Does diabetes mellitus (DM) confer an equivalent risk of coronary heart disease (CHD) to pre-existing CHD in HIV-positive individuals?

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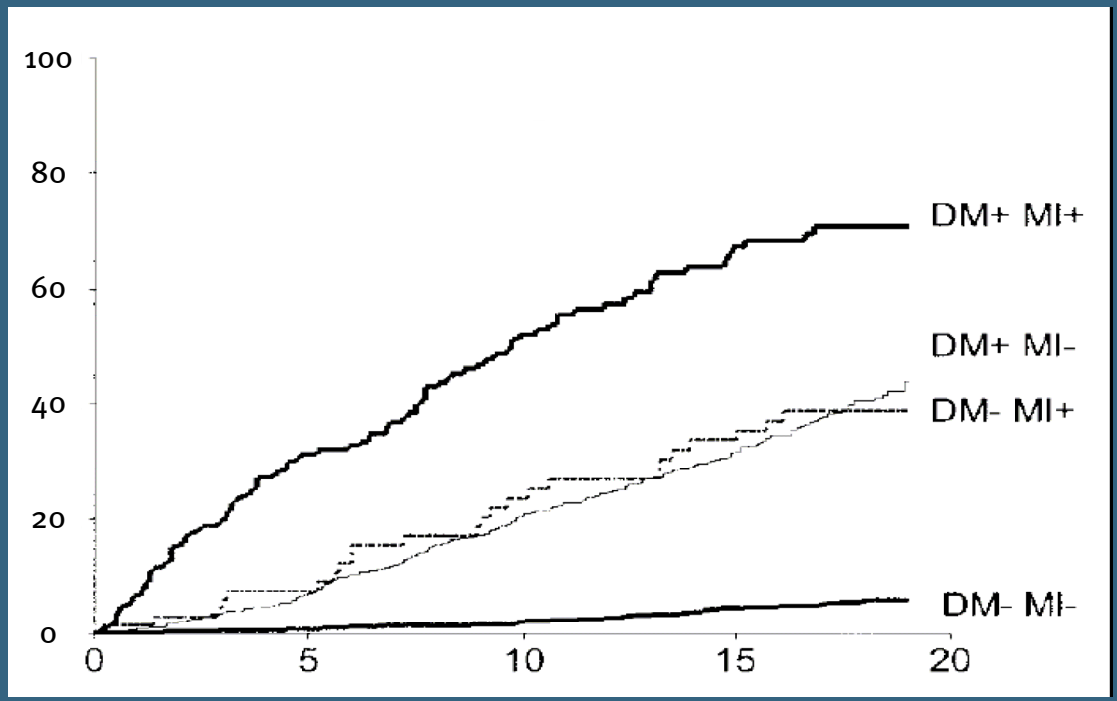
On behalf of the D:A:D study group

D:A:D

Background

- In the background population patients having DM have a high risk for CHD
- NCEP guidelines operate with a concept of **'CHD risk equivalent'**
  - a disease conferring similar risk of CHD as pre-existing CHD



DM = Diabetes mellitus
MI = Myocardial infarction
\+ = Present
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D:A:D

Update of Haffner SM: NEJM 1998, by Juutilainen A in Diabetes Care, Dec 2005

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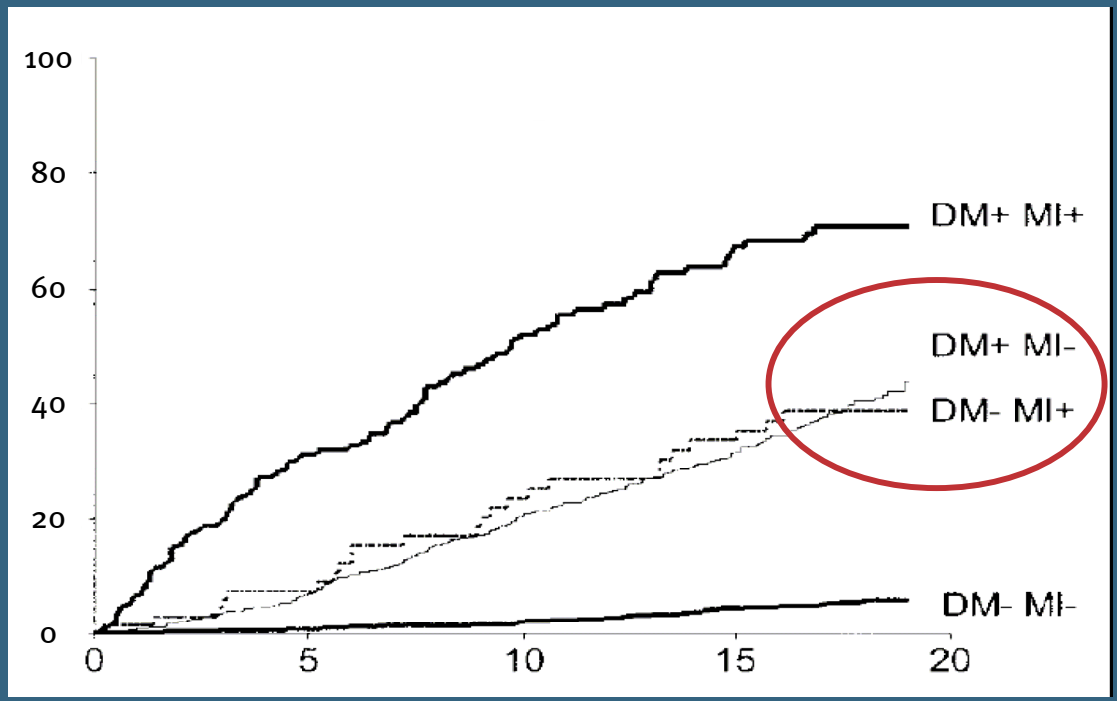

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DAD

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DM and HIV

- DM is a frequent condition in HIV
  - Prevalence 3%, incidence in D:A:D 5.72 per 1000 PY*
- In HIV, risk factors for DM may differ from those in the background population
  - e.g. ART rather than lifestyle
- It is unknown if DM should be considered a CHD risk equivalent in HIV
- Clarification may have major public health implications for the prevention of CHD in HIV

*SD Wit: 8th International Congress on Drug Therapy in HIV Infection, Glasgow 2006

Purpose

- Is DM a CHD risk equivalent in HIV?
- Is the risk of CHD in patients with DM and no history of CHD, similar to the risk of recurrence of CHD in patients with a history of CHD and no DM?

Methods

- CHD: Myocardial infarction (MI), invasive procedures (angioplasty and by-pass) and fatal cardio-vascular events
- In patients with and without prior CHD and with and without DM at entry to D:A:D (=baseline)
  - the incidence of CHD was calculated
  - Multivariable Poisson analyses compared the risk of CHD after adjustment for gender, age, cohort, HIV transmission mode, ethnicity, family history of CHD, smoking and calendar year
- Patient follow-up: from D:A:D enrolment, until the first CHD event during follow-up, 1st Feb 2007 or 6 months after the patient's last clinic visit, whichever occurred first

Sensitivity analyses

- The potential modifying effect of lipid-lowering therapy (LLT) and anti-hypertensive medication
- The impact of the duration since diagnosis of DM on the risk of CHD was assessed
  - Follow-up time and corresponding events were classified in 4 categories:
    - No DM, prior to baseline or during follow-up
    - DM during follow-up of ‹ 2 years duration
    - DM during follow-up of › 2 years duration
    - DM before baseline

Characteristics of patients in D:A:D according to history of DM or CHD

	- DM	+ DM	- CHD	+ CHD
Number	32,394	952	33,986	360
Age, med (IQR)	38 (33-44)	48 (40-56)	38 (33-44)	51 (44-59)
Male sex (%)	74	81	74	91
CD4 (cells/mm3) med (IQR)	410 (250-600)	380 (208-582)	408 (248-600)	438 (272-593)

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TG (mmol/L) med (IQR)	1.6 (1.0-2.6)	2.4 (1.4-4.0)	1.6 (1.0-2.6)	2.3 (1.5-3.5)
HDL (mmol/L) med (IQR)	1.1 (0.9-1.4)	1.0 (0.8-1.3)	1.1 (0.9-1.4)	1.0 (0.8-1.3)
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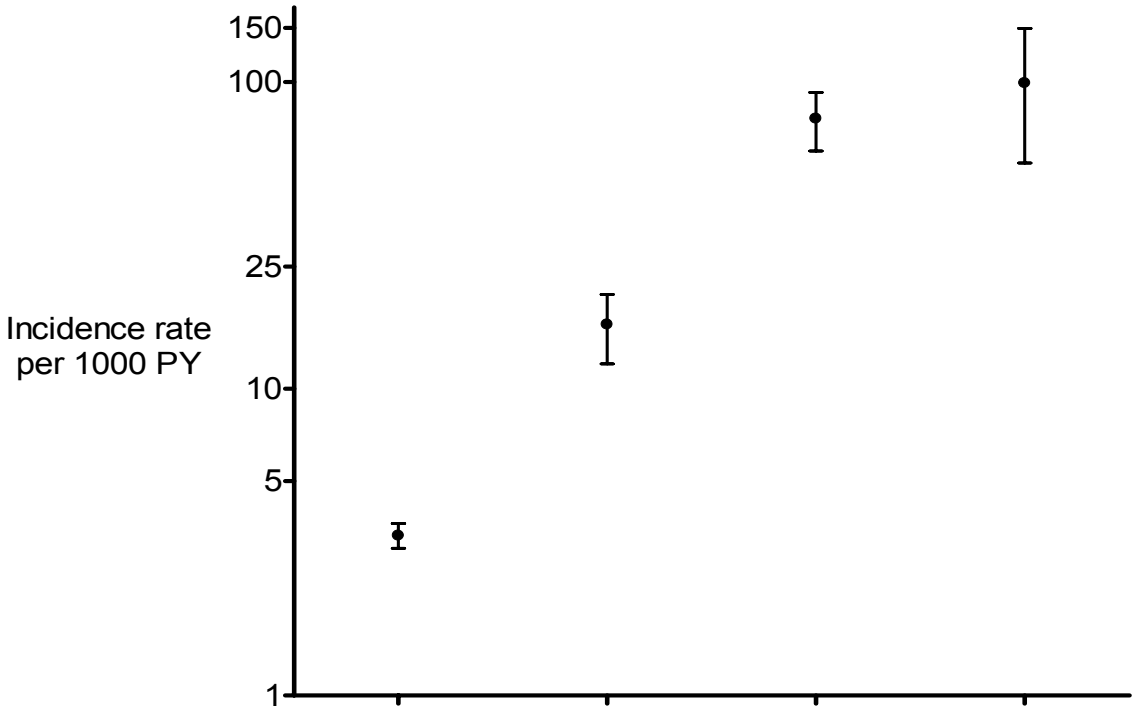
Smoker % Current / Ex	34 / 17	22 / 20	34 /17	34 /31
Fam history of CVD %	7	7	7	19
Years on - PI	2.3 (1.2-3.2)	2.6 (1.7-3.4)	2.3 (1.2-3.2)	2.6 (1.7-3.4)
- NRTI	3.0 (1.6-4.7)	3.9 (2.4-5.80)	3.0 (1.6-4.8)	4.0 (2.5-5.7)
- NNRTI	0.9 (0.4-1.6)	1.0 (0.4-1.7)	0.9 (0.4-1.6)	1.0 (0.5-1.7)

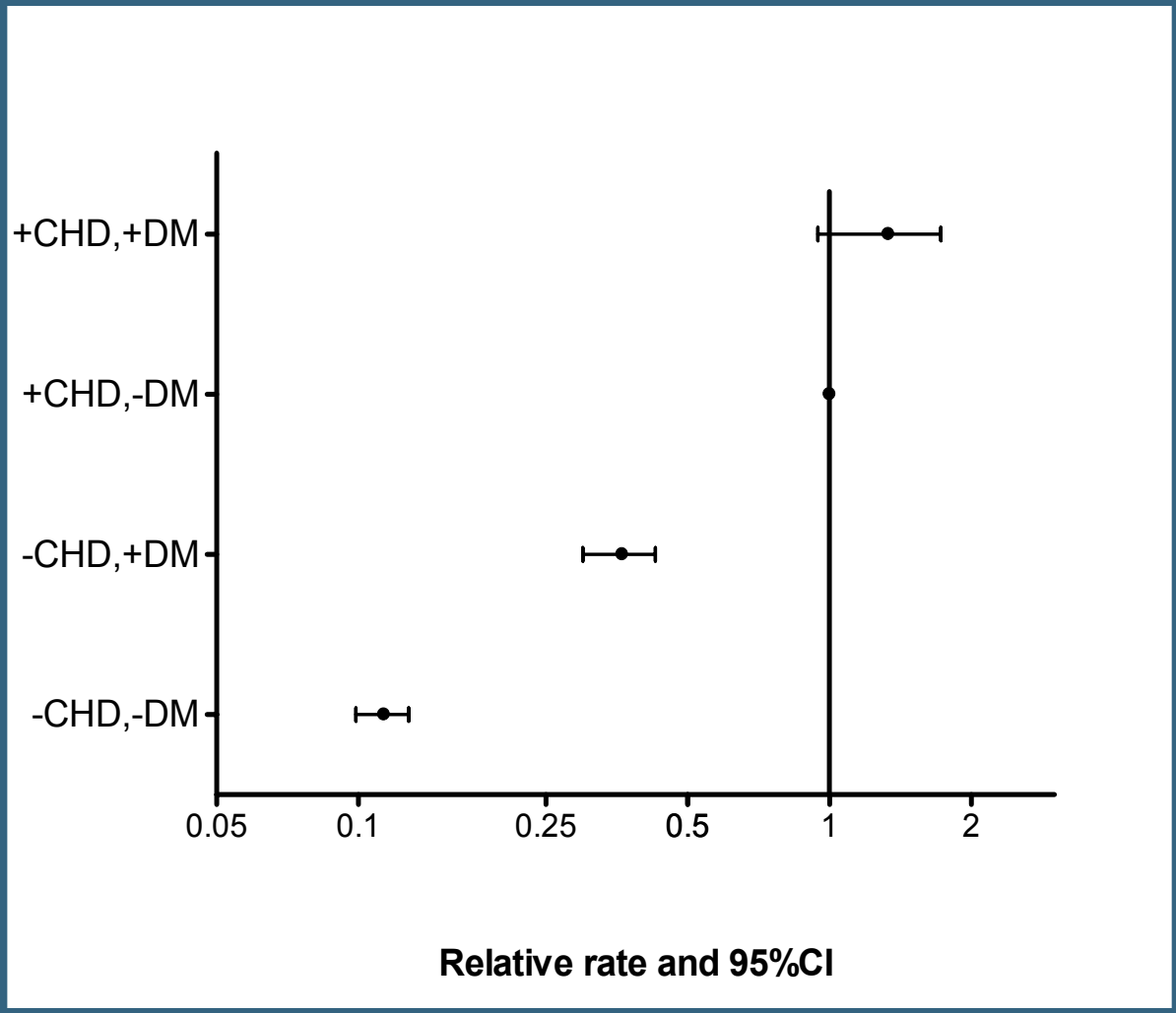
Incidence of CHD according to history of CHD and/or DM



Distribution of events (%) status at baseline

	-CHD,-DM	+CHD,-DM	-CHD,+DM	+CHD,+DM
MI	64.2	44.6	65.5	69.6
Angioplasty	31.3	41.1	19.7	26.1
Enderectomy	1	1.8	3.9	0
By-pass	3.6	12.5	10.5	4.3

Adjusted rate ratios (RR) for CHD according to history of DM and/or CHD



Adjusted for :

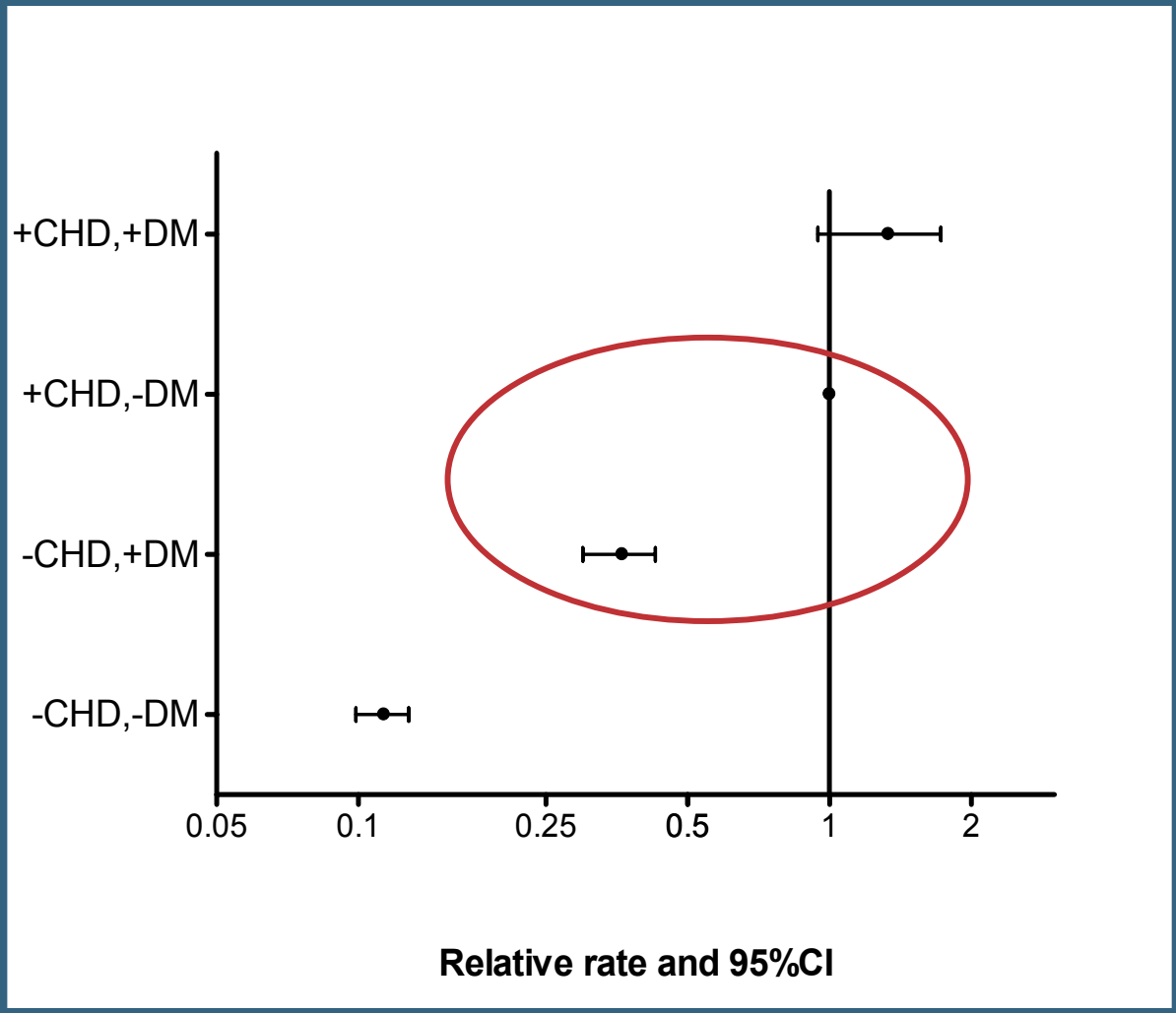
gender, age, cohort, HIV transmission mode, ethnicity, family history of CHD, smoking, calendar year

No positive interaction between age and DM was found, p= 0.59

D:A:D

Adjusted rate ratios (RR) for CHD according to history of DM and/or CHD

History of CHD and or DM



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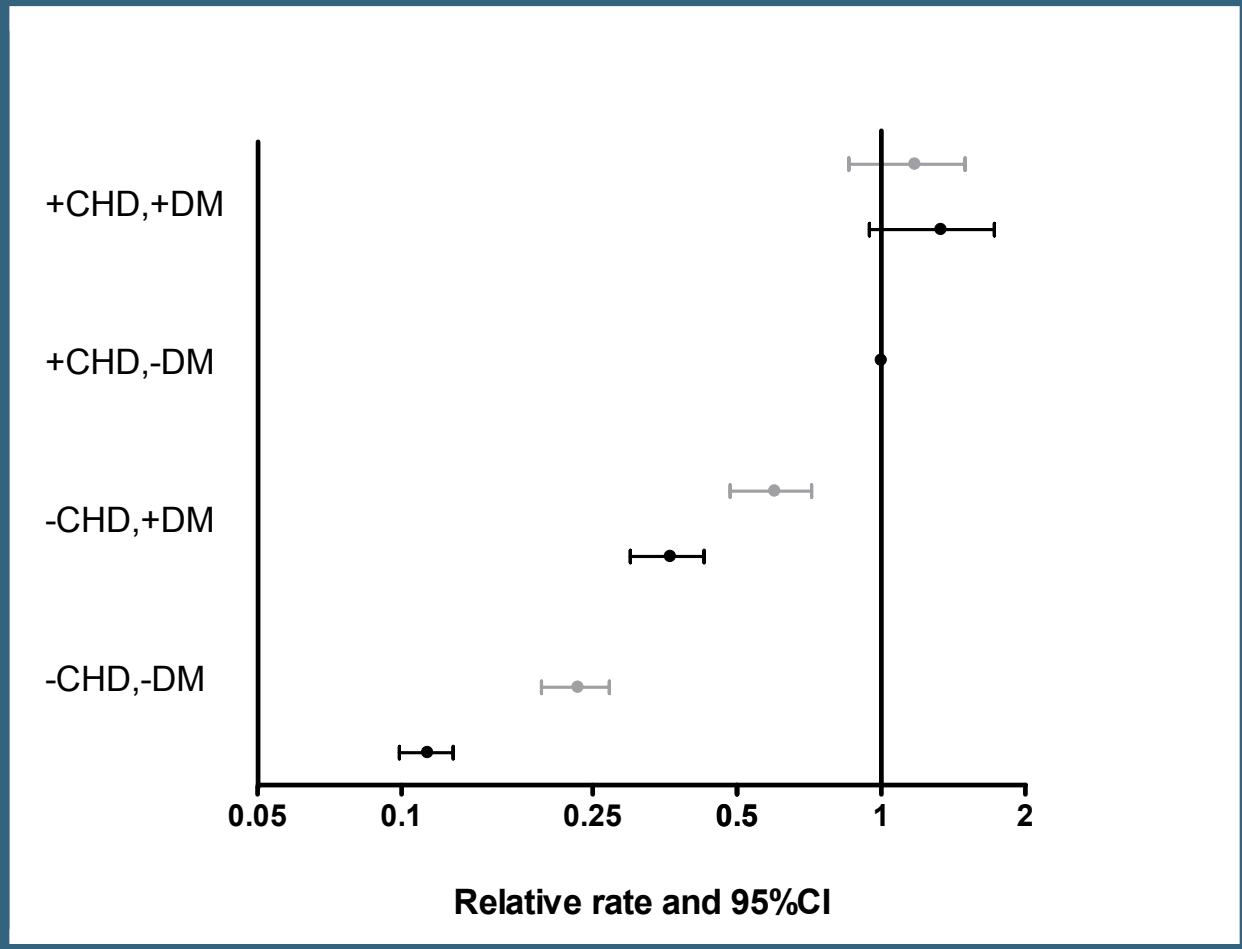
Adjusted rate ratios (RR) for CHD according to history of DM and or CHD : adjustment for use of CHD intervention*

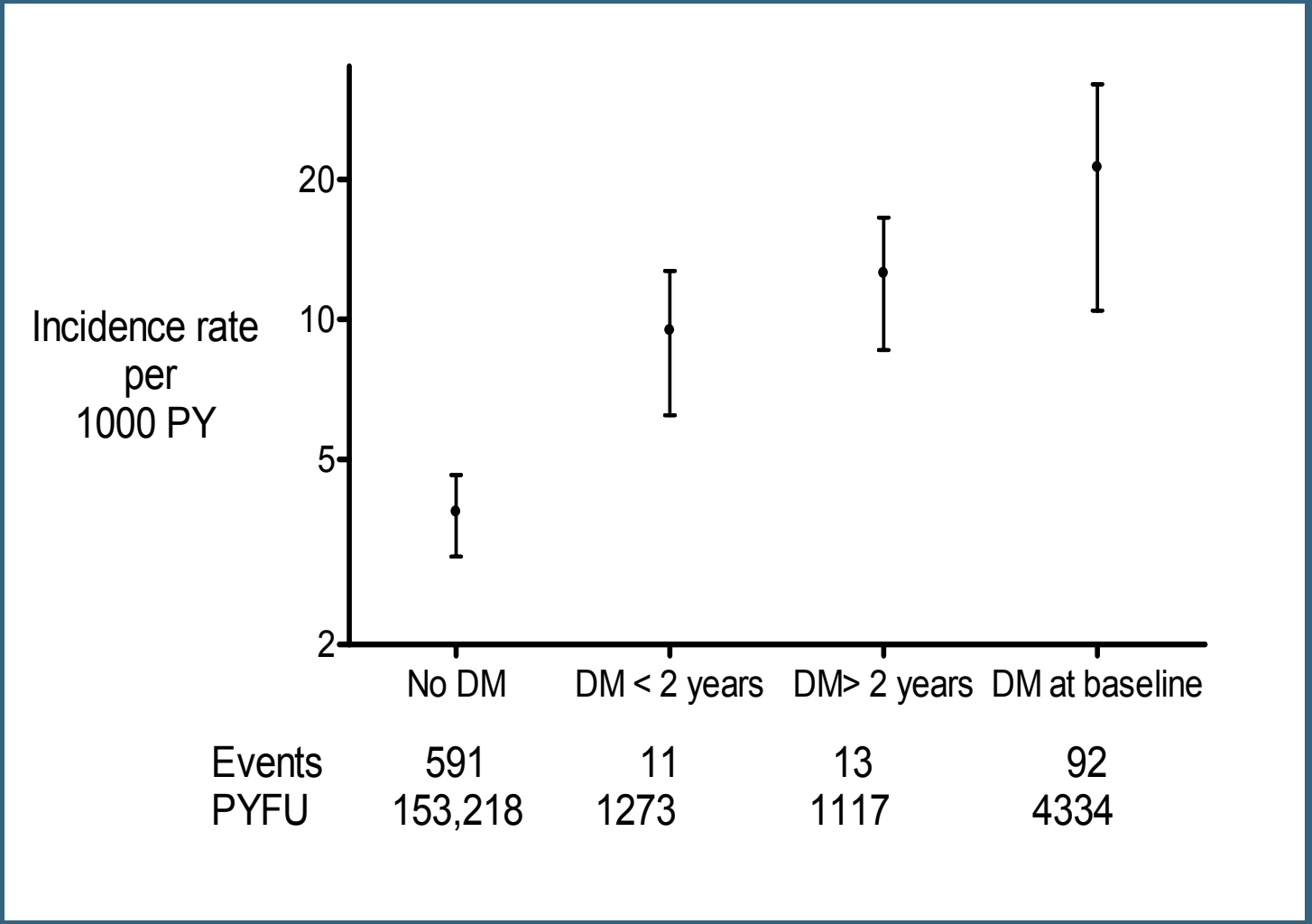


Black bars adjusted for gender, age, cohort, HIV transmission mode, ethnicity, family history of CHD smoking and calendar year

***Grey bars** furthermore adjusted for lipid-lowering therapy, anti-hypertensive treatment and anti-platelet drugs

D:A:D

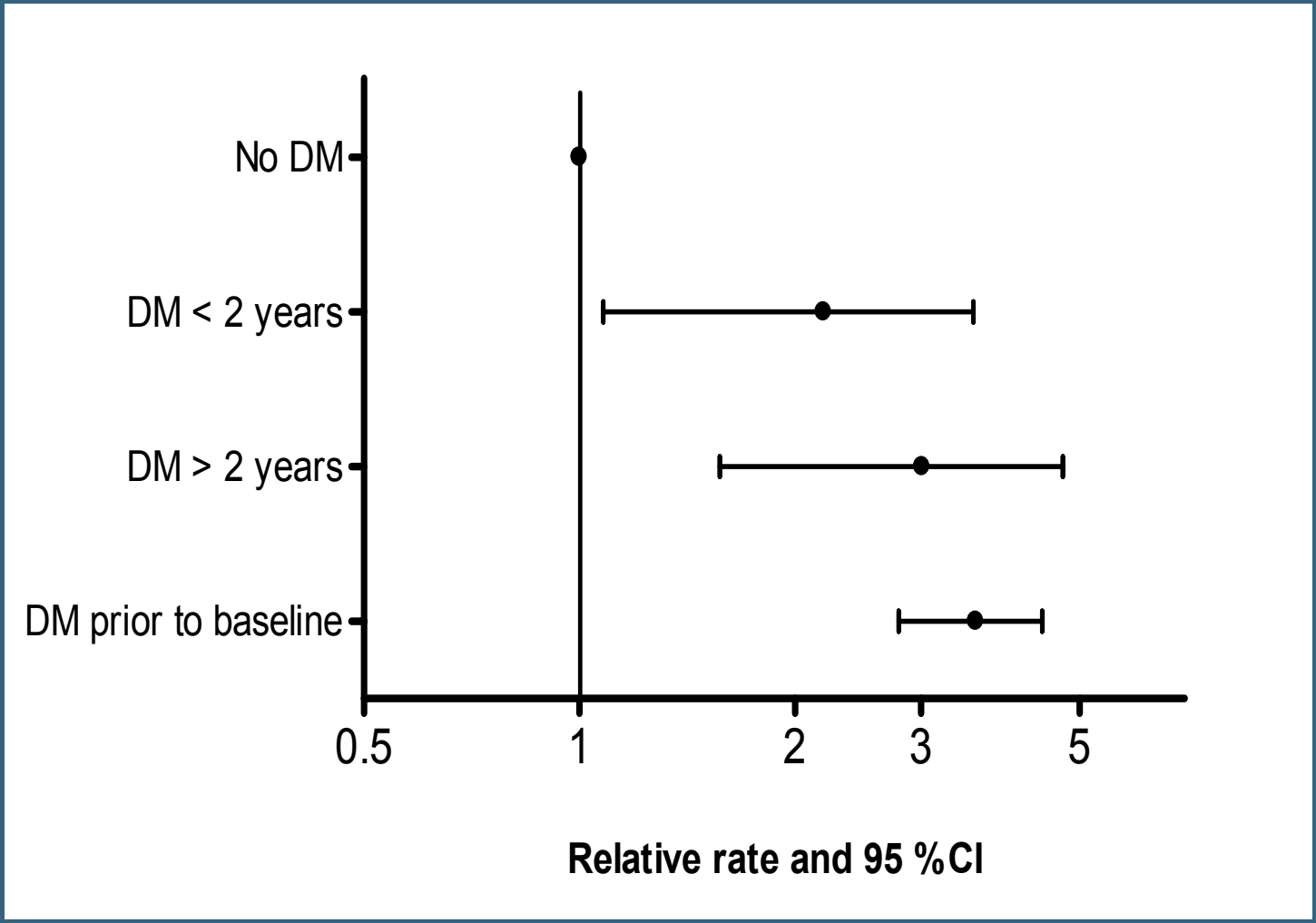
Incidence of CHD according to duration of DM



952 with DM prior to baseline; 886 developed DM during follow-up

Adjusted risk of CHD according to duration of DM

DM diagnosed during follow-up



Adjusted for gender, age, cohort, HIV transmission mode, ethnicity, family history of CHD, smoking, calendar year and CHD event at baseline

D:A:D

Limitations

- Years lived with DM in this study might be too short to demonstrate the full extent of this condition on the risk of CHD
  - As the study matures (and the population ages) this relationship will be more assessable
- Additionally, as the cohort ages, more HIV+ might be at risk of develop DM and thereby potentially CHD
- Only relative risk was assesed (not absolute)

Summary

- A previous CHD event is a far stronger predictor of CHD than a diagnosis of DM in HIV
- A history of CHD was associated with a markedly higher risk of recurrence of CHD, regardless of whether the patient also had DM or not
- Conversely, in patients without prior CHD, DM was an important risk factor for CHD, *but however not a CHD risk equivalent*
- Sensitivity analyses suggested that a higher risk of CHD may exist with longer time since diagnosis of DM

Discussion

- In HIV, DM is not a CHD risk equivalent
- Rather, intensity of preventive interventions should be guided from estimates of absolute CHD risk
    - the Framingham equation* (Anderson version)
    - the D:A:D risk equation currently under development**
- DM remains an important risk factor for CHD and has important implications for targeting interventions
    - such as lipid-lowering drugs, anti-hypertensive medication and glycemic control

* M Law: HIV Medicine 2006
** N Friis-Møller: Abstract 808, CROI 2007

Acknowledgements

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- **Statisticians:** CA Sabin, AN Phillips *
- **Community representative:** S Collins *
- **DAD coordinating office:** N Friis-Møller, S Worm, A Sawitz, JD Lundgren *¢
- **Steering Committee:** Members indicated w/*; ¢ chair;

  Additional members: S Storfer *, F Rousseau *, I Weller *
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