British HIV Association
BHIVA

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COMPETING INTEREST OF FINANCIAL VALUE > £1,000:	
Speaker Name	**Statement**
Duncan Churchill	None
Date	**22 September 2012**

# Cardiovascular disease and antiretrovirals

Duncan Churchill
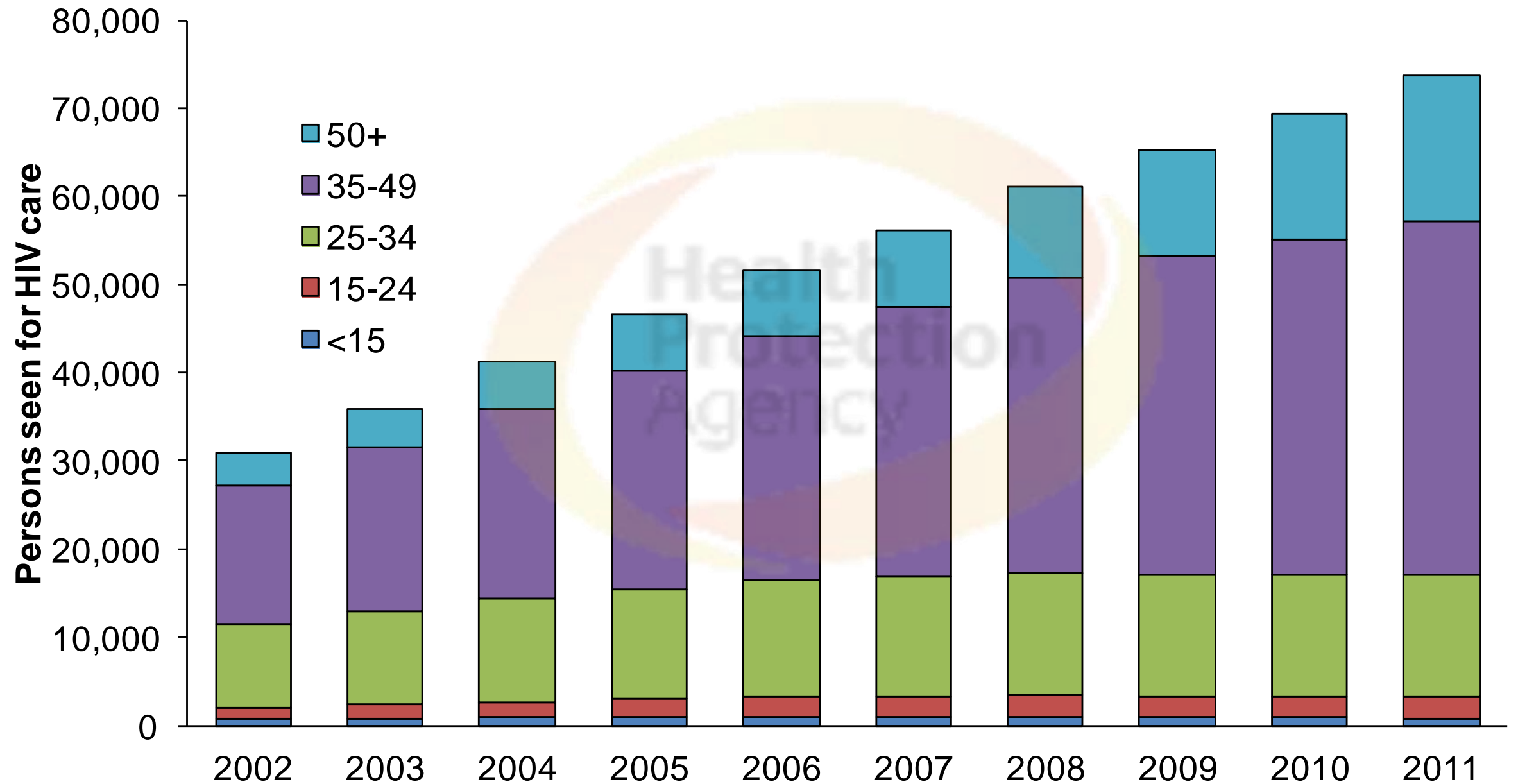
Brighton and Sussex University Hospitals NHS Trust

- Should we start ARVs earlier in people with high CVD risk?

- How should we measure CVD risk?

- Should we modify ARVs in people with high CVD risk?

New HIV and AIDS diagnoses, people living with diagnosed HIV, and deaths: United Kingdom, 2001-2010
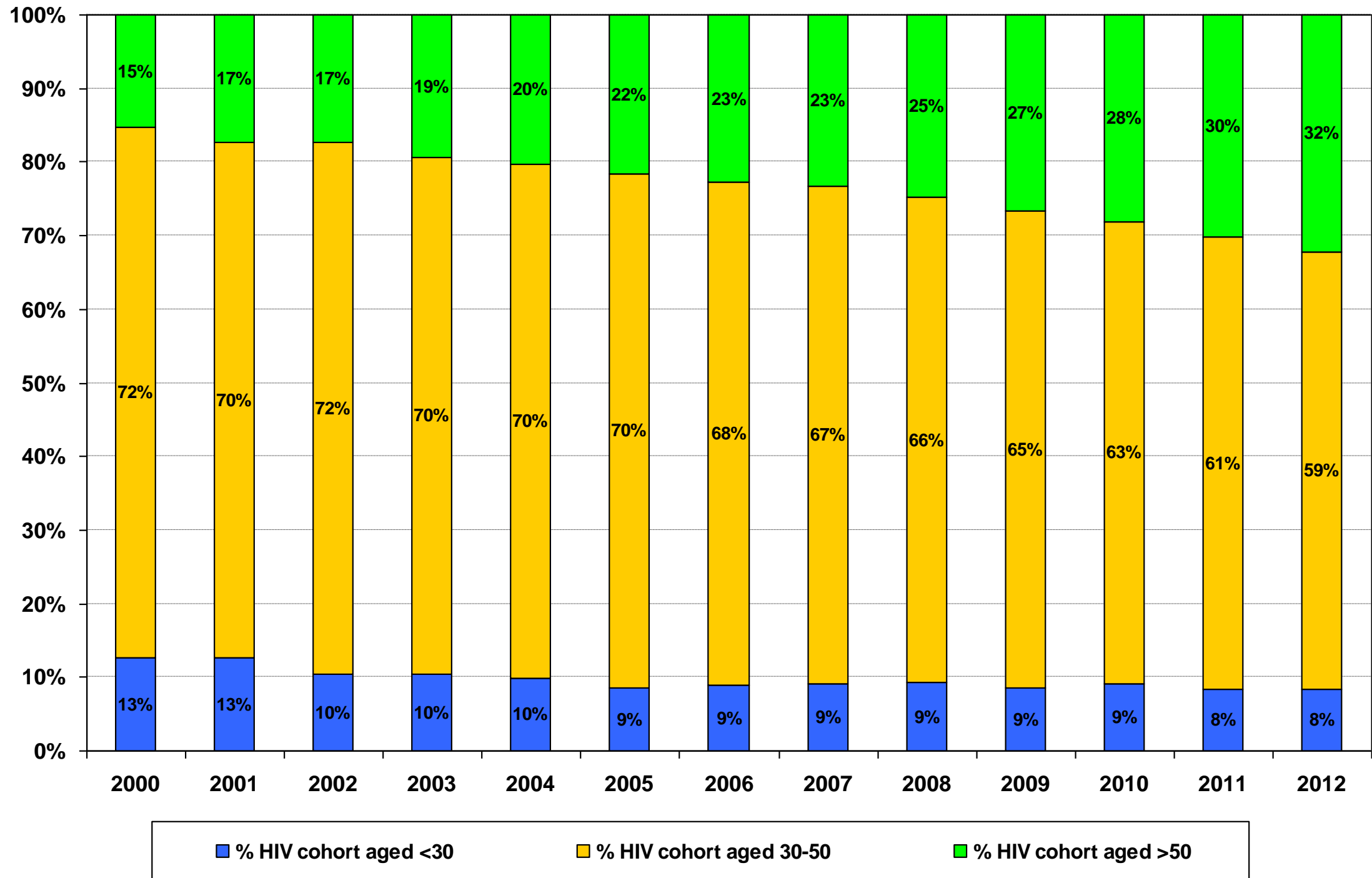
HIV and STI Department, Health Protection Agency - Colindale

Health Protection Agency
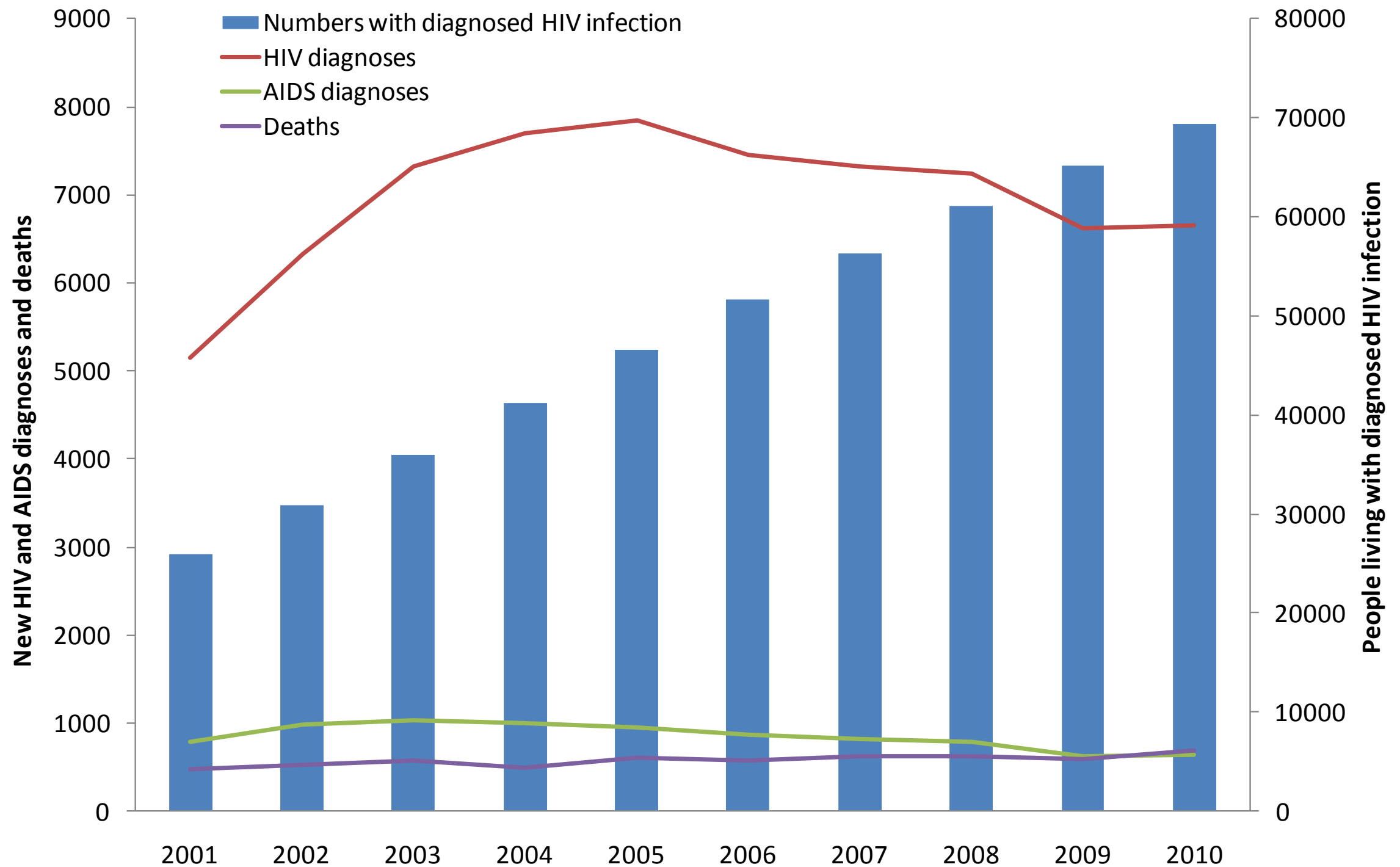
HIV diagnosed persons seen for HIV care by age group*: UK, 2002-2011

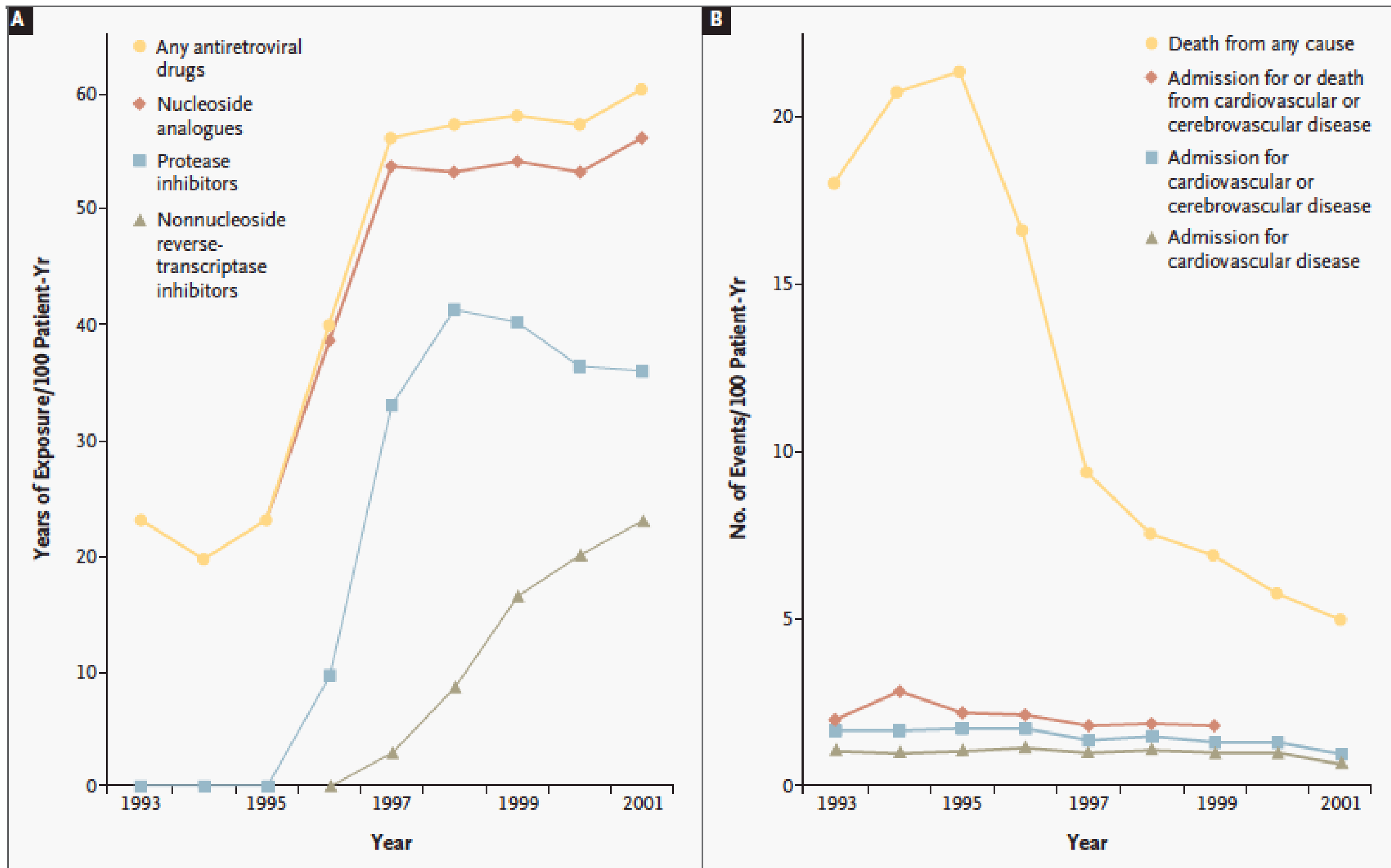*Excludes persons with age not reported, 15 in 2002 and 0 in 2011.

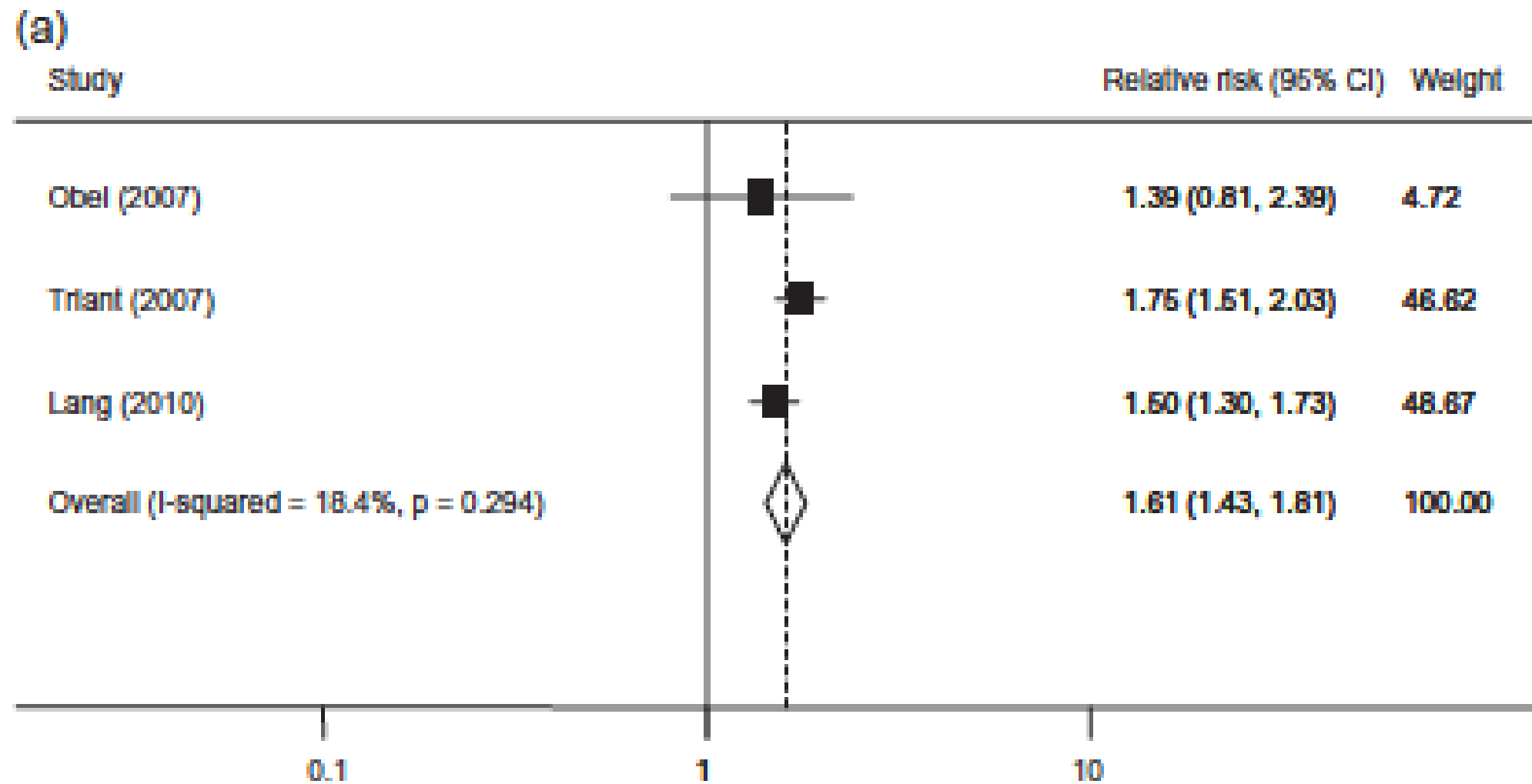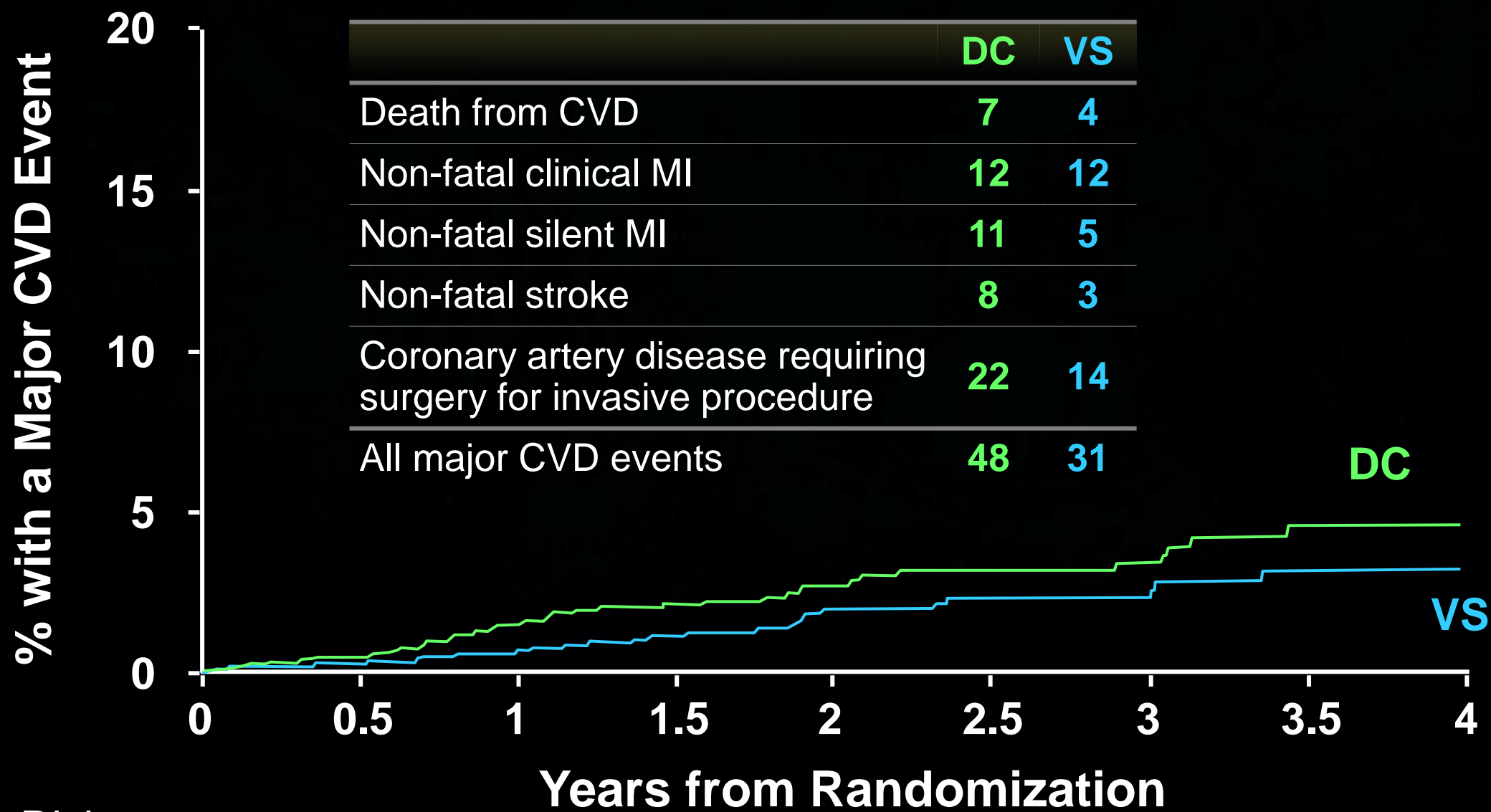HIV and STI Department, Health Protection Agency - Colindale

Health Protection Agency

Brighton cohort

Figure 1. Changing Rates of Use of Antiretroviral Drugs (Panel A) and Vascular Events and Death (Panel B).

Bozzette et al., NEJM 2003; 348: 702-710

Increased risk of CVD in HIV

(a)

Study	Relative risk (95% CI)	Weight
Obel (2007)	1.39 (0.81, 2.39)	4.72
Triant (2007)	1.75 (1.51, 2.03)	46.62
Lang (2010)	1.50 (1.30, 1.73)	48.67
Overall (I-squared = 18.4%, p = 0.294)	1.61 (1.43, 1.81)	100.00

Islam et al. HIV Medicine 2012, 13: 453-468

Should people with high CVD risk start antiretrovirals earlier?

Risk of CVD with ART Interruptions

	DC	VS
Death from CVD	7	4
Non-fatal clinical MI	12	12
Non-fatal silent MI	11	5
Non-fatal stroke	8	3
Coronary artery disease requiring surgery for invasive procedure	22	14
All major CVD events	48	31

No. at Risk

DC	2752	1306	713	379	10
VS	2720	1292	696	377	10

Baseline characteristics of deaths + controls in SMART

	Deaths (n=85)	Controls (n=170)	P-value
Age (median)	50	48	0.007
CD4 (median)	545	614	0.03
Prior AIDS (%)	31.8	26.5	0.36
Current smoker (%)	57.6	31.8	0.0001
Diabetes (%)	25.9	14.7	0.03
Antihypertensive medication (%)	38.8	25.3	0.02
Prior CVD (%)	11.8	4.7	0.04

7/85 deaths due to AIDS

Kuller et al. CROI 2008

Should people with high CVD risk start ARVs earlier?
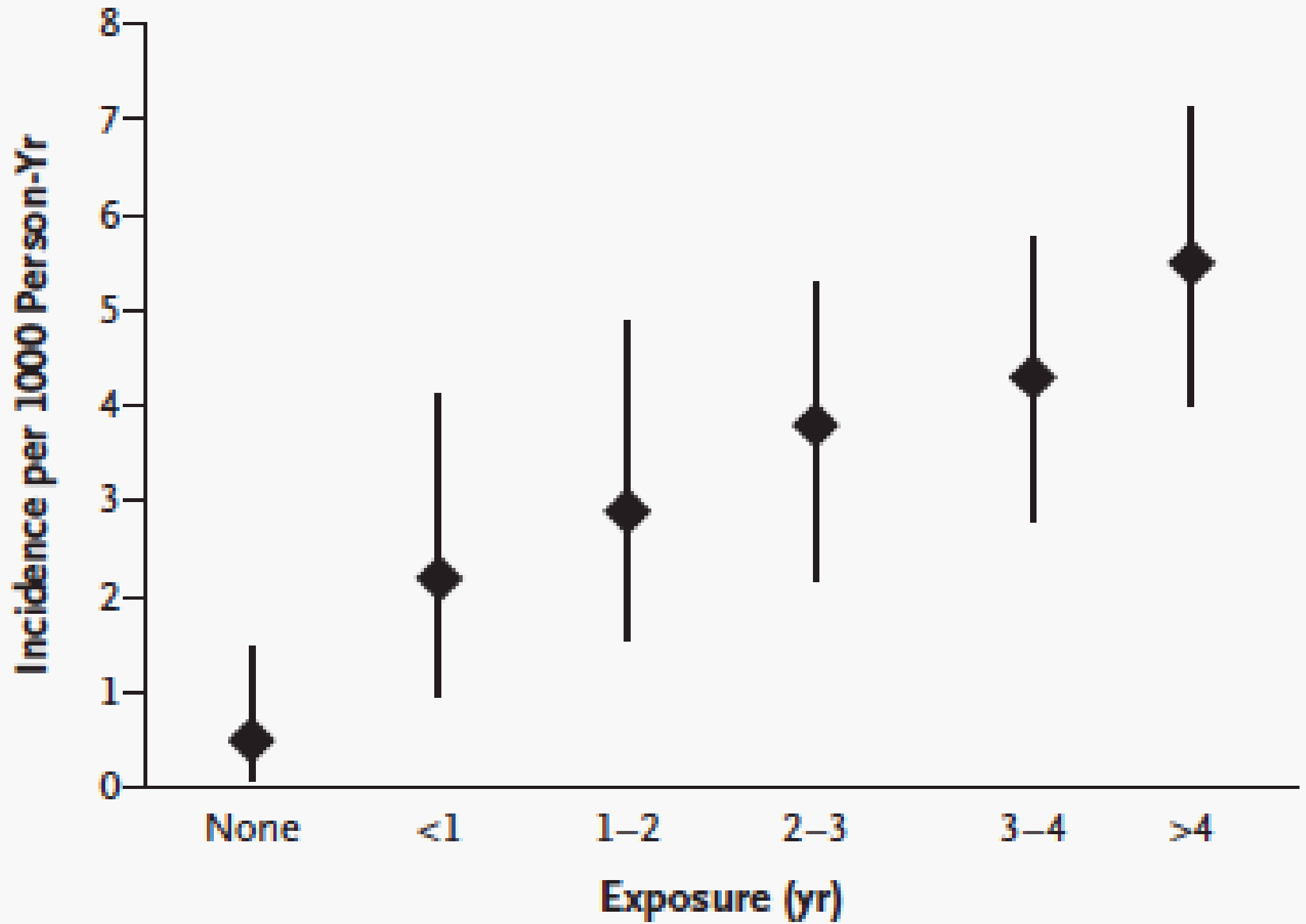
- SMART
  - Virological suppression associated with reduced CVD events (not significant)

- HOPS
  - CD4 <350 → greater risk of CVD
  - CD4 350-500 → no increased risk

- D:A:D
  - Treated HIV associated with <u>increased</u> risk of MI
  - Longer treatment associated with increased risk

Incidence per 1000 Person-Yr

8
7
6
5
4
3
2
1
0

Exposure (yr)

None   <1   1–2   2–3   3–4   >4

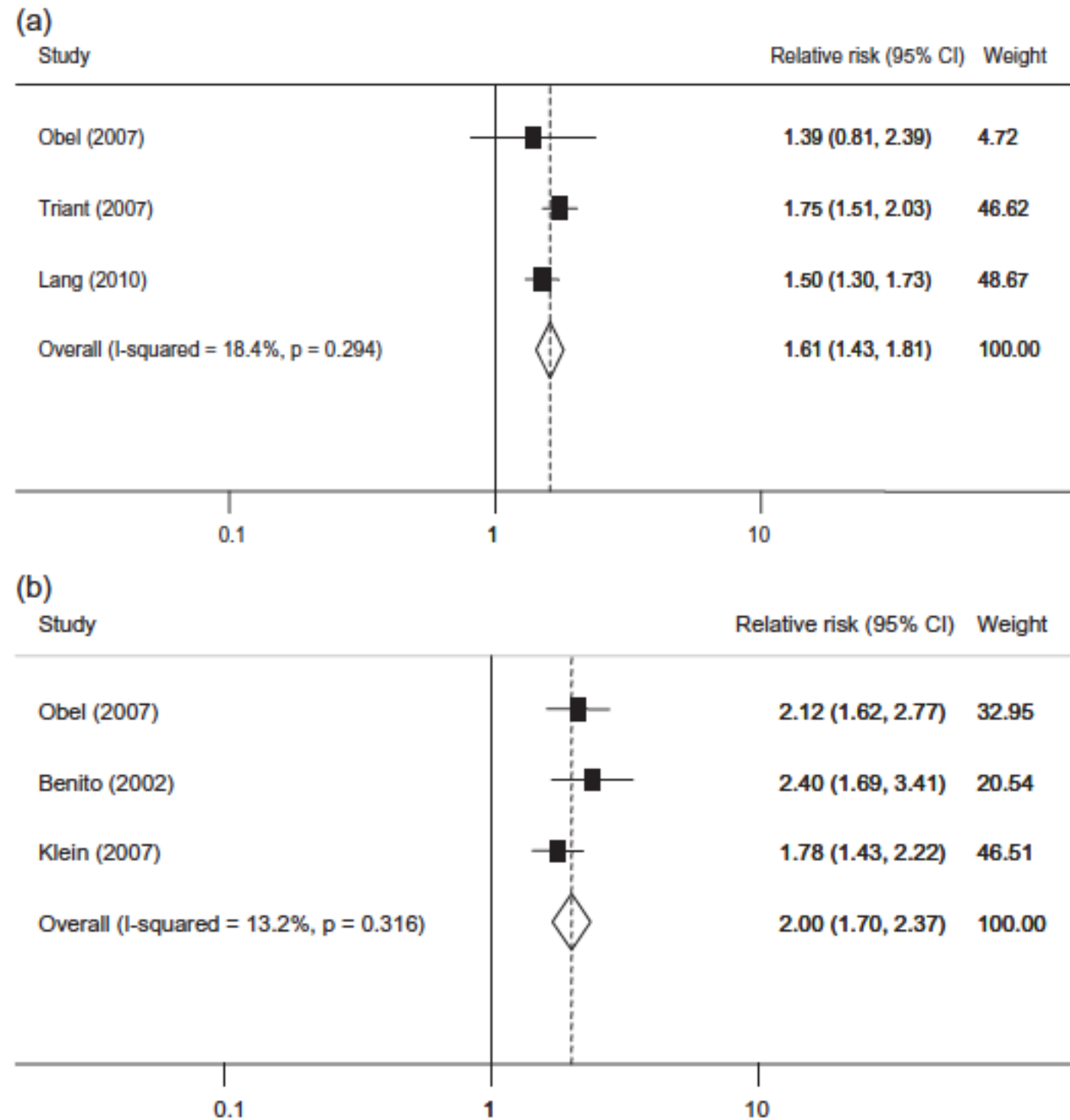|	None	<1	1–2	2–3	3–4	>4
No. of events	3	9	14	22	31	47
No. of person-years	5714	4140	4801	5847	7220	8477

Fig. 2 Forest plots of studies and pooled estimate of relative risk of cardiovascular disease (a) in people living with HIV (PLHIV) versus HIV-uninfected people and (b) in PLHIV exposed to antiretroviral treatment versus HIV-uninfected people. CI, confidence interval.

- Should we start ARVs earlier in people with high CVD risk? Probably not
- How should we measure CVD risk?

Managing cardiovascular risk

BRITISH HIV ASSOCIATION GUIDELINES

British HIV Association guidelines for the routine investigation and monitoring of adult HIV-1-infected individuals 2011

D Asboe, C Aitken, M Boffito, C Booth, P Cane, A Fakoya, AM Geretti, P Kelleher, N Mackie, D Muir, G Murphy,
C Orkin, F Post, G Rooney, C Sabin, L Sherr, E Smit, W Tong, A Ustianowski, M Valappil, J Walsh, M Williams and
D Yirrell on behalf of the BHIVA Guidelines Subcommittee*
British HIV Association (BHIVA), BHIVA Secretariat, Mediscript Ltd, London, UK

4.5 Routine monitoring on ART

- Assessment
  - CVD risk (12-monthly)

Assessment of CVD risk
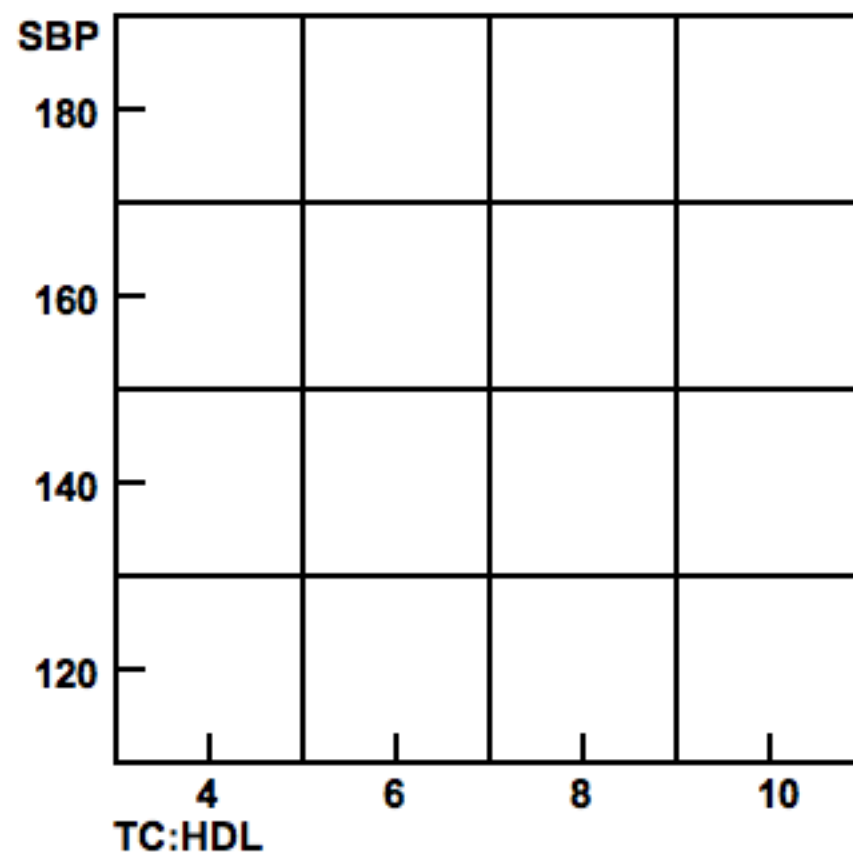
- Framingham

- CHIP

- Q risk

BHIVA monitoring guidelines 2011

cvrisk.mvm.ed.ac.uk/**calculator**/**framingham**.htm

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

ClinRisk **Welcome to the QRISK®2-2012 risk calculator: http://qrisk.org**

This calculator is only valid if you do not already have a diagnosis.

Please check out

- http://qintervention.org, which has both QRISK®2 and QDiabetes®, and will be updated to the 2012 versions of both soon; and
- http://qrisk.org/lifetime, a newer, competing risks model, which displays people's risk of heart attack or stroke over the whole of their life. QRISK®-lifetime is the risk engine used at the heart of the new JBS3 calculator.
- http://clinrisk.co.uk/ClinRisk/QRISK2_Windows_calculator.html, for a Microsoft Windows version of the QRISK®2-2012 calculator licenced for commercial/healthcare use.
- The App Store for an iPhone and iPad version of the calculator. The 2012 update has just been released.

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About you

Age (30-84): `64`

Sex: ⦿ Male ○ Female

Ethnicity: `White or not stated ▾`

UK postcode: leave blank if unknown

Postcode: `_____`

Clinical information

Smoking status: `non-smoker ▾`

Diabetic? ☐

Angina or heart attack in a 1st degree relative < 60? ☐

Chronic kidney disease? ☐

Atrial fibrillation? ☐

On blood pressure treatment? ☐

Rheumatoid arthritis? ☐

Leave blank if unknown

Cholesterol/HDL ratio: `_____`

Systolic blood pressure (mmHg): `_____`

Body mass index

Height (cm): `_____`

Weight (kg): `_____`

Calculate risk over `10 ▾` years. `Calculate risk`

Welcome to the QRISK®2-2012 cardiovascular disease risk calculator

Welcome to the QRISK®2-2012 Web Calculator. You can use this calculator to work out your risk of having a heart attack or stroke over the next ten years by answering some simple questions. It is suitable for people who do not already have a diagnosis of heart disease or stroke.

The QRISK®2 algorithm has been developed by doctors and academics working in the UK National Health Service and is based on routinely collected data from many thousands of GPs across the country who have freely contributed data for medical research. It is updated annually each April, refitted to the latest data to remain as accurate as possible.

Whilst QRISK2 has been developed for use in the UK, it is being used internationally. For non-UK use, if the postcode field is left blank the score will be calculated using an average value. Users should note, however, that CVD risk is likely to be under-estimated in patients from deprived areas and over-estimated for patients from affluent areas. All medical decisions need to be taken by a patient in consultation with their doctor. The authors and the sponsors accept no responsibility for clinical use or misuse of these score.

The science underpinning the QRISK®2 equations has been published here:

- Predicting cardiovascular risk in England and Wales: prospective derivation and validation of QRISK2, BMJ 2008;336:1475-82.

Click here for more information on QRISK®2.

http://www.qrisk.org

- 41 year old MSM
- Ex-smoker
  - (stopped 10 cigarettes/day 10 years ago)
- BP 120/82
- Total cholesterol 4.3
- HDL cholesterol 1.3

Heart

JBS 2:
JOINT BRITISH SOCIETIES' GUIDELINES ON PREVENTION OF CARDIOVASCULAR DISEASE IN CLINICAL PRACTICE

Prepared by:
British Cardiac Society
British Hypertension Society
Diabetes UK
HEART UK
*Primary Care Cardiovascular Society*
The Stroke Association

www.heartjnl.com

BMJ

JBS2 - Thresholds for intervention

- Everyone:
  - Stop smoking
  - Increase aerobic exercise
  - Achieve optimal weight and weight distribution
  - Make healthier food choices

- Clinical evidence of CVD
- Diabetes mellitus
- CVD risk of >20%
- BP > 160 systolic, or >100 diastolic or target organ damage
- Cholesterol: HDL >6.0
- Familial dyslipidaemia
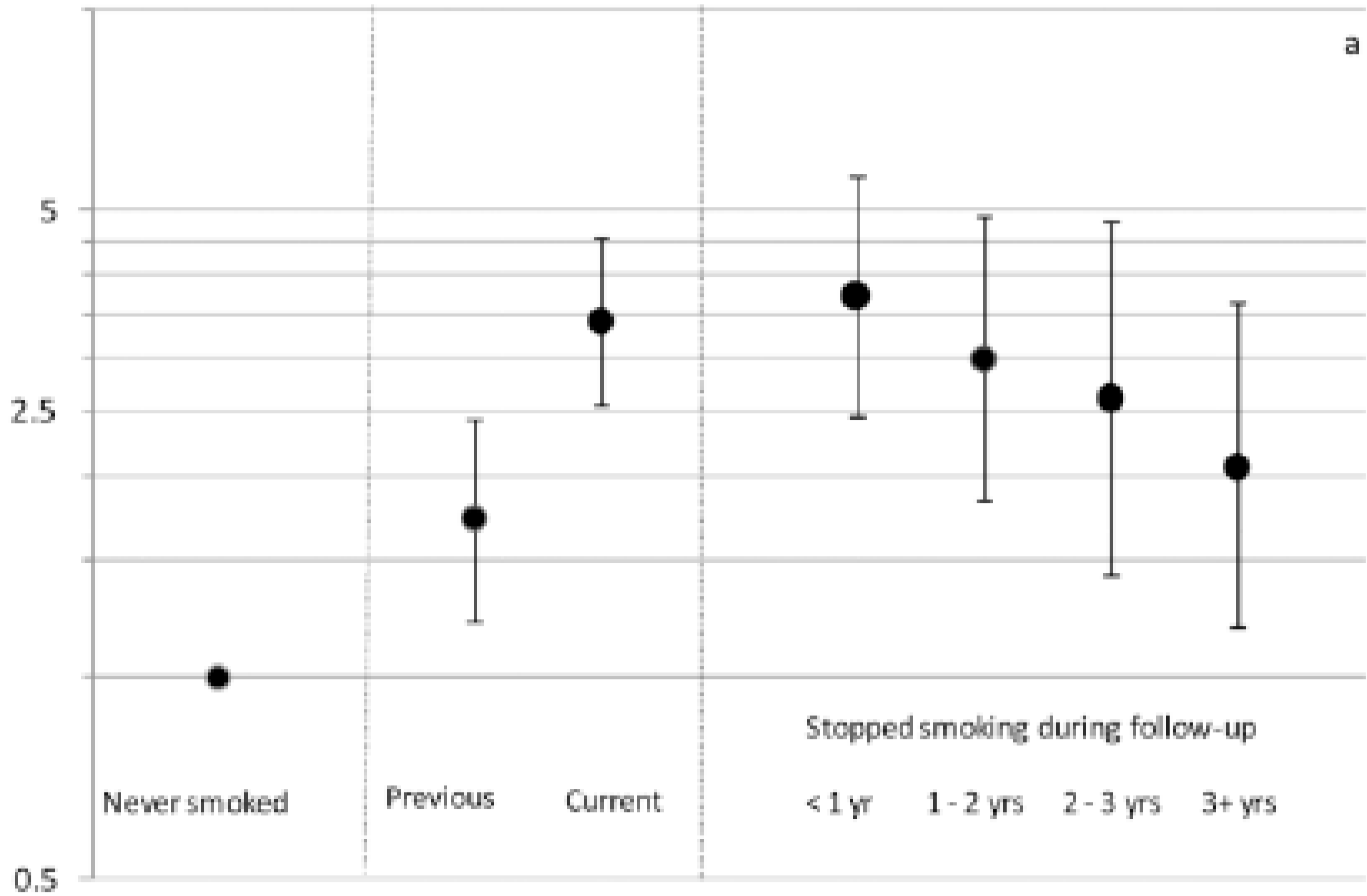
Incidence rate ratio of MI related to smoking history in the D:A:D study

How would you assess CVD risk?

- Framingham calculator
- JBS/BNF calculator
- CHIP CVD risk assessment tool
- Qrisk
- Other
- Don't know
- I wouldn't – his risk is low

- Vote

Which calculator?

	Advantage	Disadvantage
Framingham	Different time scales Different end points	Not validated for other populations
JBS2	Corresponds to JBS guidance	
ASSIGN	Tailored to Scottish population Uses family history, deprivation	
CHIP	Developed for HIV Incorporates drug history	
Qrisk	Widely used in general practice Incorporates postcode, rheumatoid, diabetes, renal disease etc.	

The University of Edinburgh
Cardiovascular Risk Calculator

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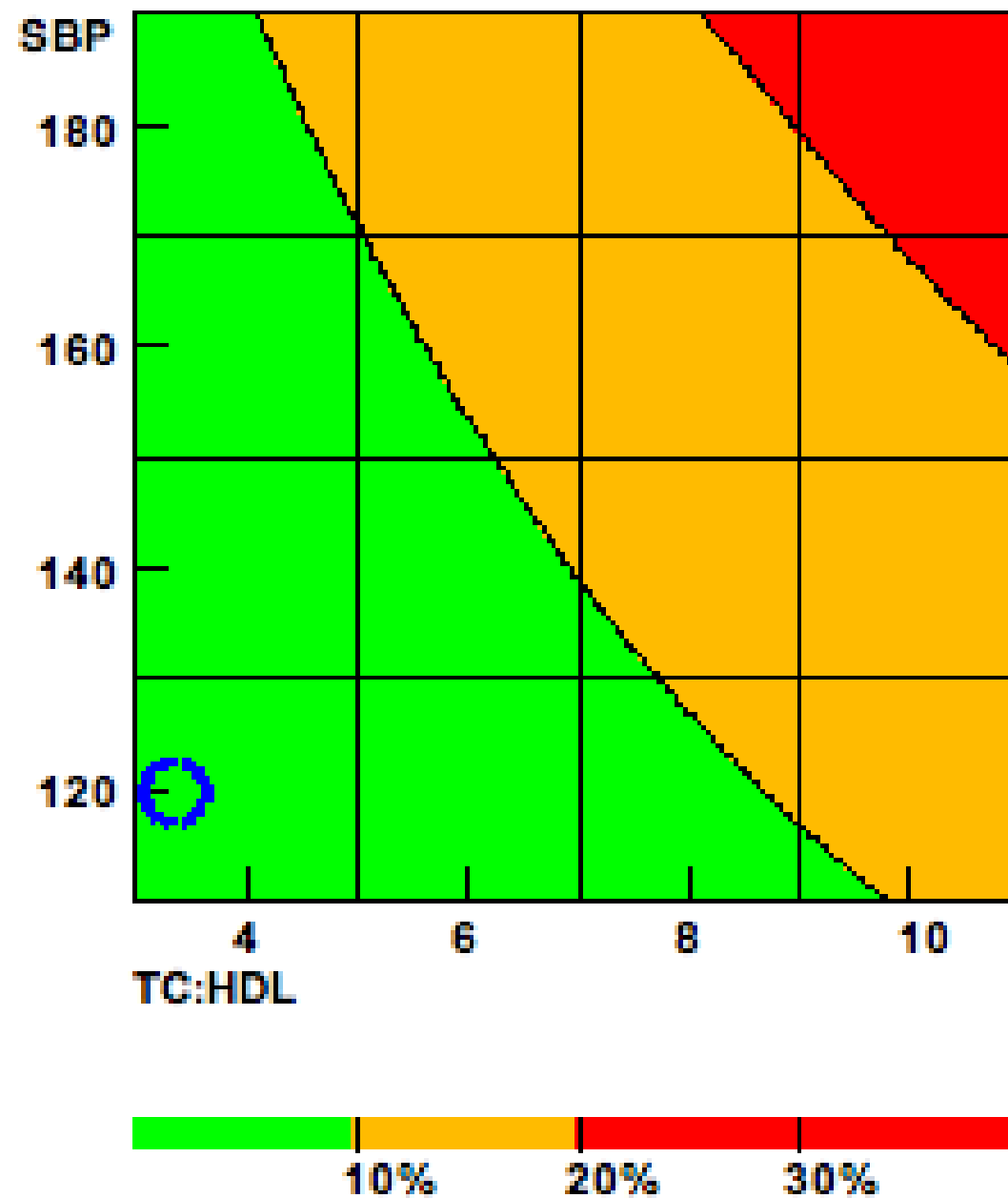
Old calculators

Excel calculator

Help

Print friendly

Chart style

BNF charts

Smiley faces

Comparison bars

Thermometer

SBP

180

160

140

120

4   6   8   10

TC:HDL

10%   20%   30%

Calculate risk of CVD (BNF) ⬍

Time period 10 years

Age 41 years

☑ Male

☐ Smoker

Systolic Blood Pressure 120 mmHg

Cholesterol

Total 4.3 : HDL 1.3 mmol/L

Use pre-treatment BP/cholesterol values

Probability of developing cardiovascular disease in next 10 years is 2.5%

Calculated using Joint British Societies (BNF) equation

Risk calculator graphs based on Joint British Societies risk prediction charts. Written by Dr Rupert Payne © 2005-2010.

Last modified: 19 May 2010

smoker will be at lower risk than an ex-smoker (especially in the early years following smoking cessation). The "non-smoker" bar is only visible if the current patient is a smoker.

Thermometer

The thermometer provides a similar means of comparing risk values to that of the comparison bar graph described above, with similar caveats. The colour coding corresponds to that used in the BNF-style charts. "Non-smoker" will only appear if the patient is a smoker. The effects of a lower BP and statin treatment are only shown if the current patient risk is out-with the lowest (green) risk area.

Important notes on using the charts

These charts are designed as an aid to making clinical decisions, with respect to the use of lifestyle and drug interventions for modifying risk. They should **NOT** replace clinical judgement. For a detailed overview, users are advised to read the relevant section of the BNF. Users of the ASSIGN score are also referred to the SIGN-97 guidelines.

- Use of charts is inappropriate in patients with existing disease (e.g. renal dysfunction, CHD, etc.)
- Treatment of persistently/marked elevated BP or TC:HDL ratio is generally indicated regardless of estimated risk
- Smoking status should reflect lifetime tobacco exposure, rather than current use
- LVH refers to the original Framingham ECG criteria. It is important to distinguish this from echocardiographic findings of LVH, which are more common, or other ECG criteria such as the Sokolow-Lyon criteria or those employed by automated ECG reporting systems
- Decision to treat with drugs should be based on repeated assessment of risk factors rather than a single measurement
- Risk estimates are based on untreated levels of BP and cholesterol, and can only be used as a guide in persons already receiving treatment
- Risk will be underestimated in the following groups
    - Elevated triglycerides (>1.7mmol/L)
    - Premature menopause
    - Impaired glycaemic function, despite no overt diabetes
- For Framingham/BNF calculations, a family history of premature CVD will also result in underestimation of risk
- Risk estimates have not been validated in ethnic minorities

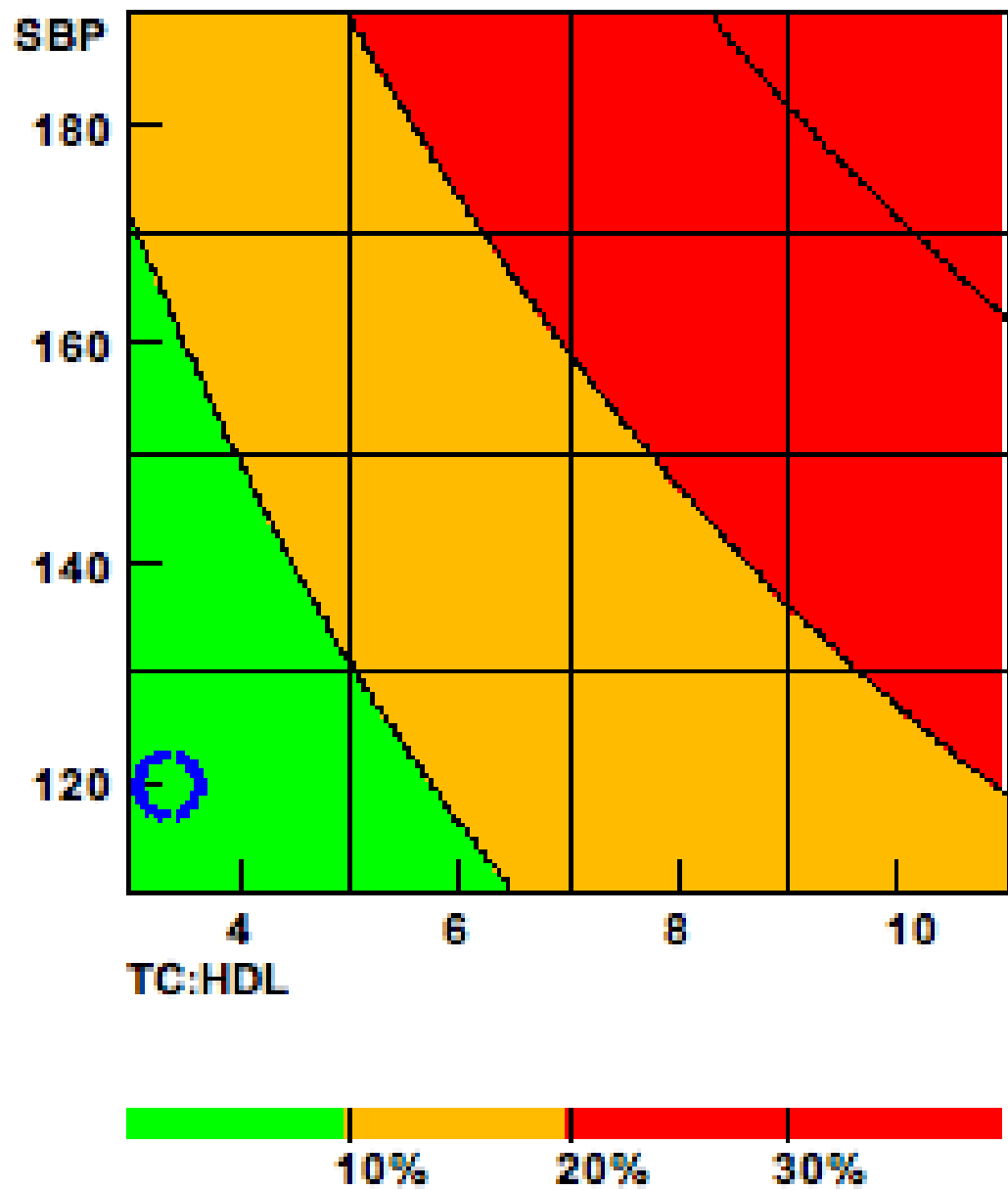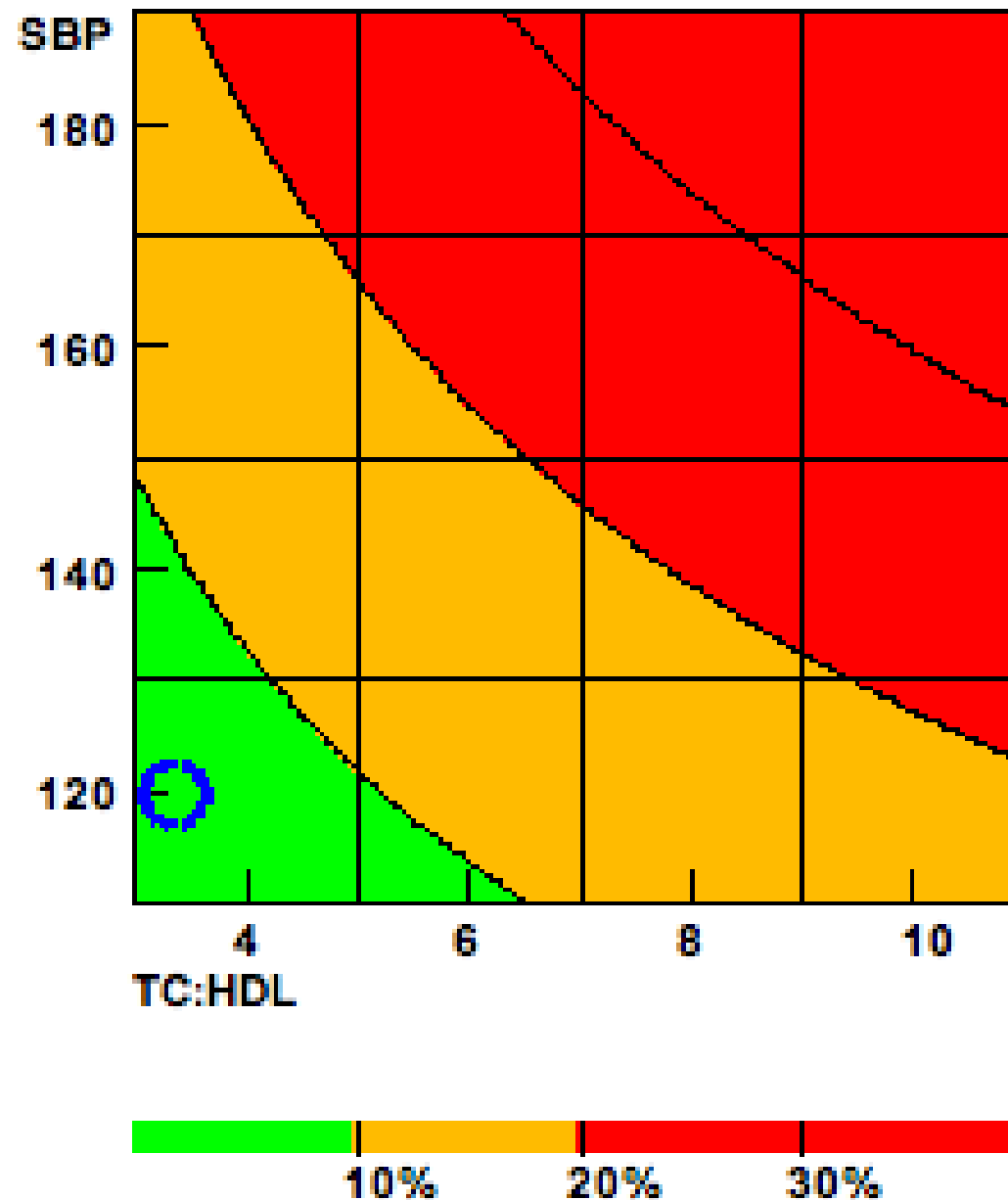# The University of Edinburgh
Cardiovascular Risk Calculator

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Chart style

BNF charts
Smiley faces
Comparison bars
Thermometer

SBP

180

160

140

120

4   6   8   10

TC:HDL

10%   20%   30%

Calculate risk of [CVD (Framingham) $\updownarrow$]

Time period [10] years

Age [41] years
☑ Male

☑ Smoker
☐ Diabetes
☐ LVH (strict Framingham criteria)

Systolic Blood Pressure [120] mmHg
Cholesterol
Total [4.3] : HDL [1.3] mmol/L
Use pre-treatment BP/cholesterol values

Probability of developing cardiovascular disease in next 10 years is 6.3%

Calculated using Framingham equation

http://www.qrisk.org/index.php

Google

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QRISK2-2012

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About you

Age (30-84): 41

Sex: ● Male   ○ Female

Ethnicity: White or not stated

UK postcode: leave blank if unknown

Postcode: BN13FS

Clinical information

Smoking status: ex-smoker

Diabetic? ☐

Angina or heart attack in a 1st degree relative < 60? ☐

Chronic kidney disease? ☐

Atrial fibrillation? ☐

On blood pressure treatment? ☐

Rheumatoid arthritis? ☐

Leave blank if unknown

Cholesterol/HDL ratio: 3.3

Systolic blood pressure (mmHg): 120

Body mass index

Height (cm): 175.9

Weight (kg): 82

Calculate risk over 10 years.   Calculate risk
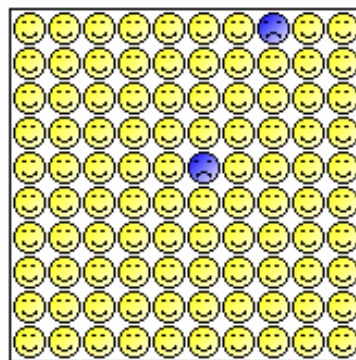
Your results

Your risk of having a heart attack or stroke within the next 10 years is:

2.4%

In other words, in a crowd of 100 people with the same risk factors as you, 2 are likely to have a heart attack or stroke within the next 10 years.

Risk of

heart attack or stroke

Your score has been calculated using the data you entered.

Your body mass index was calculated as 26.5 kg/m^2.

How does your 10-year score compare?

Your score	
Your 10-year QRISK®2 score	2.4%
The score of a typical person with the same age, sex, and ethnicity[*]	2.3%
Relative risk[**]	1.1
Your QRISKage[TM***]	42

[*] This is derived from all people of your age, sex and ethnic group, whatever their clinical information.

[**] Your relative risk is your risk divided by the typical person's risk.

[***] Your QRISKage[TM] is the age at which a typical person of your sex and ethnicity has your 10-year QRISK®2 score.

Internet   100%

- Should we start ARVs earlier in people with high CVD risk? Probably not

- How should we measure CVD risk? That depends

- Should we modify ARVs in people with high CVD risk?

Managing cardiovascular risk

British HIV Association guidelines for the treatment of HIV-1-positive adults with antiretroviral therapy 2012

2.1.6.15 *Cardiovascular disease: what to start*

8.6.4   We suggest avoiding: ABC, FPV/r and LPV/r in patients with a high cardiovascular disease (CVD) risk, 2C
         if acceptable alternative ARV drugs are available.

D:A:D: Recent and/or Cumulative Antiretroviral Exposure and Risk of MI
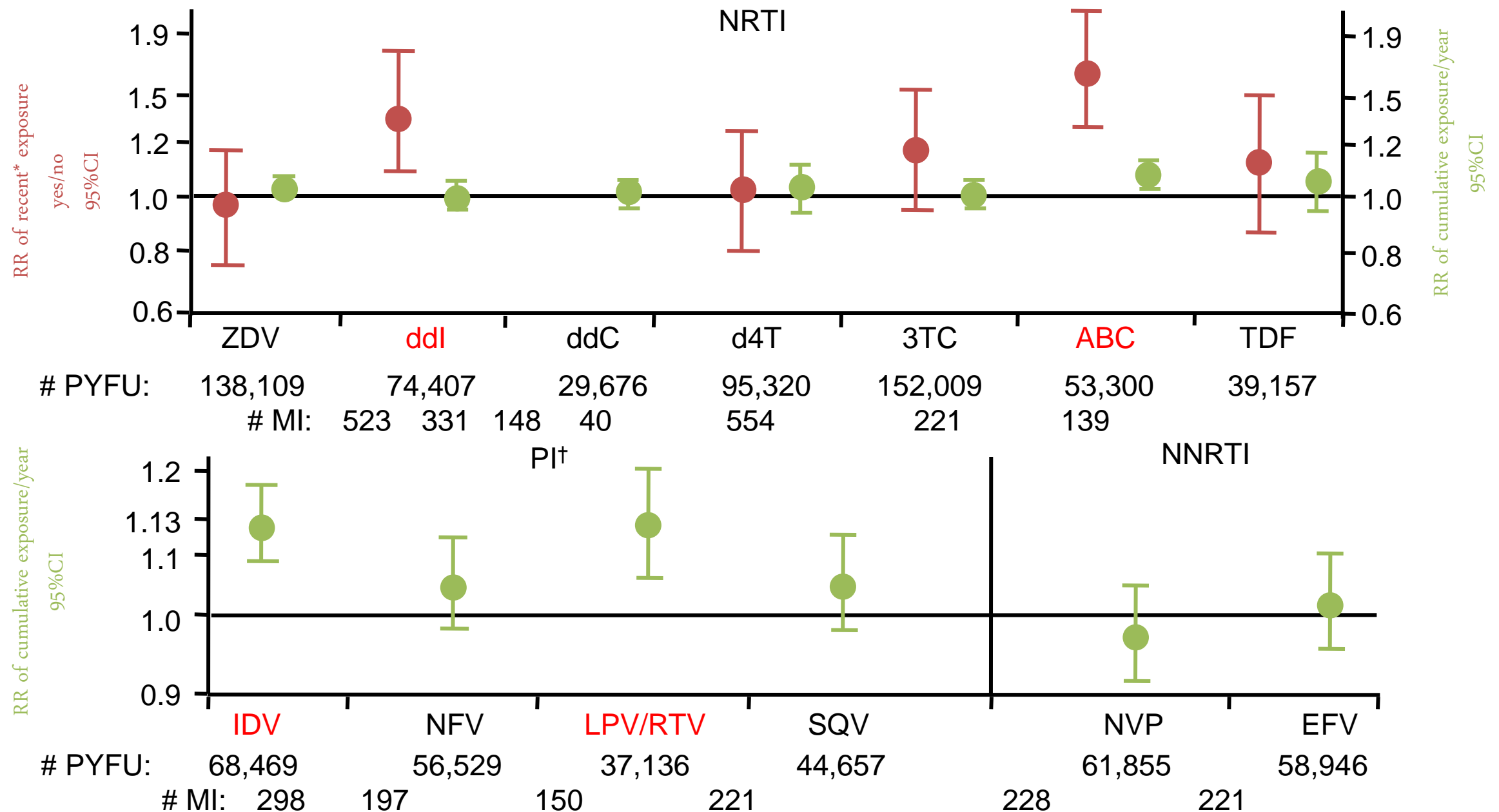
*Current or within last 6 months. †Approximate test for heterogeneity: $P = 0.02$

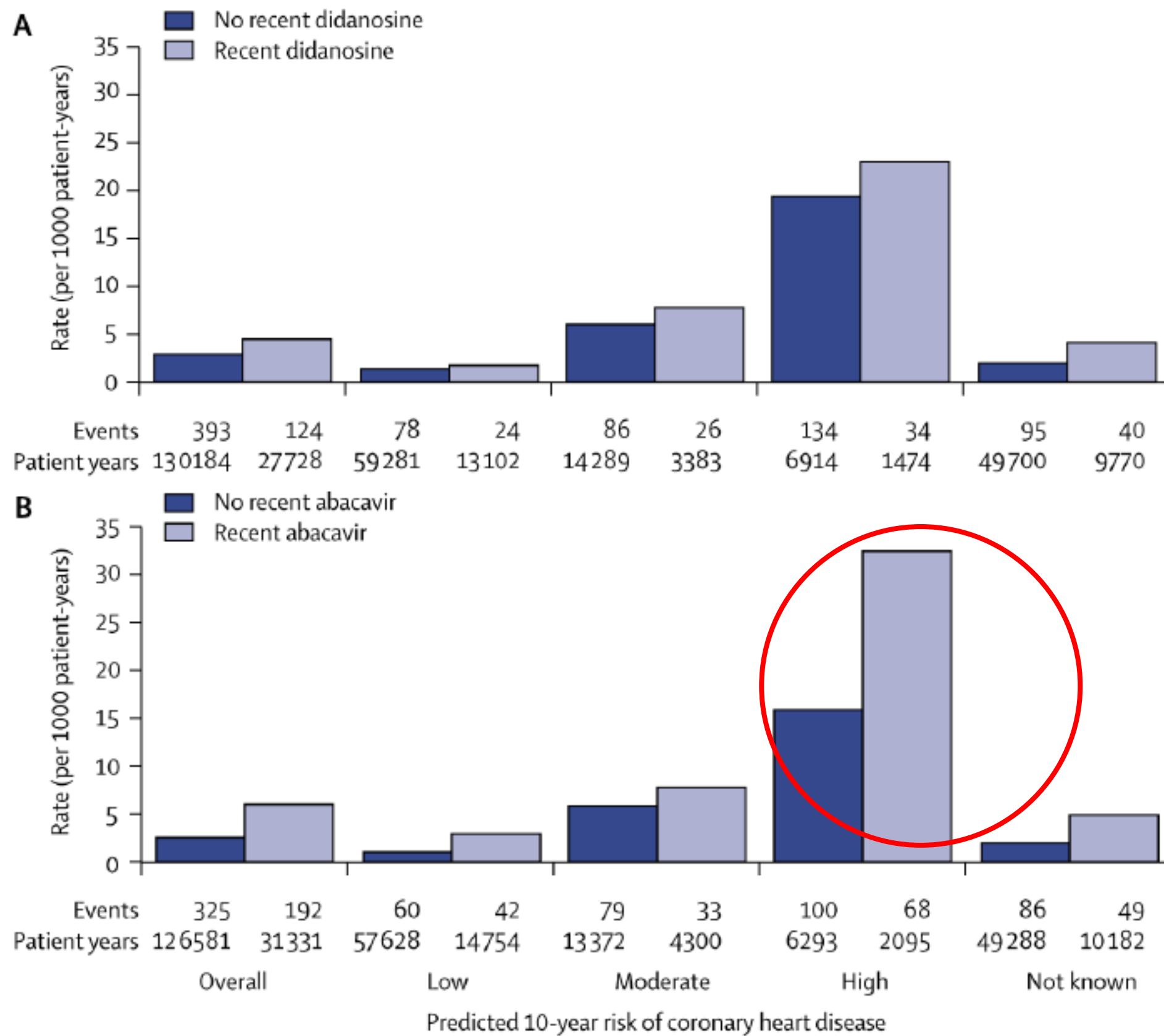Lundgren JD, et al. CROI 2009. Abstract 44LB. Graphics reproduced with permission.

Figure 1.
Rates of myocardial infarction, stratified by predicted 10-year risk of coronary heart disease, and recent use of either (A) didanosine or (B) abacavir

- 41 year old MSM
- Ex-smoker
  - (stopped 10 cigarettes/day 10 years ago)
- BP 120/82
- Total cholesterol 4.3
- HDL cholesterol 1.3
- On Kivexa and Kaletra for 9 years

Would you

- Leave him on Kivexa/Kaletra
- Switch Kivexa only
- Switch Kaletra only
- Switch both drugs

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DAD 5 Year Estimated Risk calculator ⊟

The risk during the next   5 years
                    of CHD is: 3.6%

Number of years on:

indinavir: `0`

lopinavir: `9`

Currently on:

indinavir?:   ⦿ No   ◯ Yes

lopinavir?:   ◯ No   ⦿ Yes

abacavir?:   ◯ No   ⦿ Yes

Gender: ◯ Female   ⦿ Male

Current age in years: `41`

Current cigarette smoker?:   ⦿ No   ◯ Yes

Previous cigarette smoker?:   ◯ No   ⦿ Yes

Diabetic?:   ⦿ No   ◯ Yes

Family CVD history?:   ⦿ No   ◯ Yes

Systolic blood pressure: `120`   unit: ⦿ mm/Hg ◯ cm/Hg ◯ kPa

Total cholesterol: `4.3`   unit: ⦿ mmol/L ◯ g/L ◯ g/dL ◯ mg/dL

HDL: `1.3`   unit: ⦿ mmol/L ◯ g/L ◯ g/dL ◯ mg/dL

Calculate