

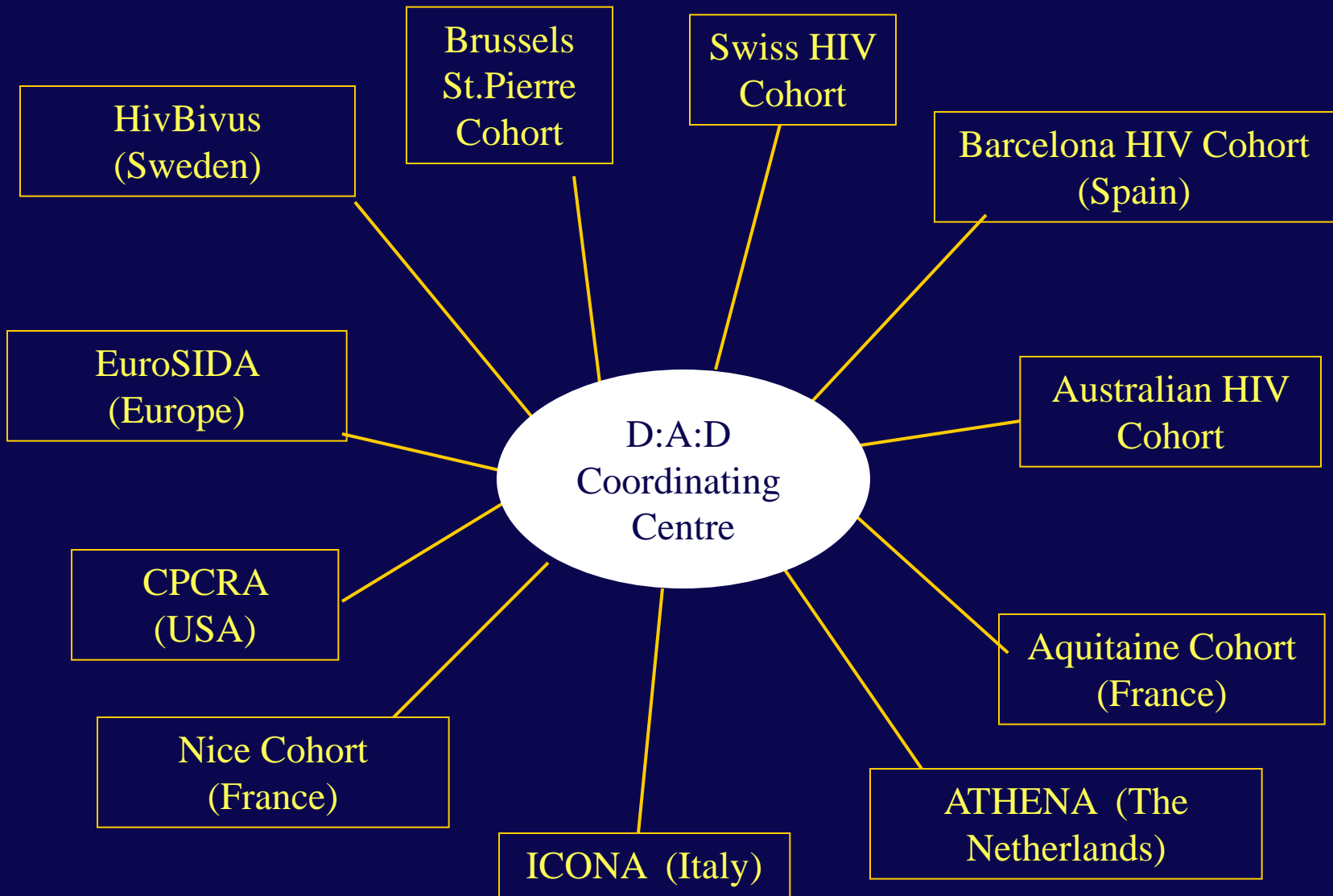
D:A:D

D:A:D Study Teaching Material

“Data Collection of Adverse events of anti-HIV Drugs”
(D:A:D) study

Background

- The D:A:D Study, is a prospective cohort study (collaboration) initiated in 1999 as part of an EMEA initiative
 - 11 cohorts participating from Europe, Australia and USA
 - > 49.000 persons are under follow-up from > 200 participating clinics
 - > 330.000 PYFU, 3 enrolment cohorts
 - The Coordinating centre is located at Copenhagen HIV programme (CHIP), Denmark
- D:A:D



D:A:D

The D:A:D study

- The study originally aimed to assess whether exposure to combination antiretroviral treatment, cART, was associated with an increased risk of myocardial infarction (MI)
 - Definition of cART: NNRTI and/or PI in combination with NRTI
- In later years the research agenda was broadened to also include other cardiovascular- and other organ diseases

D:A:D events

Primary:

- Myocardial Infarction (MI)

Other Endpoints;

- Stroke
- Invasive Cardiovascular procedures (ICP)
- Diabetes Mellitus (DM)
- Death (using CoDe methodology)
- Cancers
- End-stage renal disease (ESRD)
- End-stage liver disease (ESLD)

D:A:D

CoDe – Coding Causes of Death

The goal of the CoDe Project is to develop a uniform coding system that can be applied universally to studies of individuals with HIV infection, including:

- a detailed data collection
- a centralised review process

The data collection on causes of death in D:A:D has changed to implement CoDe

Protocol, forms and instructions are available at:
www.cphiv.dk/CoDe

D:A:D events

- All events are reported 'real time' to the DAD Study Coordinating Office at CHIP
- Reimbursement of 253 US\$ per form
- Event reporting forms at: www.cphiv.dk
- Annual monitoring; includes random monitoring and monitoring of events
- Events centrally adjudicated and supervised by external experts (cardiologist, nephrologist, oncologist)

Other information collected systematically:

- HIV: CD4 counts, VL, risk group, time of diagnosis, opportunistic infections, ART regime details
- Demographics and CV risk factors: age, sex, ethnicity, cohort, CVD dispositions and previous events, smoking status, height, weight, hypertension
- Lab values: blood gluceses, creatinine, hgb, lipids, bilirubin, ALAT/ASAT, platelets
- Other drugs: i.e. Lipid lowering drugs, anti-hypertensive, anti-diabetic drugs, drugs used to treat opportunistic infections
- Hepatitis serology

Baseline demographics

Number of patients		49734	(100.0)
Female		13018	(26.2)
Mode of infection:	Homo/bisexual	21901	(44.0)
	IDU	7631	(15.3)
	Heterosexual	16133	(32.4)
	Other	1012	(2.0)
	Unknown	3057	(6.2)
Ethnicity	White	25189	(50.7)
	Black	4852	(9.8)
	Other	1408	(2.9)
	Not known	18285	(36.8)
Age at recruitment:	Median (IQR)	38.1	(32.5-45.0)
BMI at recruitment:	Median (IQR)	23.0	(21.0-25.3)
AIDS at recruitment:		11032	(22.2)

CARIOVASCULAR DISEASE (CVD)

Definition of MI

- Definition as applied in the WHO MONICA study
- Diagnosis based on information on:
 - Cardiac pain, cardiac enzymes, troponine, ECG changes, autopsy findings
- Categories:
 - Fatal and non-fatal (survival 28 days)
 - Definite, possible or unclassifiable

Event Checking Chart Cases of MI

Example of completed event checking chart

Name of centre and cohort XX Hospital (999), EuroSIDA

Patient ID code: 714 Gender: MALE

Year of birth (yyyy) [REDACTED] Date of event (dd/mm/yy): 01/06/00

1. Number of available ECG's, copies of which are included.

Total (aim 3-6) 5 Prior to MI (aim 1-2) 0 From time of MI (aim 1-2) 3 After MI (aim 1-2) 2

Are all ECG's marked with: pt ID-code, date & time, ecg-velocity?

2. Serological markers.

Register sequence of and/or peak-values of measurements performed within 72 hours of the event. (For iso-enzymes: peak-value of CK-MB and the corresponding value of CK, peak-value of LDH-1 and the corresponding value of LDH-2).

CK unit / U/L (0-190)	CK-MB / unit U/L (2-23)	Troponin T / unit	Troponin I / unit ng/ml (0.01-0.10)	LDH-1 / unit	LDH-2 / unit U/L (200-480)	Other serology marker-which? <small>nyq 620 0.12 unit ng/L</small>	Time from MI / hours
505	55		0.520	484		430	H 5
410	467			1445			H 10
225	289		17.36	1693			H 19
668	94			1566			H 43
174				960		18	H 91

3. Narrative description of the event/ Summary of symptoms.

Duration of symptoms (> 20 min.?): yes, ≈ 5 h

Quality of symptoms, summary:

retrosternal pain not totally cured by TNT, left arm

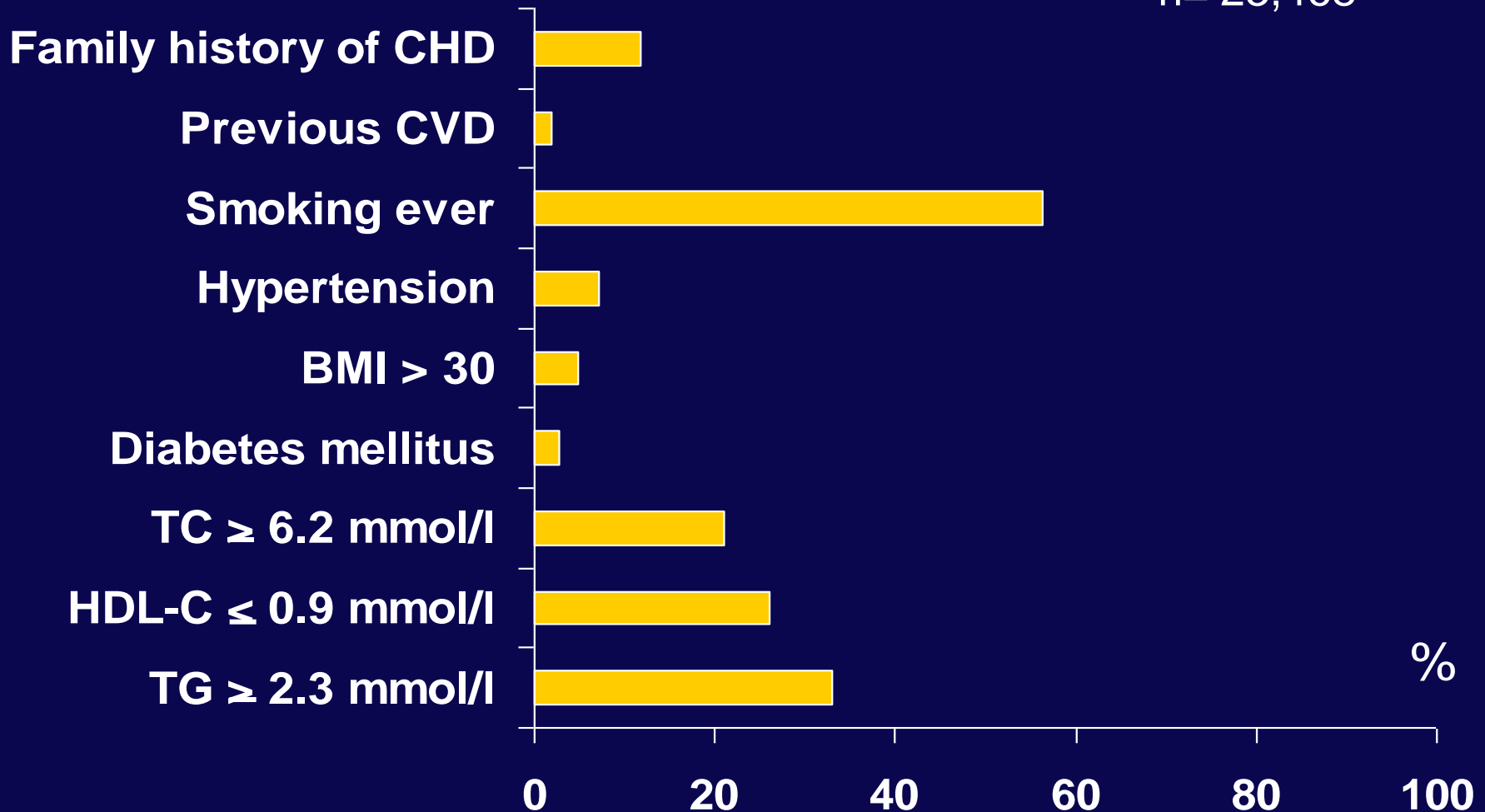
Typical Atypical Incomplete Missing

All available information regarding this event has been collected,

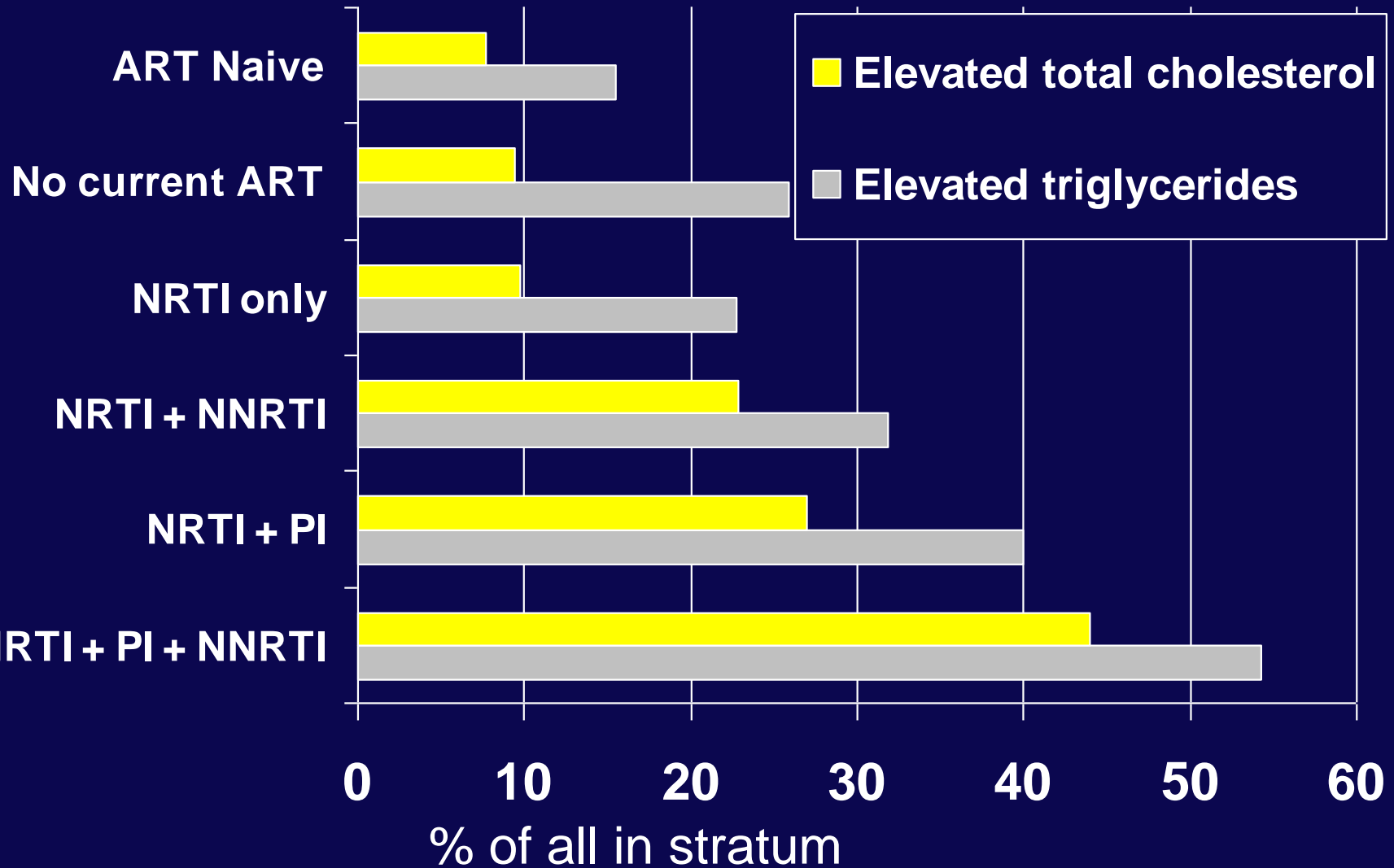
(dd/mm/yyyy)

Baseline Risk Factors for CVD in D:A:D

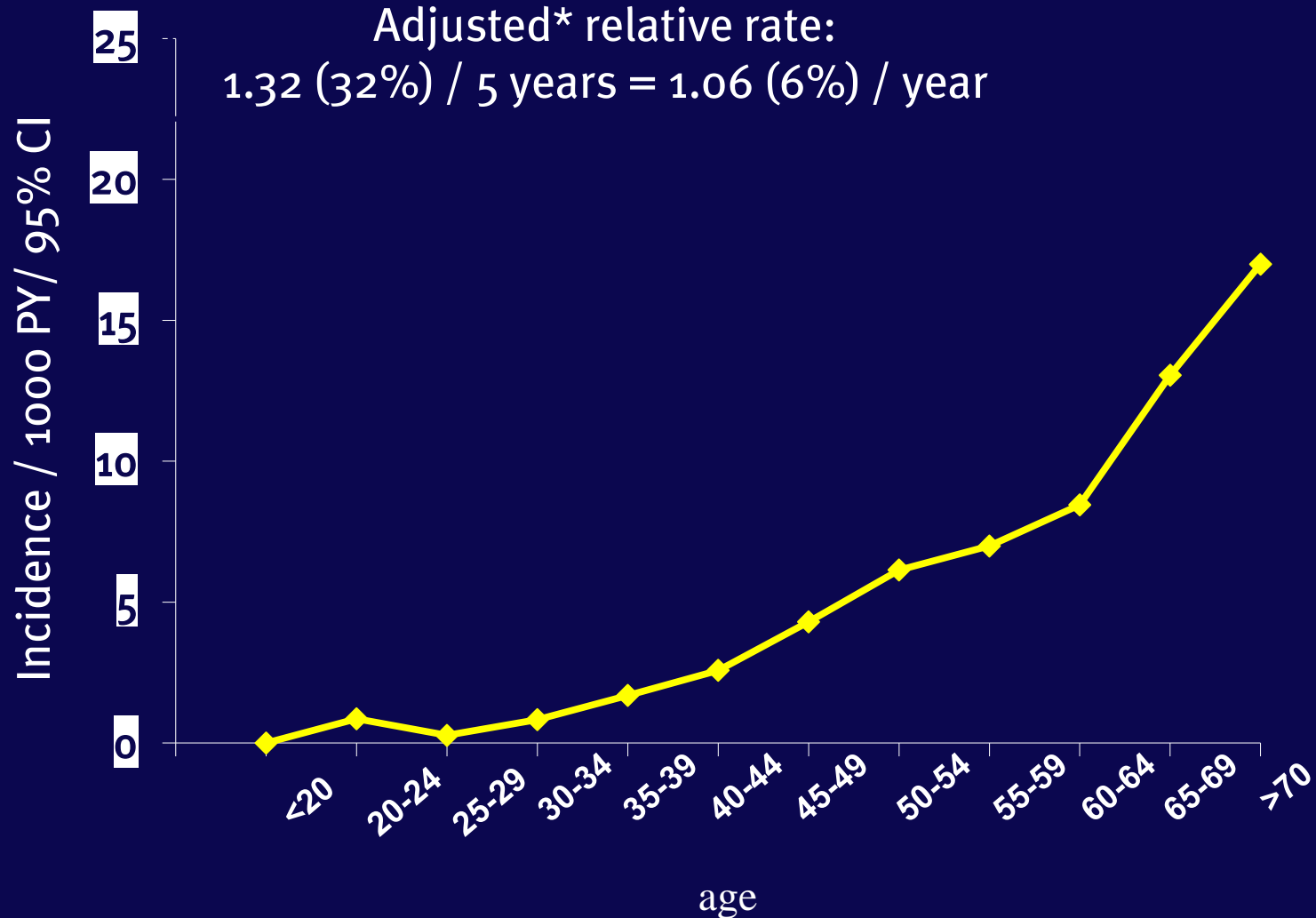
n= 23,468



Lipid elevation and ART status at baseline



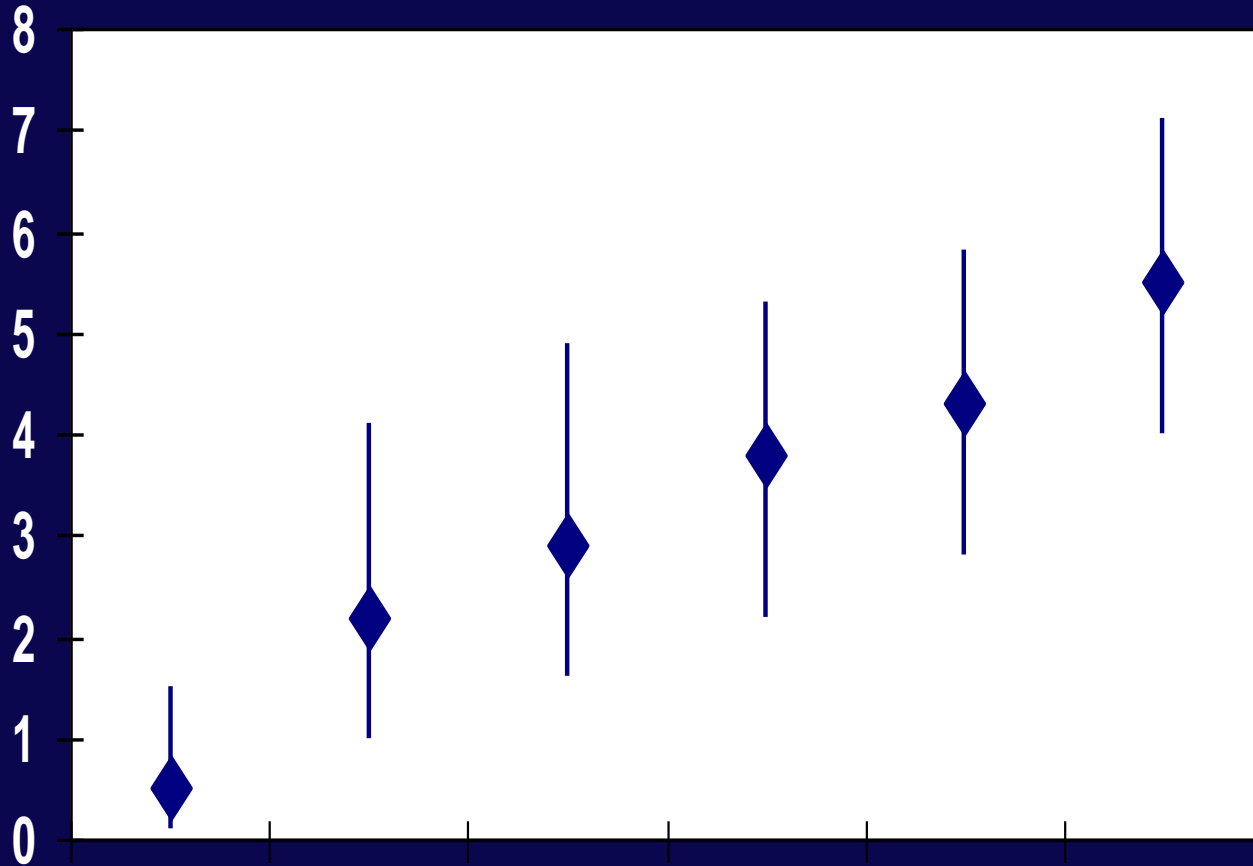
Incidence of MIs according to age in D:A:D



*: Adjusted for sex, age, cohort, calendar year, prior CVD, family history of CVD, smoking, body-mass index, PI exposure, lipids, diabetes, hypertension

MI by CART exposure

MIs per
1,000 PY
(95% CI)



Years on CART

None

<1

1-2

2-3

3-4

>4

Total

No. MIs

3

9

14

22

31

47

126

No. PY

5,714

4,140

4,801

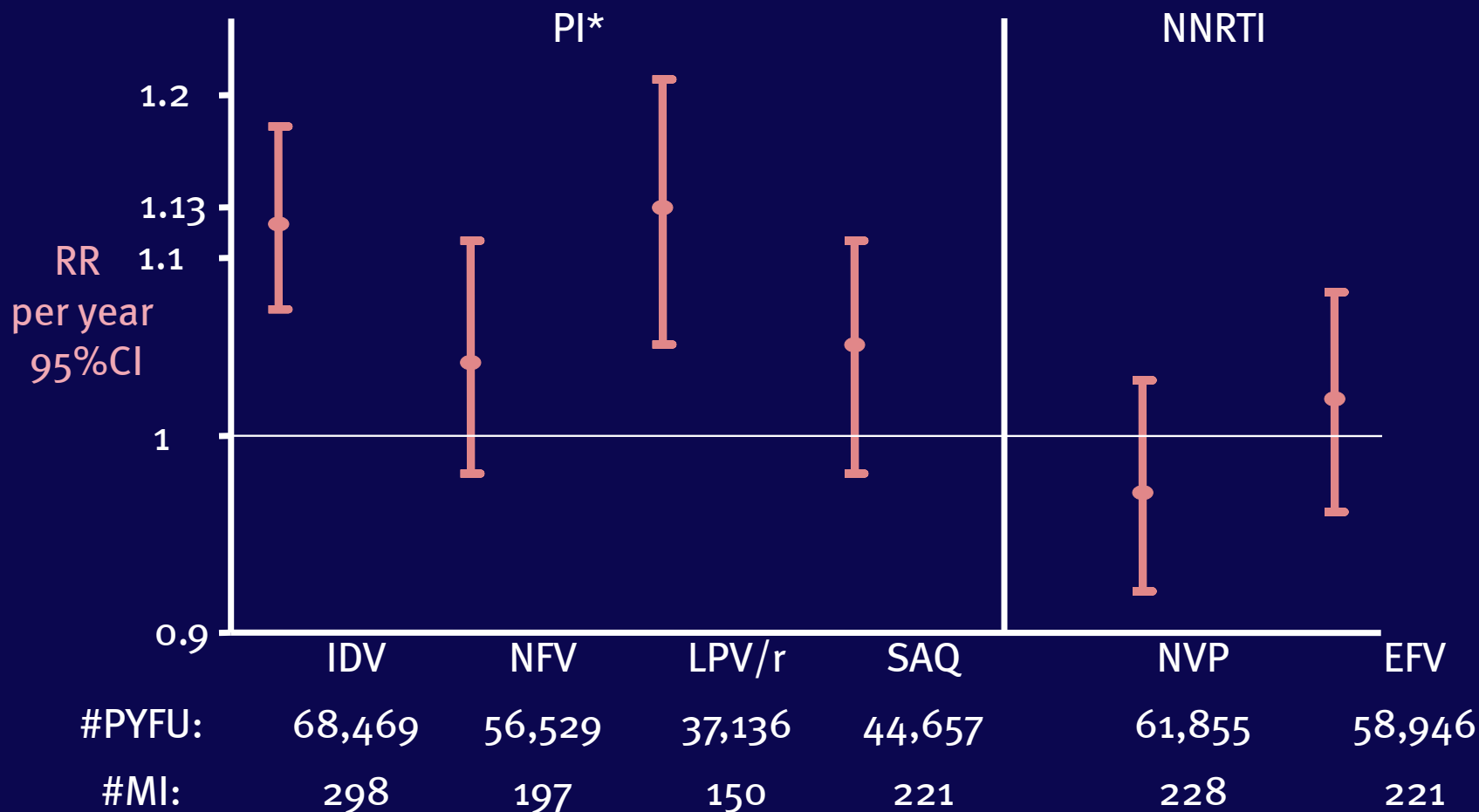
5,847

7,220

8,477

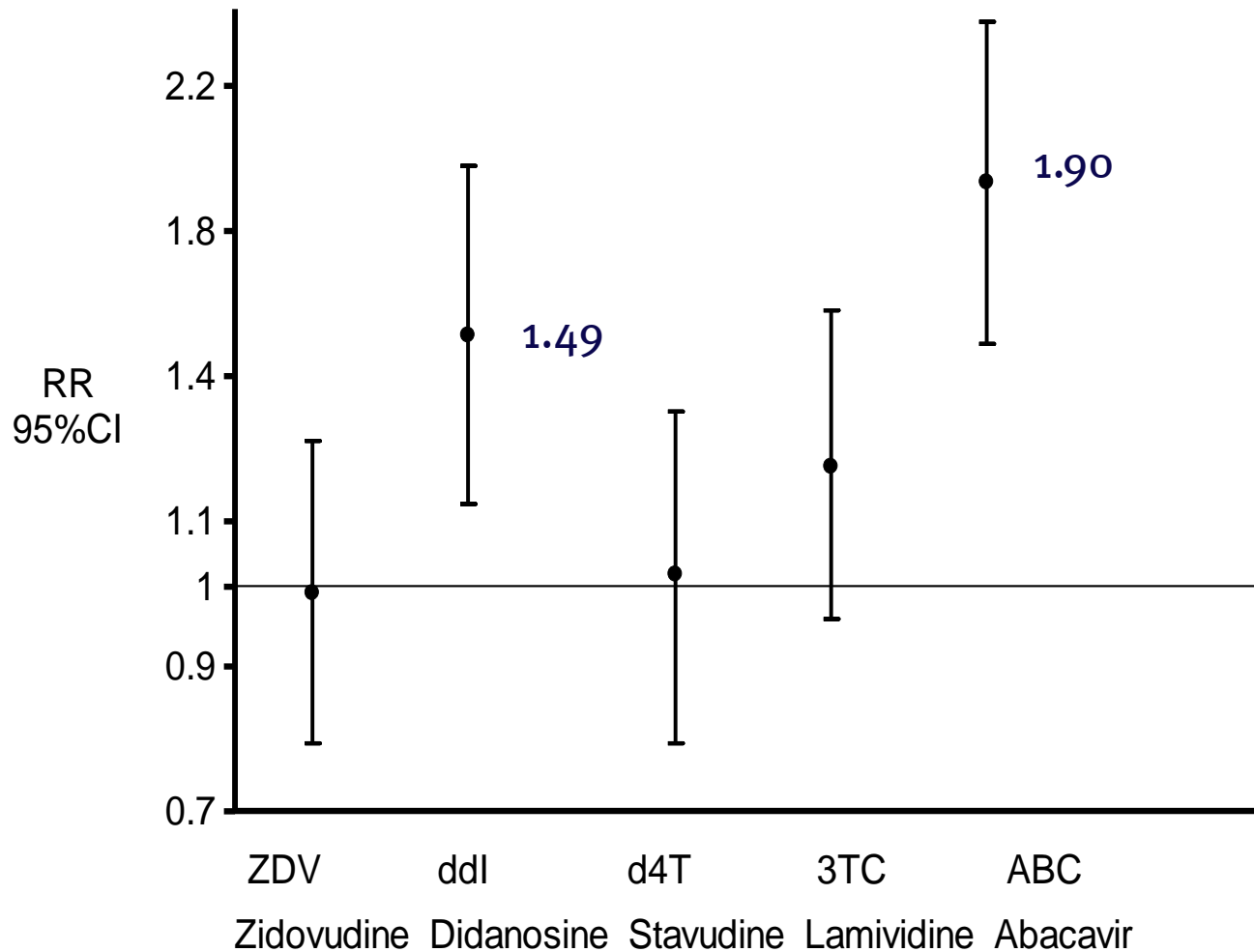
36,199

PIs/NNRTIs and risk of MI: cumulative exposure to each drug



*: Approximate test for heterogeneity: $P=0.02$

Risk of MI associated with recent exposure to 5 drugs from the NRTI drug class



Recent use=
still using or
stopped
within last 6 months

THE STUDY COORDINATING OFFICE

Copenhagen HIV Programme (CHIP)

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