D:A:D

PREDICTION OF GLOBAL CVD RISK IN HIV-POSITIVE PERSONS

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for the D:A:D Study Group

Background

- With the aging of the population living with HIV, the absolute risk of cardiovascular disease (CVD) is increasing
- There is a need to further facilitate the identification of HIV-positive persons at increased risk of CVD

Purpose of study:

- Updated CVD prediction models
  - Global CVD risk *
  - Baseline CVD risk factors
  - Full and reduced D:A:D models (+/- ARVs)

* D'Agostino et al. Circulation 2008

Methods – participants and outcome

- 32,663 HIV-positive persons from 20 countries in Europe and Australia, who
  - ✓ were free of CVD at entry into the D:A:D Study
  - ✓ had complete information on CVD risk factors
- Outcome: A composite CVD endpoint that included
  - Myocardial infarction
  - Stroke
  - Invasive coronary artery procedure (including coronary artery by-pass or angioplasty)
  - Carotid artery endarterectomy
  - Death from other CVD
- All CVD outcomes are reported real time, and are centrally validated

Methods – Participant follow-up

- Predictive risk equations based on Cox regression models
- Individuals were followed from D:A:D entry to the first of:
  - CVD
  - Six months after last clinic visit
  - 1st February 2011
- Full and reduced D:A:D models (+/- ARVs)
  - Estimated 5-year risk of CVD
- Comparison: Recent Framingham model re-calibrated to the D:A:D dataset

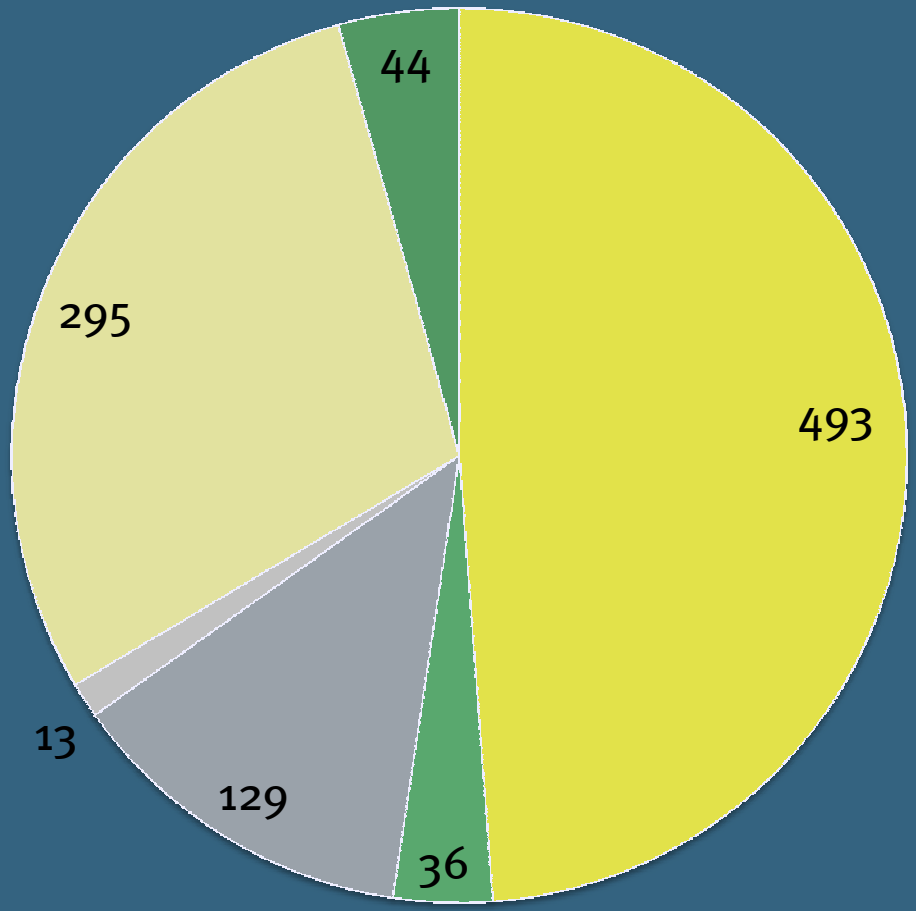
Overall rate of composite CVD

There were 1,010 CVD in 32,663 individuals followed for 186,364.5 person-years

Rate: 5.42 per 1,000 person-years

95% CI: 5.09-5.76

Components of Composite CVD Outcome



n=1010

D:A:D

Baseline Characteristics

		No CVD (n=31,653)	CVD (n=1,010)
Age	years	39 (33-46)	47 (41-57)
Female	%	26.0	12.5
Smoking current / former	%	51.9 / 16.7	61.5 / 17.4
Diabetes	%	2.8	10.4
Systolic BP	mmHg	120 (110-130)	130 (120-140)
Total cholesterol	mmol/L	4.8 (4.1-5.7)	5.6 (4.8-6.5)
HDL cholesterol	mmol/L	1.14 (0.91-1.42)	1.06(0.85-1.34)
cART/PI/ NRTI	years	1.75 / 0.68 / 2.42	3.19 / 1.44 / 4.34
CD4 count	cells/µL	440 (290-630)	402(260-611)
HIV RNA <50 copies/mL	%	53.8	47.6

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Risk Factors Considered

- Age
- Sex
- Blood pressure (systolic and diastolic)
- Smoking (current, former)
- Diabetes
- Family history of CVD
- Serum values of
  - Total (TC) and HDL cholesterol (TC:HDL ratio)
  - Triglycerides
  - CD_4 / HIV-RNA
- HIV-exposure category
- cART
  - IDV/r, LPV/r, PI, NRTI as cumulative exposure
  - Abacavir as current exposure
- Body-mass index (BMI)
- Lipodystrophy

Risk Factors Included

- Age
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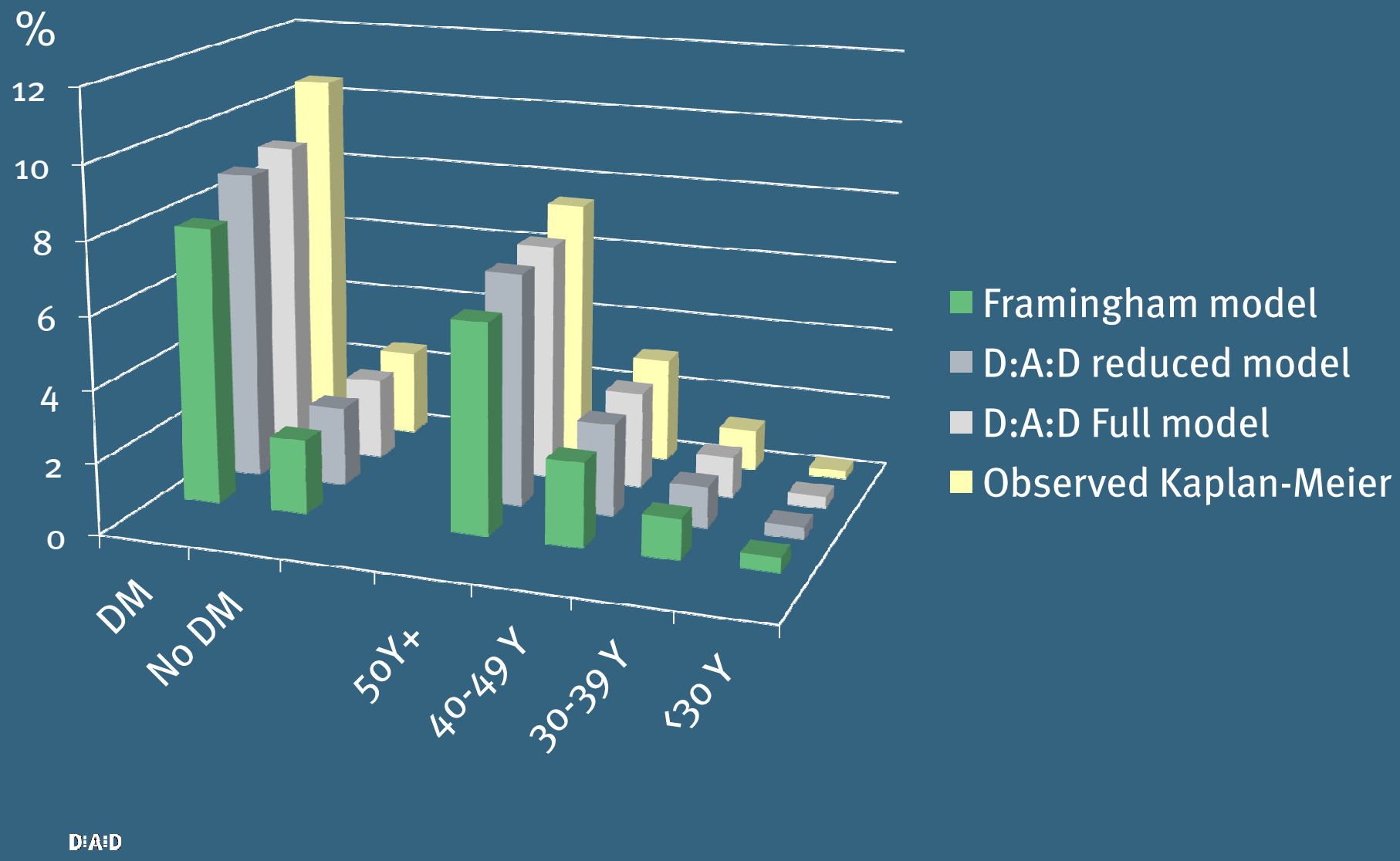
Three Models

Risk factor	D:A:D Full	D:A:D Reduced	Framingham
Age	+	+	+
Sex	+	+	Seperate models by sex
Diabetes	+	+	+
Smoking	Current and former	Current and former	Current
Total and HDL cholesterol	+	+	+
Systolic BP	+	+	+
Family History CVD	+	+	
CD_4 cell count	+	+	
Abacavir - current	+		
PI - cum. exposure	+		
NRTI – cum. exposure	+		

Three Models – Hazard Ratios from Cox Models

Risk factor	Per unit	D:A:D Full	D:A:D Reduced	Framingham (men)
Age	ln	22.0	24.0	21.4
Sex		1.37	1.41	-
Diabetes		1.96	2.08	1.78
Smoking current / former		2.25 / 1.24	2.26 / 1.27	1.92 / -
Total and HDL cholesterol	ln	2.58 / 0.61	2.98 / 0.59	3.08 / 0.39
Systolic BP (#: if treated)	ln	4.59	4.56	6.91 / 7.38 #
Family History CVD		1.37	1.39	
CD4 cell count	2-fold higher	0.89	0.89	
Abacavir - current		1.47		
PI - cum. exposure	year	1.05		
NRTI – cum.exposure	year	1.03		

5-year CVD risk – Age and Diabetes



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Summary (I)

D:A:D models tailored to HIV-positive persons

- based on observed data in HIV-positive persons

What's new:

- Additional 80,000 PY of follow-up (total of 186,000 PY)
- One outcome only: Global CVD risk
- Based on baseline rather than time-updated risk parameters (Cox model)
- Full and reduced D:A:D models (+/- ARVs)
  - CD_4 count included

Summary (II)

- The recent Framingham model for global CVD risk can be re-calibrated to predict well in HIV-positive persons in the D:A:D Study population
- However, our analyses suggest that risk equations developed from the D:A:D dataset are superior in HIV-positive persons, in particular for the accuracy of prediction in subgroups

- Generalizability of the D:A:D prediction models require external independent validation in cohorts of HIV positive persons

Perspectives

Holistic approach

- Assessment of global CVD risk

- Individual level: In the clinical context to inform doctor patient discussions on CVD risks and interventions
  - Moderate-high CVD risk: more targeted interventions to reduce this risk
- Population level: for research purposes of estimations of predicted risk at population levels

Updated D:A:D models will become available at :

http://www.cphiv.dk/TOOLS/tabid/437/Default.aspx

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