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

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

- 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

![Graph showing the comparison of different modelled age effects](image-url)
Relative risk of CHD from age 40 years
Relative risk of CVD from age 40 years
Relative risk of MI from age 40 years

![Graph showing the relative risk of MI from age 40 years with age on the x-axis and relative hazard on the y-axis. The graph includes lines for DAD and FHS_A, with shaded areas indicating the upper and lower confidence limits (UCL/LCL).]
Comparison with Triant et al, 2007

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

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

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

![Graph showing the relative hazard of smoking across different ages. The graph indicates a significant increase in relative hazard with age.]

- Relative Hazard
- Age
- 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
Acknowledgements

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