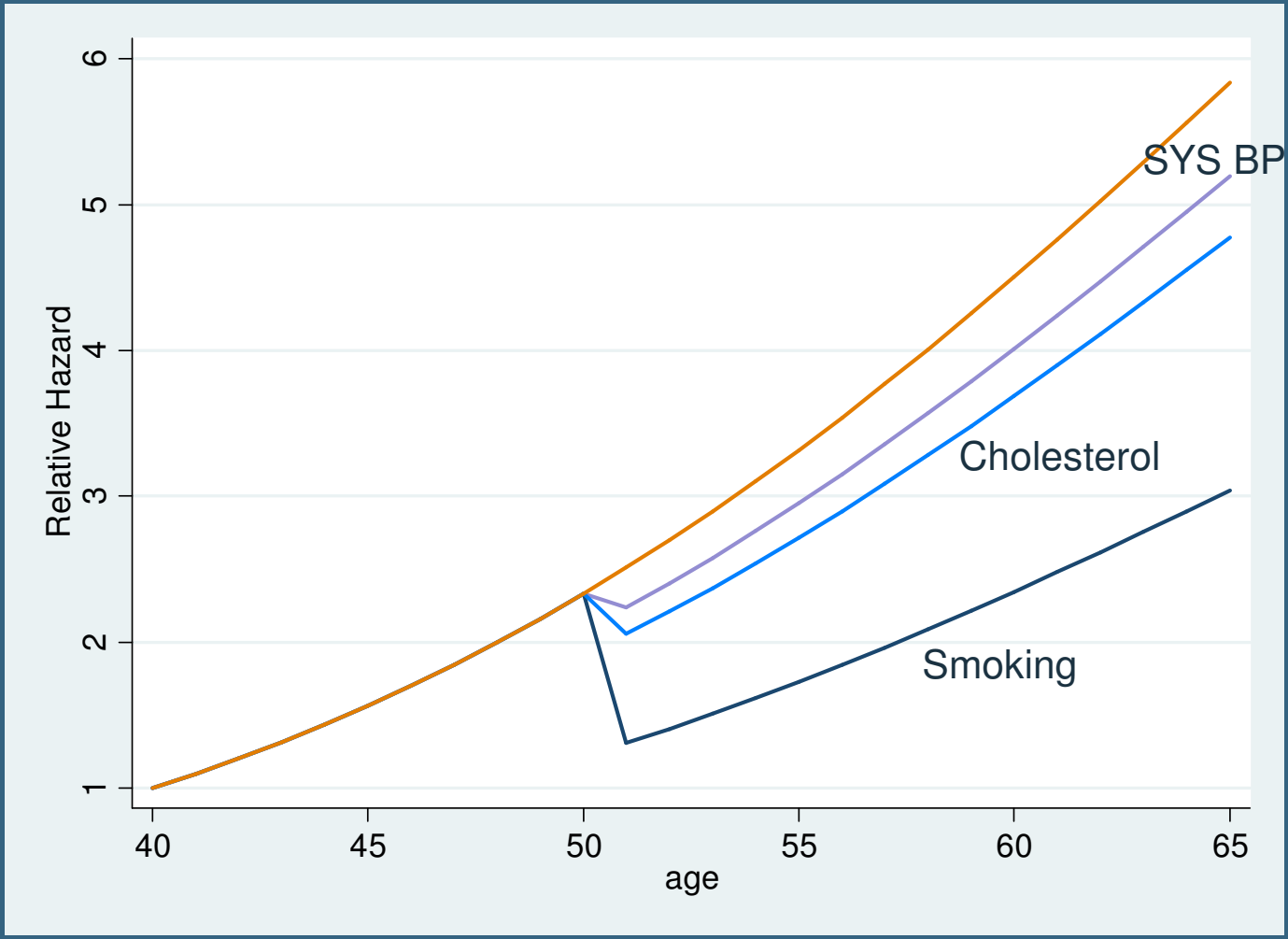
Modifying risk: stop smoking



Modifying risk: stop smoking, cholesterol (↓1 mmol/L)



Modifying risk: stop smoking, cholesterol (↓ 1 mmol/L), SYS BP (↓ 10 mmHG)



Limitations

- Unable to perform statistical comparisons of the age effects with the general population
  - D:A:D 95% CI range
  - Assessed a number of endpoints and against several general population equations – evidence of consistency
- Models extrapolate over a 25+ year age range based on a median of 6 years of follow-up
- Comparison with HIV negative population risk equations

Conclusion

- We found an increased relative risk for CVD with age in D:A:D, but only slightly faster in D:A:D compared with the general population risk equations
  - Our analysis suggests that the additional risk of HIV infection is not unlike other risk factors such as smoking
- Risk may be reduced
  - HIV+ people in routine clinical care – early intervention to reduce CVD risks

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