D:A:D

Rates of Cardiovascular Disease Following Smoking Cessation in Patients with HIV Infection: Results from the D:A:D Study

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On behalf of the D:A:D study group

Background (1)

- Rates of tobacco smoking in HIV-positive patients are very high across virtually all populations in developed countries
- In the era of cART increased risk of smoking associated disease (eg cardiovascular disease, pulmonary disease and non-AIDS malignancies) and death
- Smoking tobacco is independently associated with mortality and morbidity in HIV-positive patients
- Despite this evidence rates of smoking remain high in HIV-positive patients

Background (2)

- In HIV-negative smokers there is a substantial reduction in coronary heart disease within one to two years of stopping smoking
- Clinical benefits from stopping smoking have not previously been reported in an HIV-positive population
- If similar evidence could be found among HIV-positive smokers, this might provide further incentive for quitting

Objective

- To estimate the rates of cardiovascular disease events and mortality after stopping smoking among patients in the D:A:D study

Methods (1)

- The D:A:D study is a prospective, multi-national observational study formed by the collaboration of 11 cohorts of HIV-infected patients.
- 33,308 HIV-positive patients are followed in 212 clinics in Europe, the US and Australia
- Primary objective: to establish whether the use of cART is associated with an increased risk of CVD
- Secondary objectives: diabetes-mellitus, stroke and invasive cardiovascular procedures; non-AIDS cancers, renal failure and liver failure

Methods (2)

- All D:A:D patients who report smoking status at baseline, and no prior CVD, were included
- *Current* (yes/no) and *ever* (yes/no) smoking status is collected at each visit
- Duration of stopping smoking determined only for current smokers at baseline:
  - Calculated from the mid-point between the last visit where patients reported being a current smoker to the first visit s/he reported being a non-smoker
  - Patients who reported that they re-started smoking were assumed to do so at the mid-point of the respective visits

Methods (3)

Endpoints

- Myocardial infarction (MI): fatal and non-fatal cases
- Coronary heart disease (CHD): MI plus invasive coronary artery procedure (including coronary artery by-pass or angioplasty), or death from other CHD
- Cardiovascular disease (CVD): CHD plus carotid artery endarterectomy, or stroke
- All-cause mortality

Statistical Methods

- Event rates were calculated for never smokers, ex-smokers at D:A:D study entry, current smokers, and smokers who stopped during D:A:D follow-up
- Incidence rate ratios (IRR) were determined using Poisson regression adjusted for:
  - age, sex, cohort, calendar year, family history of CVD, diabetes, and time-updated lipids and blood pressure assessments, antiretroviral treatment
  - Mortality endpoint also adjusted for: HCV, HBV, mode of HIV exposure, ethnicity and incidence of CVD during follow-up

Results (1)

	Smoking status at baseline			Reported stopping smoking during D:A:D follow-up[1] (n=8197)
	Never smoked (n=8920)	Ex-smoker (n=6265)	Current smoker (n=11951)	
Age (years)	38 (33, 46)	39 (34, 46)	38 (33, 43)	41 (37, 47)
Female	35.2%	21.1%	23.3%	21.5%
Transmission group				
Heterosexual	45.1%	28.2%	26.0%	27.5%
Homosexual	41.8%	47.9%	37.9%	47.2%
Injecting drug use	5.0%	17.6%	32.2%	20.3%
White	47.9%	46.1%	70.3%	54.0%
HCV Positive	8.4%	19.2%	33.8%	23.9%
HBV Positive	14.3%	14.5%	17.1%	17.2%
CD4 count	406 (255, 591)	410 (250, 603)	440 (278, 642)	480 (320, 680)
Viral load >50 copies/ml	62.9%	65.6%	63.7%	47.7%
cART exposure (years)	1.5 (0, 3.0)	1.5 (0, 3.1)	1.8 (0, 3.1)	4.1 (1.8, 6.1)
PI exposure (years)	1.0 (0, 2.7)	0.7 (0, 2.7)	1.3 (0, 2.8)	2.5 (0, 4.7)

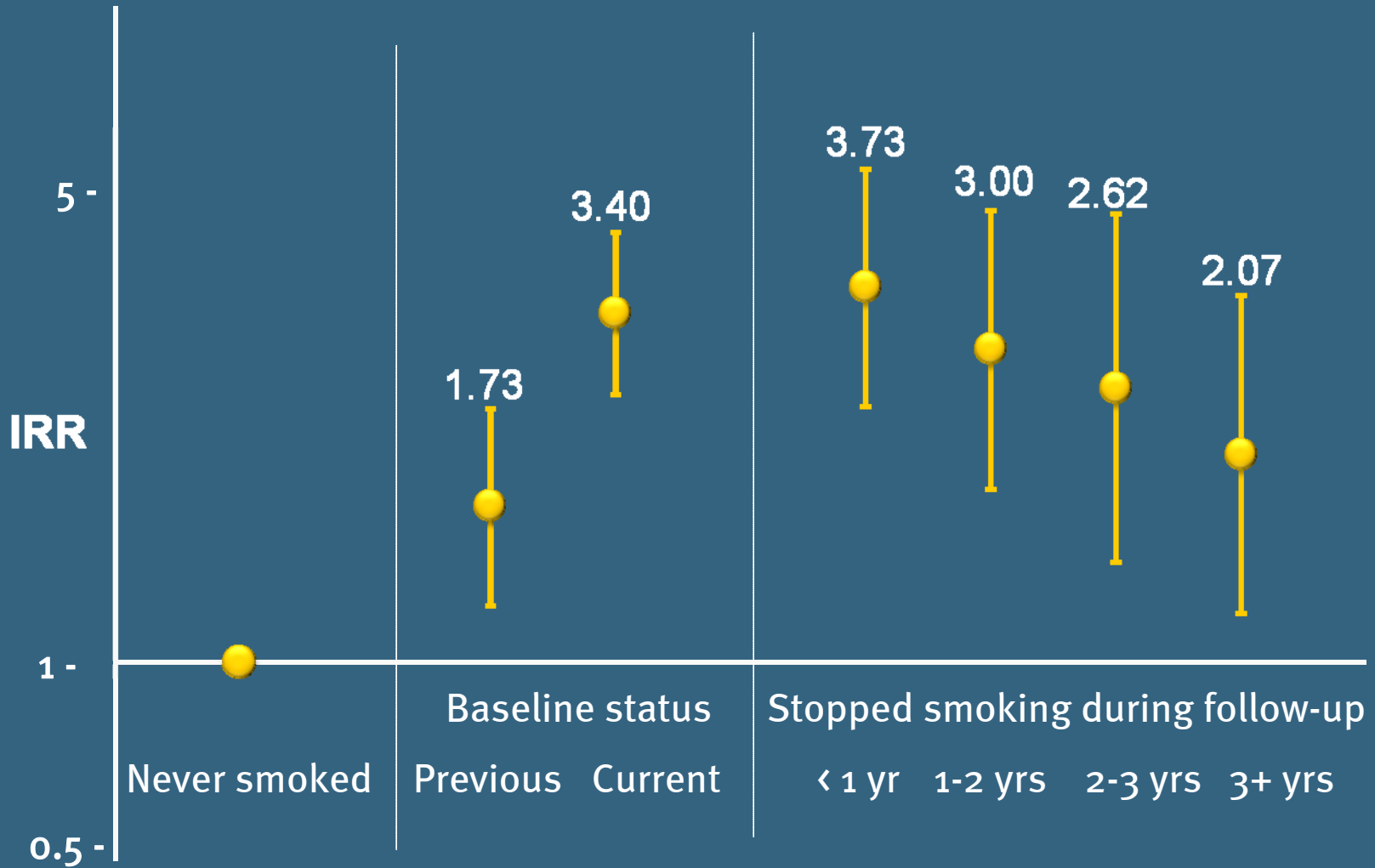
1. Characteristics at first attempt to stop smoking. Figures are medians (inter quartile ranges) unless otherwise specified

Results (2)

	Smoking status at baseline			Reported stopping smoking during D:A:D follow-up[1] (n=8197)
	Never smoked (n=8920)	Ex-smoker (n=6265)	Current smoker (n=11951)	
Systolic BP (mmHg)	120 (115, 130)	120 (110, 130)	120 (110, 130)	120 (110, 130)
Diastolic BP (mmHg)	80 (70, 84)	80 (70, 82)	80 (70, 80)	80 (70, 80)
Total cholesterol (mmol/L)	5.0 (4.2, 6.0)	5.0 (4.2, 6.0)	4.9 (4.0, 5.8)	5.0 (4.2, 5.8)
HDL (mmol/L)	1.2 (0.9, 1.4)	1.1 (0.9, 1.4)	1.1 (0.9, 1.4)	1.2 (0.9, 1.4)
Cholesterol:HDL ratio	4.4 (3.4, 5.7)	4.6 (3.4, 6.0)	4.4 (3.4, 5.7)	4.3 (3.3, 5.6)
Triglycerides (mmol/L)	1.5 (1.0, 2.6)	1.6 (1.1, 2.7)	1.6, (1.1, 2.6)	1.7 (1.1, 2.7)
BMI (kg/m^2)	23.5 (21.5, 25.8)	23.0 (21.1, 25.2)	22.5 (20.7, 24.6)	22.8 (20.9, 25.0)
Family history of CVD	6.4%	7.9%	9.7%	9.9%
Diabetes	3.2%	3.1%	1.9%	4.8%

1. Characteristics at first attempt to stop smoking. Figures are medians (inter quartile ranges) unless otherwise specified

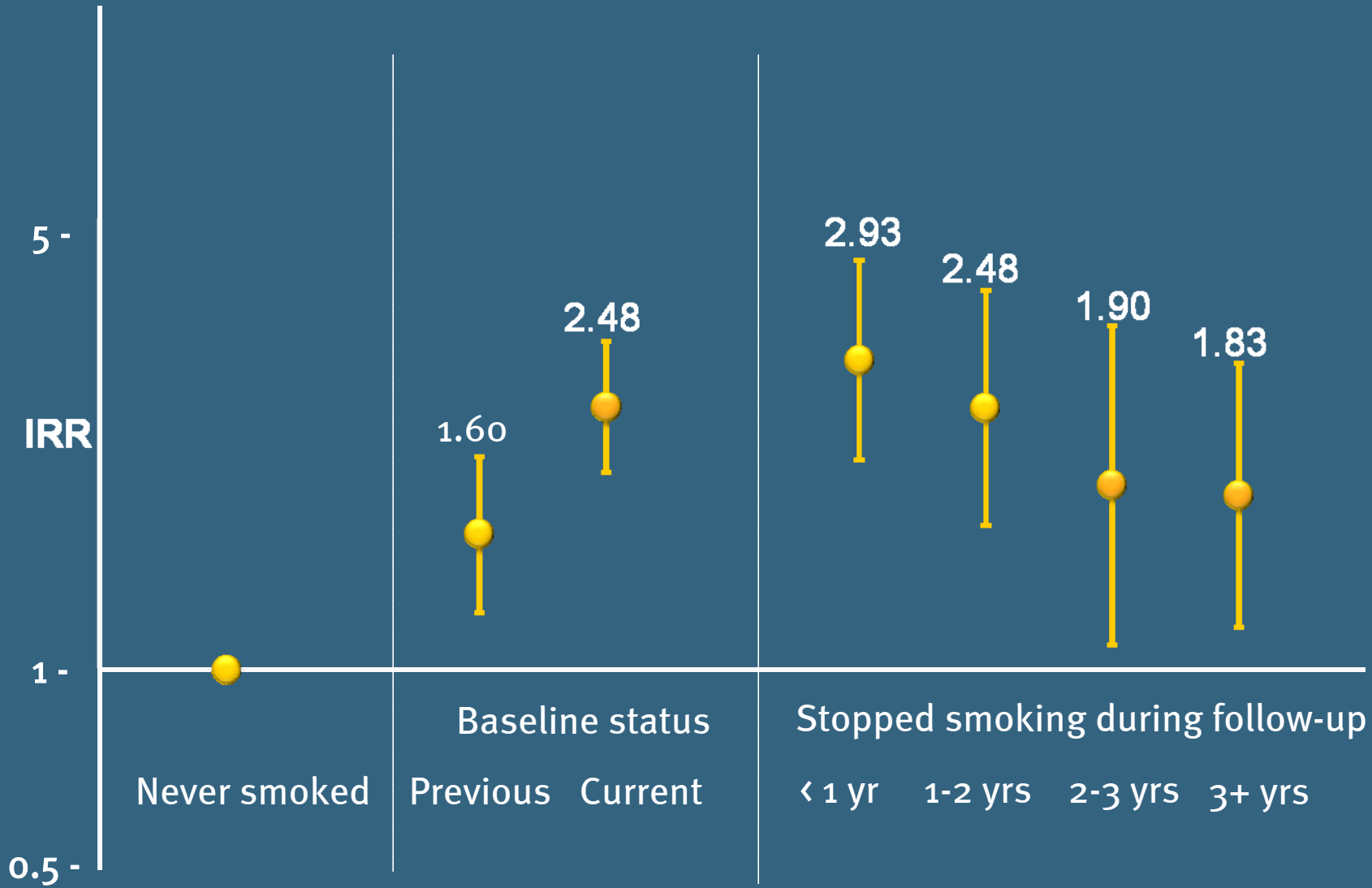
Myocardial Infarction



Adjusted for: age, sex, cohort, calendar year, antiretroviral treatment, family history of CVD, diabetes, and time-updated lipids and blood pressure assessments

D:A:D

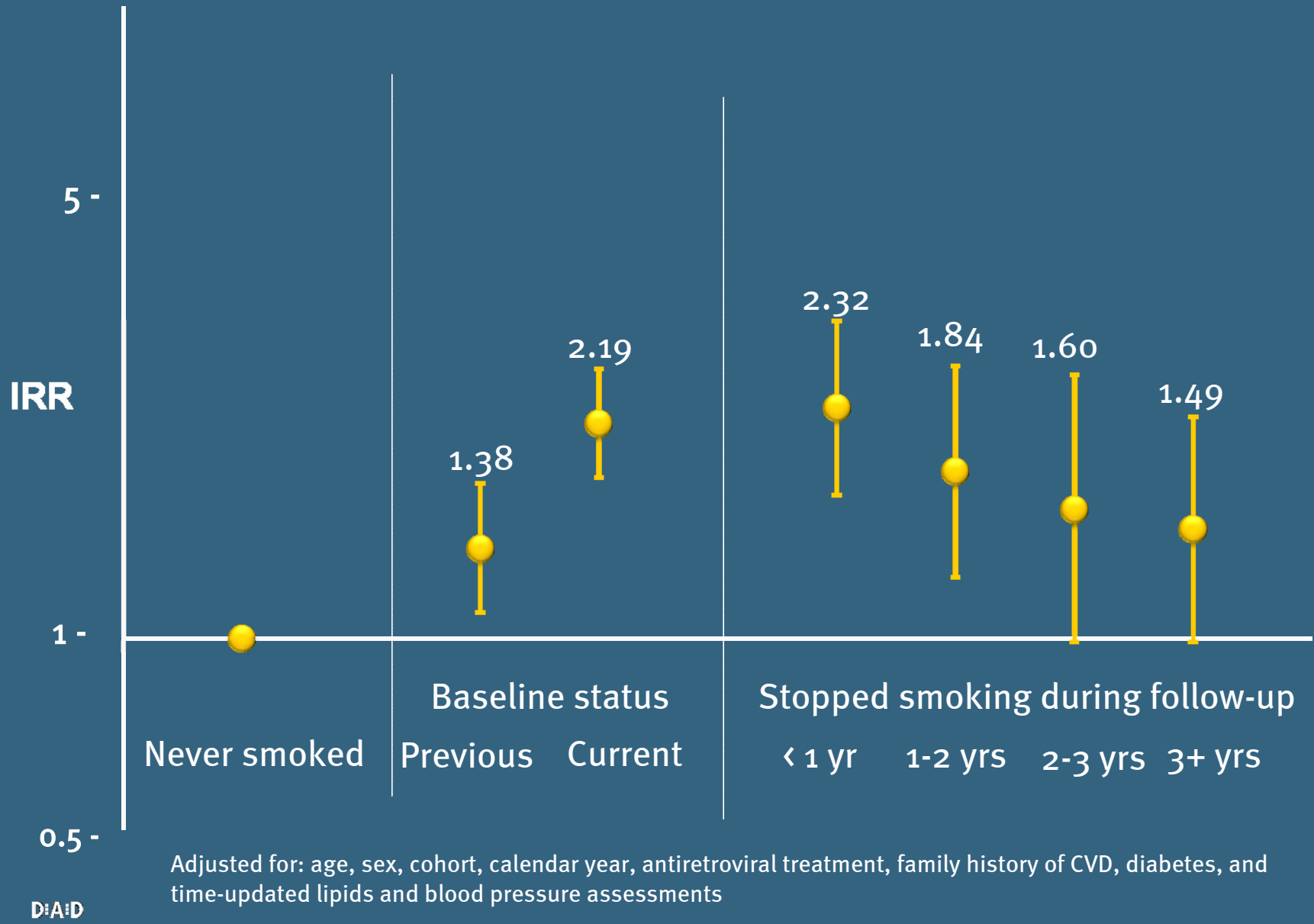
Coronary heart disease



Adjusted for: age, sex, cohort, calendar year, antiretroviral treatment, family history of CVD, diabetes, and time-updated lipids and blood pressure assessments

D:A:D

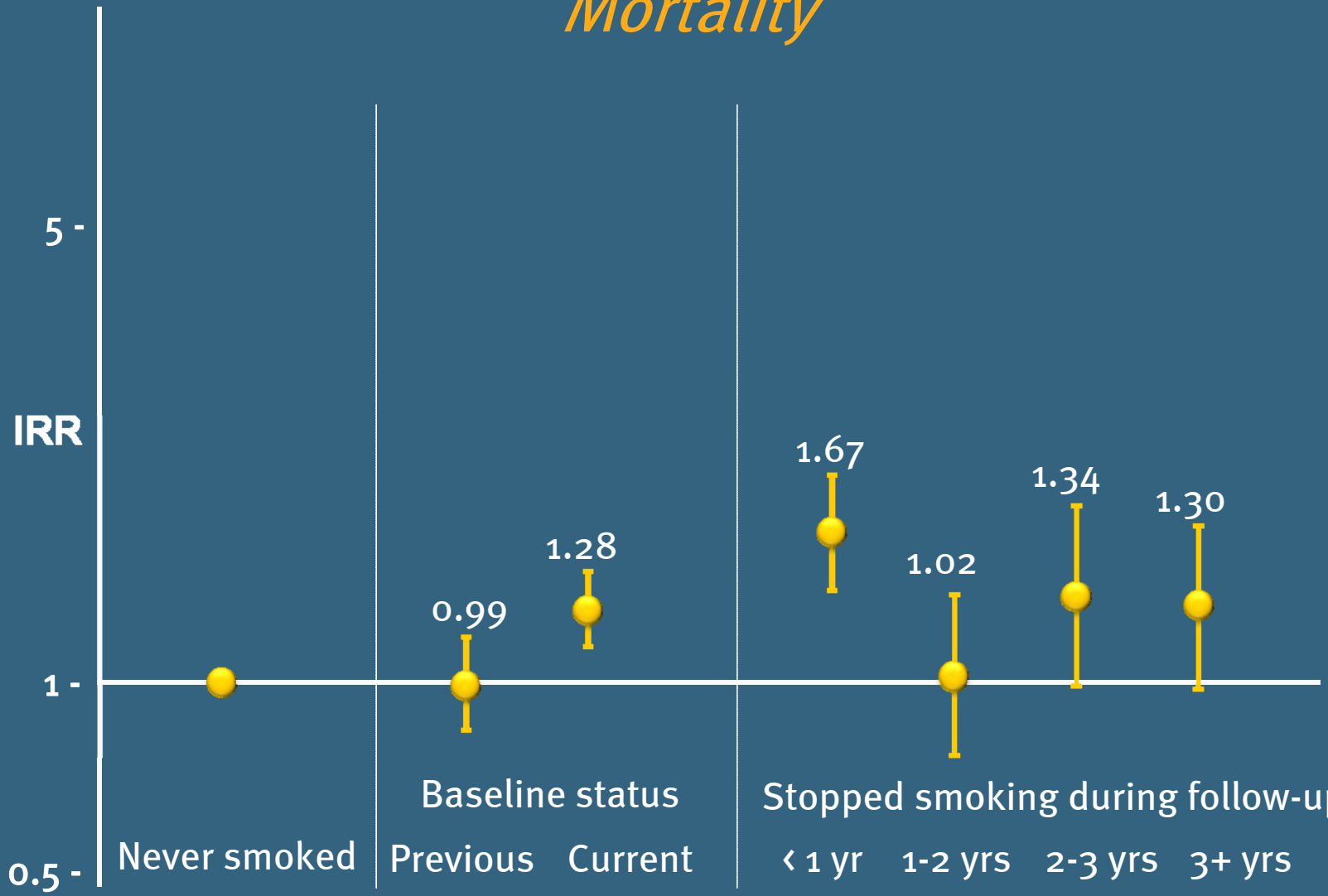
Cardiovascular disease



Adjusted for: age, sex, cohort, calendar year, antiretroviral treatment, family history of CVD, diabetes, and time-updated lipids and blood pressure assessments

D:A:D

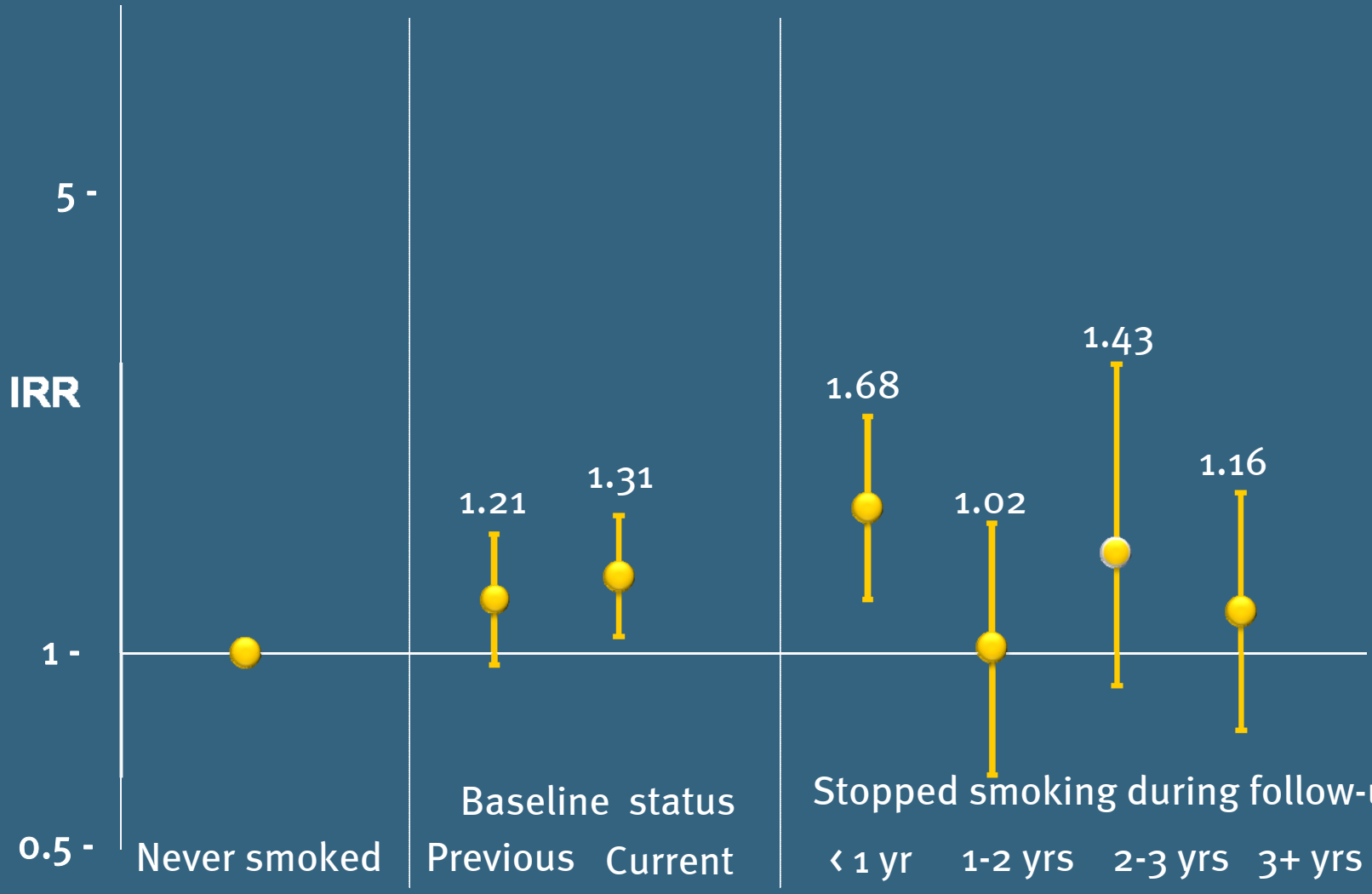
Mortality



Adjusted for: age, sex, cohort, calendar year, antiretroviral treatment, family history of CVD, diabetes, and time-updated lipids and blood pressure assessments, HCV, HBV, mode of HIV exposure, ethnicity and incidence of CVD during follow-up

D:A:D

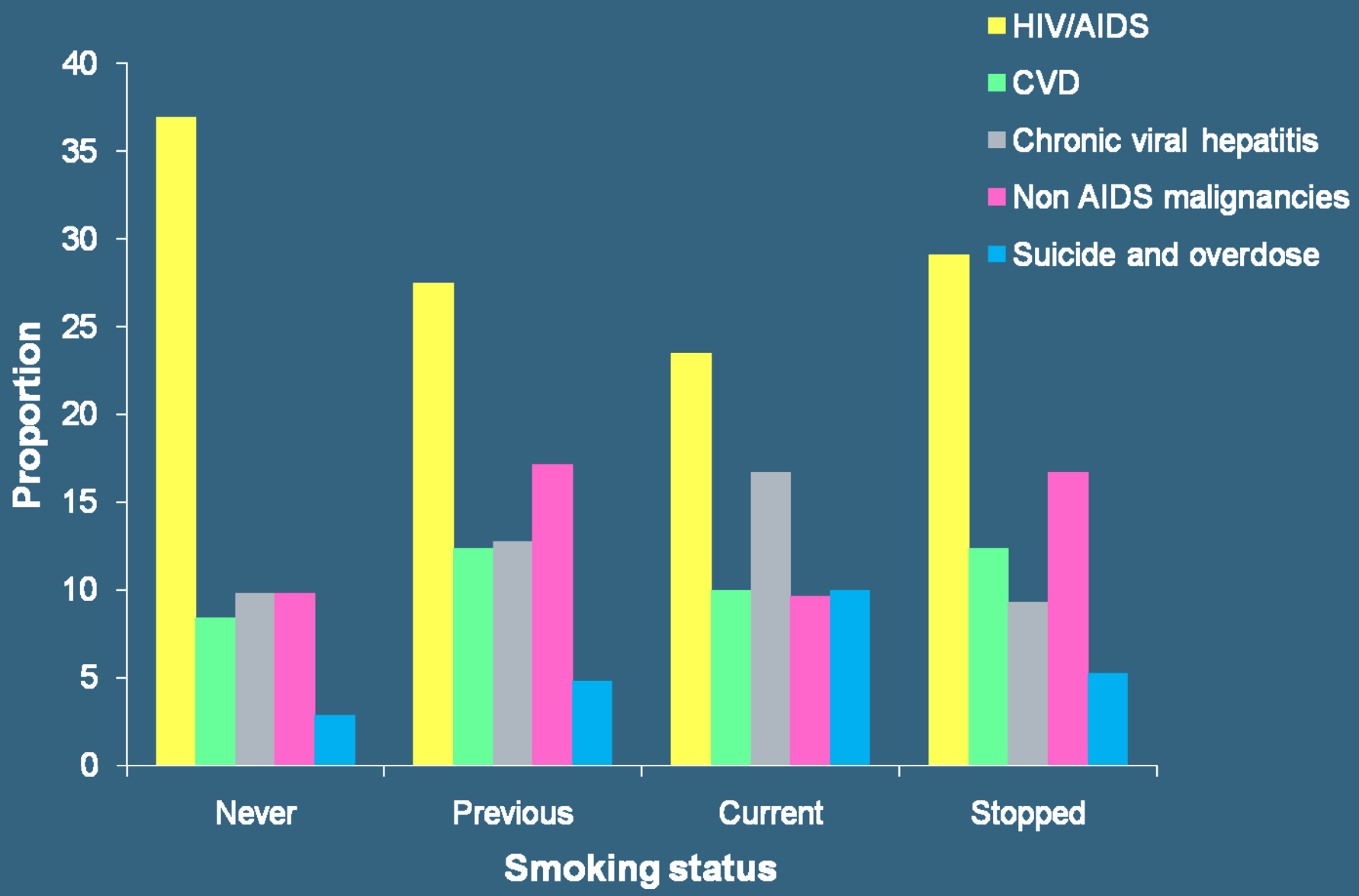
Mortality (>50 years)



Adjusted for: age, sex, cohort, calendar year, antiretroviral treatment, family history of CVD, diabetes, and time-updated lipids and blood pressure assessments, HCV, HBV, mode of HIV exposure, ethnicity and incidence of CVD during follow-up

D:A:D

Causes of death



D:A:D

Limitations

- Smoking data collected as Yes/No at each visit, no start/stop dates; no pack/years
  - *Akin to measurement error, though difficult to see how this might generate an association*
- Patients with smoking status reported at baseline but not during follow-up
  - *Sensitivity analysis excluding these patients reached similar conclusions*
- Difficult to establish cause and effect when assessing mortality
  - *Future analyses of other serious non-AIDS events might help*

Conclusion

- The risk of CVD events in HIV-positive patients decreased with increasing time since stopping smoking
- However, we did not see this in terms of mortality
- Smoking cessation efforts should be a priority in the management of HIV-positive patients
- Further research needed regarding smoking cessation in this population:
  - Clinical research
  - Behavioural research

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