15th International Workshop on Adverse Drug Reactions and Co-Morbidities in HIV.

Management of Cardiovascular risk in HIV positive individuals in Europe

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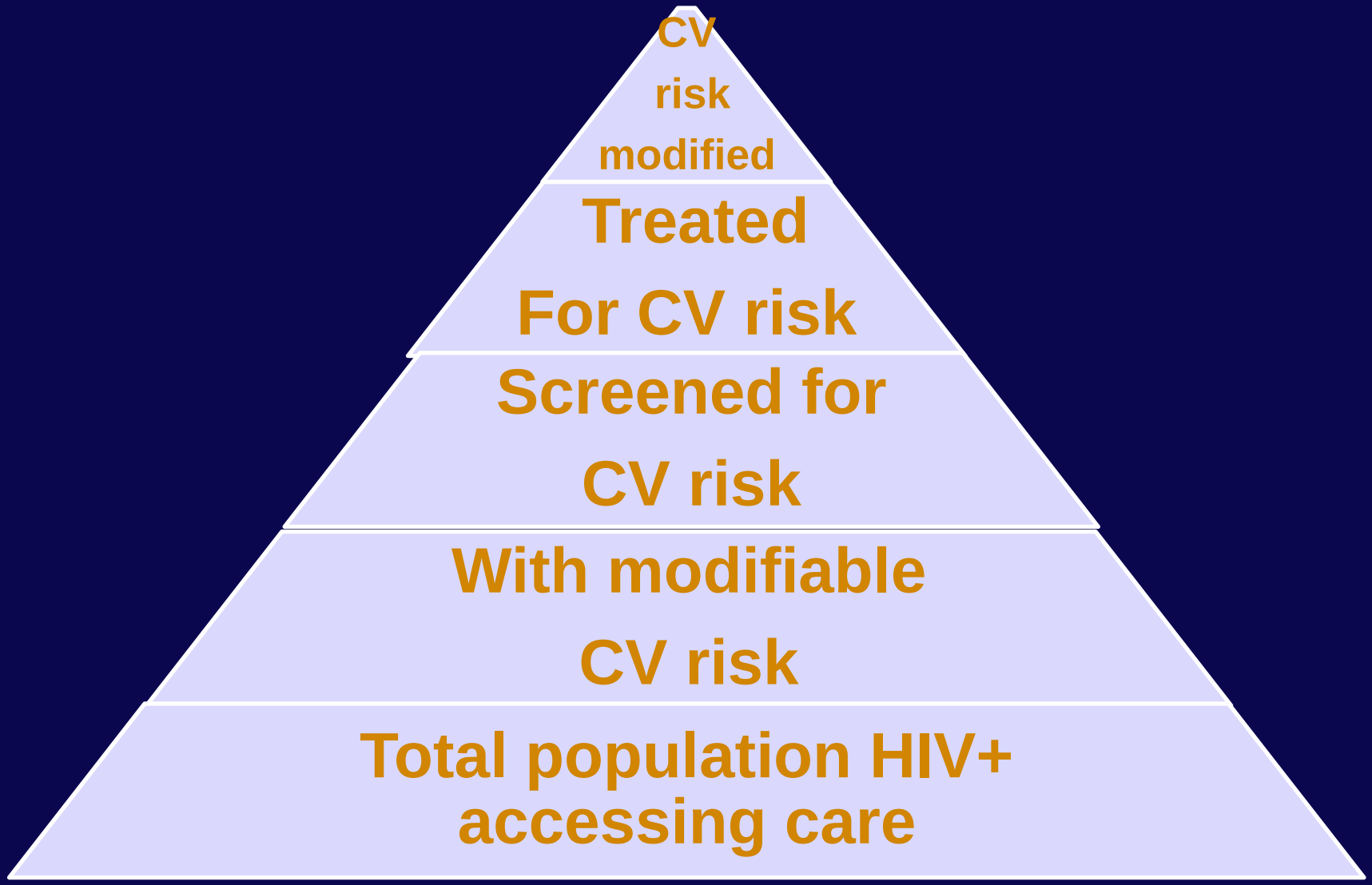
on behalf of EuroSIDA in EuroCoord

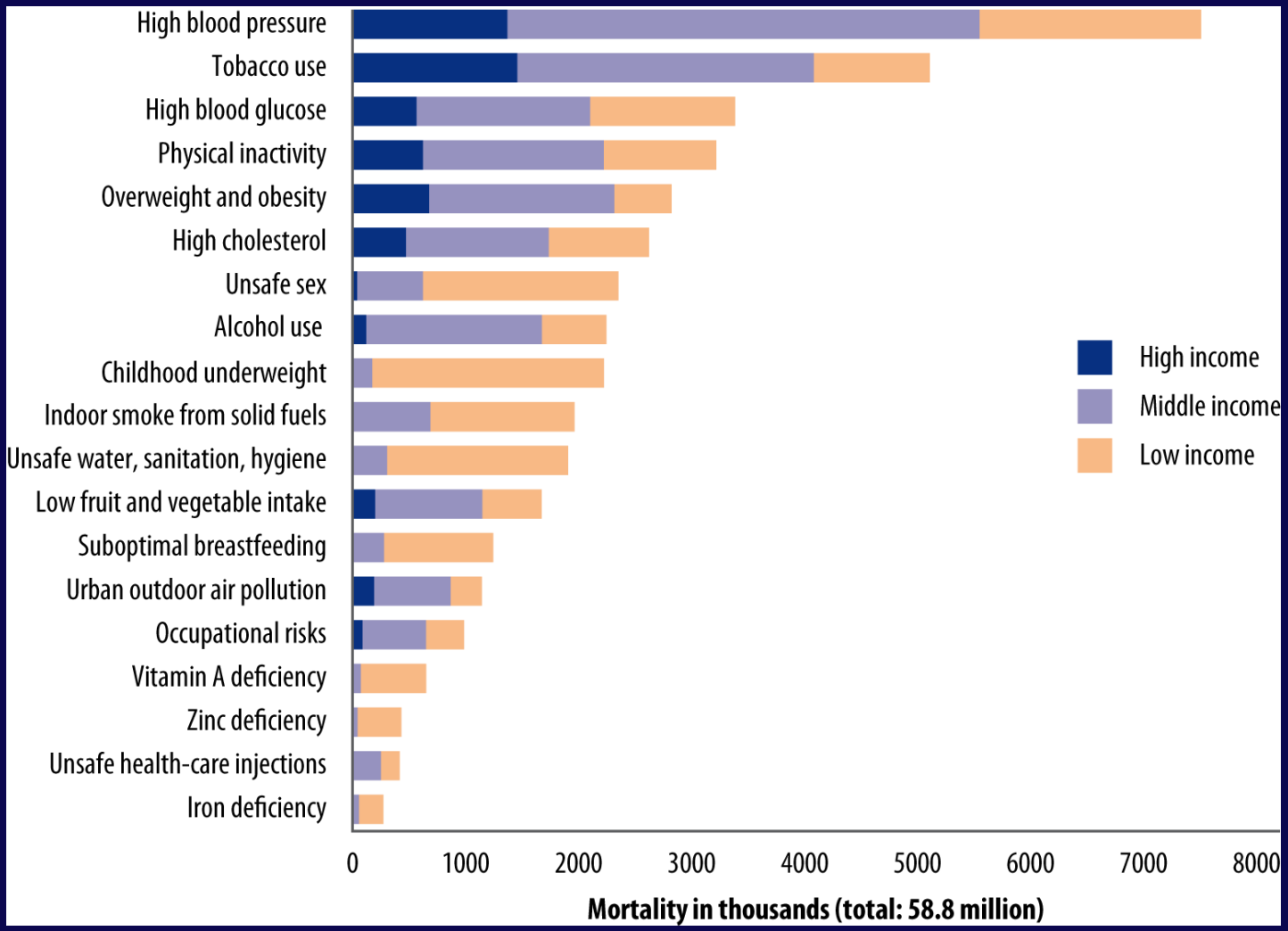
Background

- Antiretroviral therapy results in an aging cohort
- High prevalence of cardiovascular disease in HIV+
- Stepped approach to cardiovascular disease
  - Primary prevention
  - Screening for risk factors
  - Non-pharm management of modifiable risk
  - Pharmacological management of modifiable risk
  - Specialist care
- Understanding cv risk management in HIV + will inform improved care

Chronic disease paradigm for cv disease



Deaths attributed to 19 leading factors, by country income level, 2004



Aims

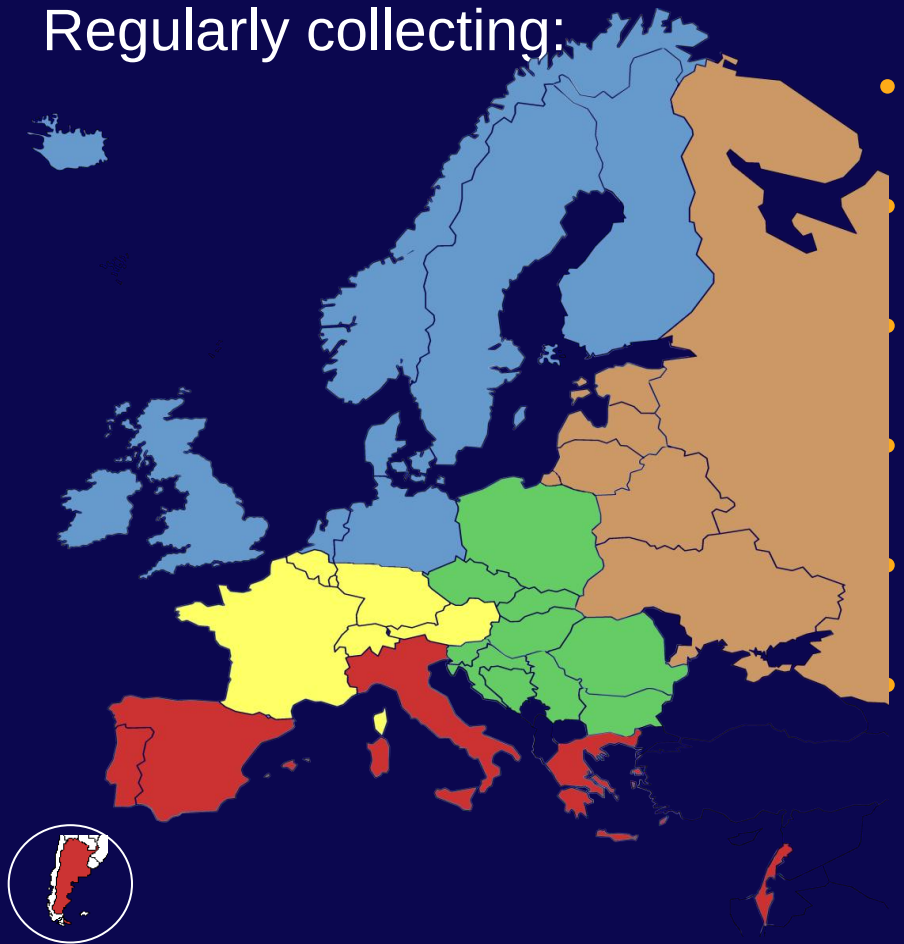
- Describe patterns of cardiovascular (CV) risk and successful CV risk modification in a European HIV Cohort

- Specific objectives
  1. Prevalence and incidence of CV risk
  2. Factors associated with CV risk
  3. Factors associated with successful CV risk modification

Methods (setting)

EuroSIDA is a large prospective cohort with 18,791 patients from 108 clinics in 34 European countries, Israel and Argentina.

Regularly collecting:



- HIV transmission risk group
- CD4 counts, HIV viral loads
- All treatment start/stop dates
- Clinical AIDS events
- Non-AIDS events (since 2001)
- Deaths and causes of death

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Methods (population)

- Population:
  - EuroSIDA patients (from 1/1/2000)
  - > 2 time points CV risk can be calculated

- Follow-up
  - Baseline: 1st date CV risk can be calculated
  - Censor: outcome of interest, month of last CV risk factor measurement, or 31/12/2011

Methods (measurement & analysis)

- Outcome variables
  1. High CV risk defined as 5-year CV risk > 5% using D.A.D. equation

     (Duration of lopinavir & Indinavir, current Abacavir, age, gender, family history of CVD, systolic blood pressure, lipid profile, smoking status and diabetes)

  2. Risk modification defined as two consecutive measurements meeting EACs guidelines

- Analysis: Poisson regression

Table 1: definitions of modifiable CV risk factors & risk modification outcomes

Modifiable CV risk factors	Clinical indication for treatment of modifiable risk (EACS guidelines)	Successful risk modification (Two consecutive measures)
Hypertension **Systolic blood pressure (BP) >140 mm Hg,** **Diastolic BP >90 mm Hg** **Antihypertensive treatment**	Treatment of BP Systolic BP >140 Diastolic BP >90 mm Hg)	 Systolic BP <140 (130 if diabetic), Diastolic BP <90 (<80 if diabetic) mm Hg
High cholesterol **Total cholesterol>6 mmol/l** **Cholesterol:HDL ratio >5** **Receiving statins**	Predicted 10 year CV risk of over 20%, diabetic, or established CV disease	 Lowering total cholesterol to less than 4 mmol/l
Current smoker	Current smoker	Stopped smoking
Overweight **Body Mass Index (BMI) over 25 kg/m^2**	Diet and exercise	Marker of lifestyle change Lowering BMI to less than 25 kg/m^2

Modifiable Risk Factors N=5719

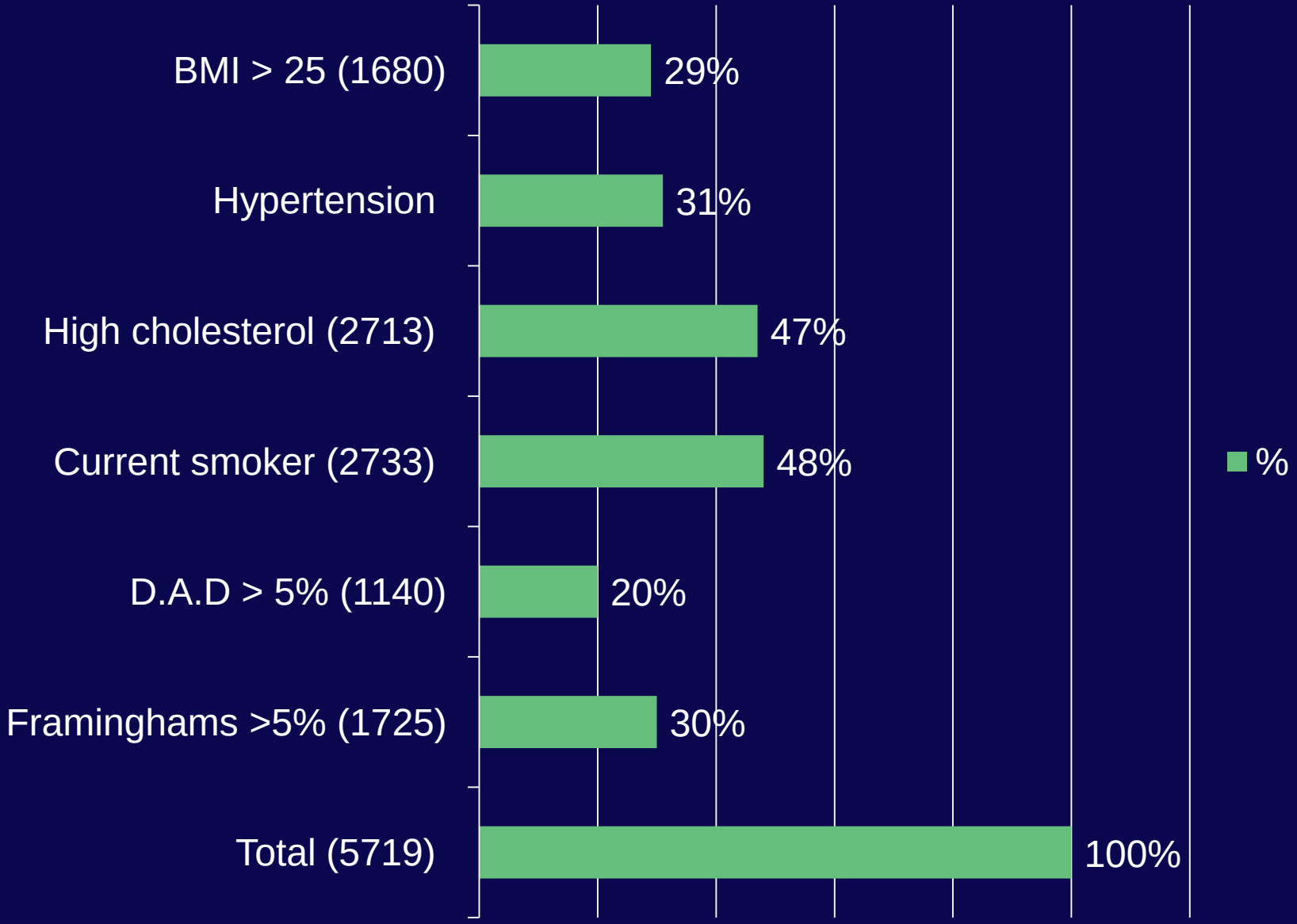

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Table 2. Baseline characteristics according to predicted CV risk

		Total	(n/N %)	5 year DAD risk > 5% (n/N%)	
Total (N)		5719		1140	
Age (Median ,IQR)		41	(36-50)	54	(48-61)
Gender	Male	4405	(77)	1075	(94)
Ethnicity	White	5080	(89)	1055	(92)
Mode of Infection	MSM	2589	(45)	644	(56)
	IDU	934	(16)	88	(8)
	Het	1726	(30)	281	(25)
Region	South	1613	(28)	254	(22)
	Central	1623	(28)	386	(34)
	North	1138	(20)	353	(31)
	East	1215	(21)	131	(11)
	Argentina	130	(2)	16	(1)

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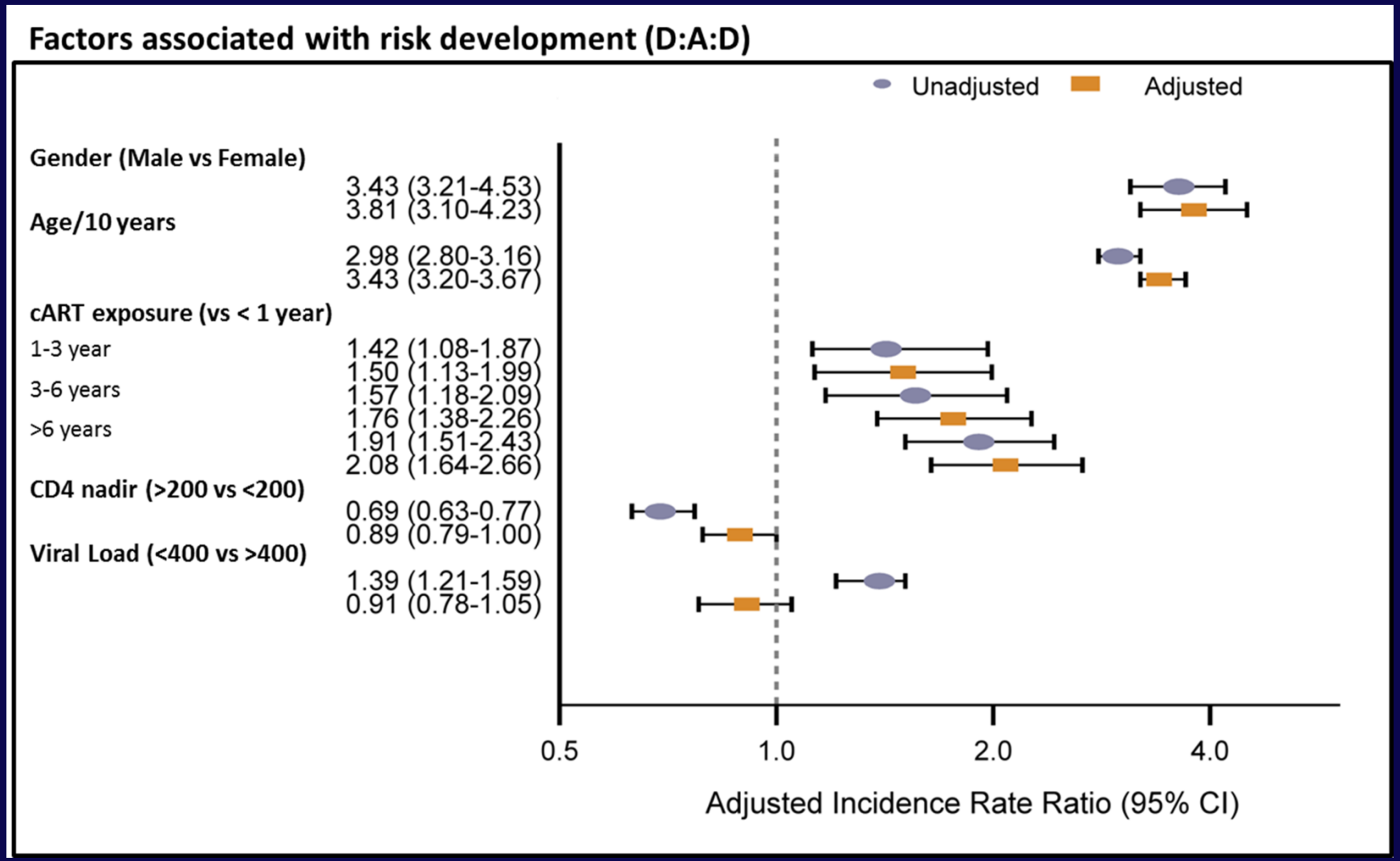
CV Risk Development

1157/4142 **(28%)** develop 5 year CV risk > 5% (using D.A.D)

Incidence rate of **6.6** (CI 6.3-6.9)/ 100 PY

Factors associated with 5%, 5 year CV risk development (N=1140)



Adjusted for gender, ethnicity, risk group, region, calendar year, CD4-cell count, CD4 nadir, prior AIDS diagnosis, prior AIDS or non-AIDS event, cumulative cART exposure, viral load suppression, hepatitis B and C

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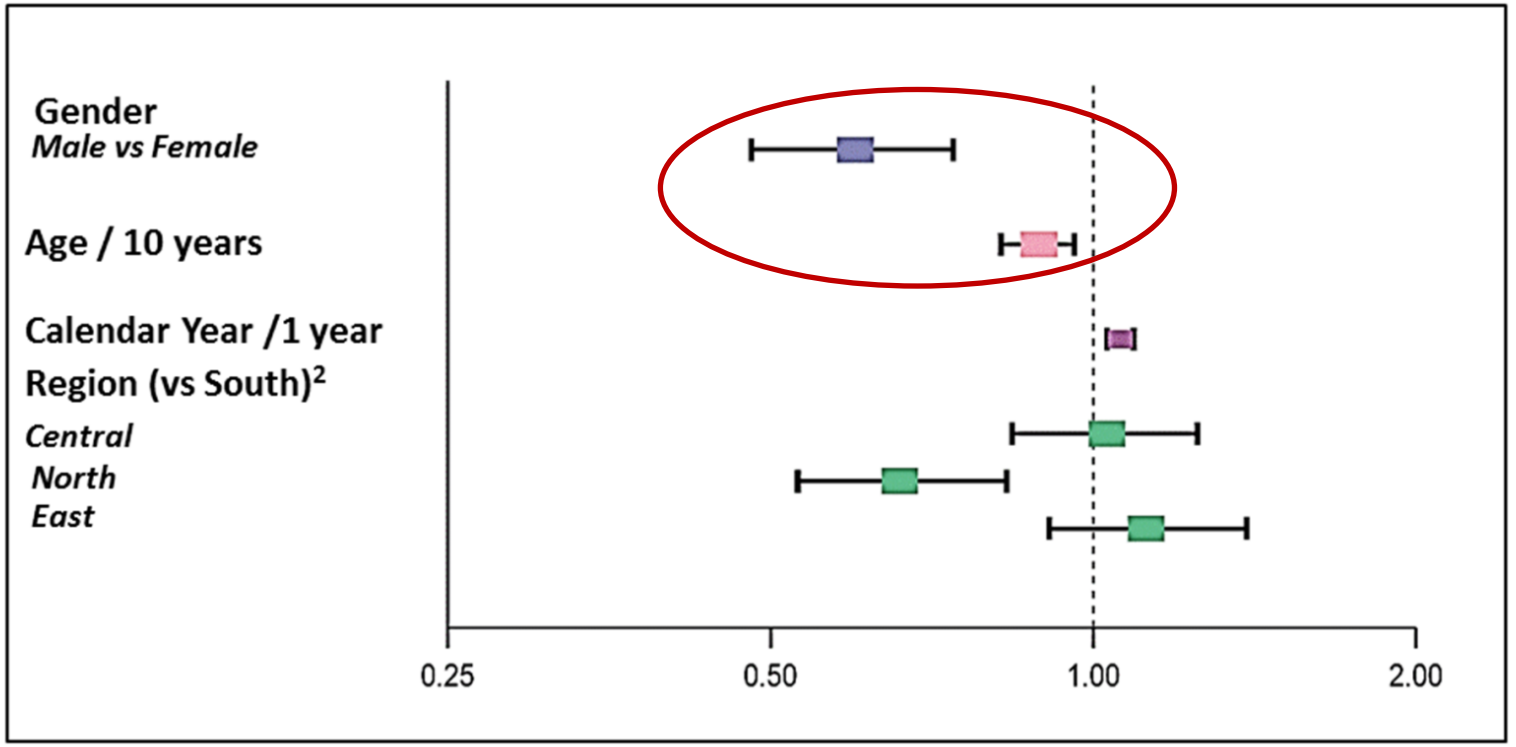
Table 3. Incidence Rates of Risk Factor Modification				
Risk Factor	Indicated for modification n (%)	Modified n (%)	PYFU	Incidence Rate / 100 PYFU
Blood Pressure	1533 (31)	819 (46)	5557	14.7
Smoking	2709 (48)	803 (30)	15107	5.5
Cholesterol	910 (16)	172 (19)	5115	3.4
BMI	1663 (29)	418 (25)	8395	5.0

Adjusted Rate Ratios for risk modification

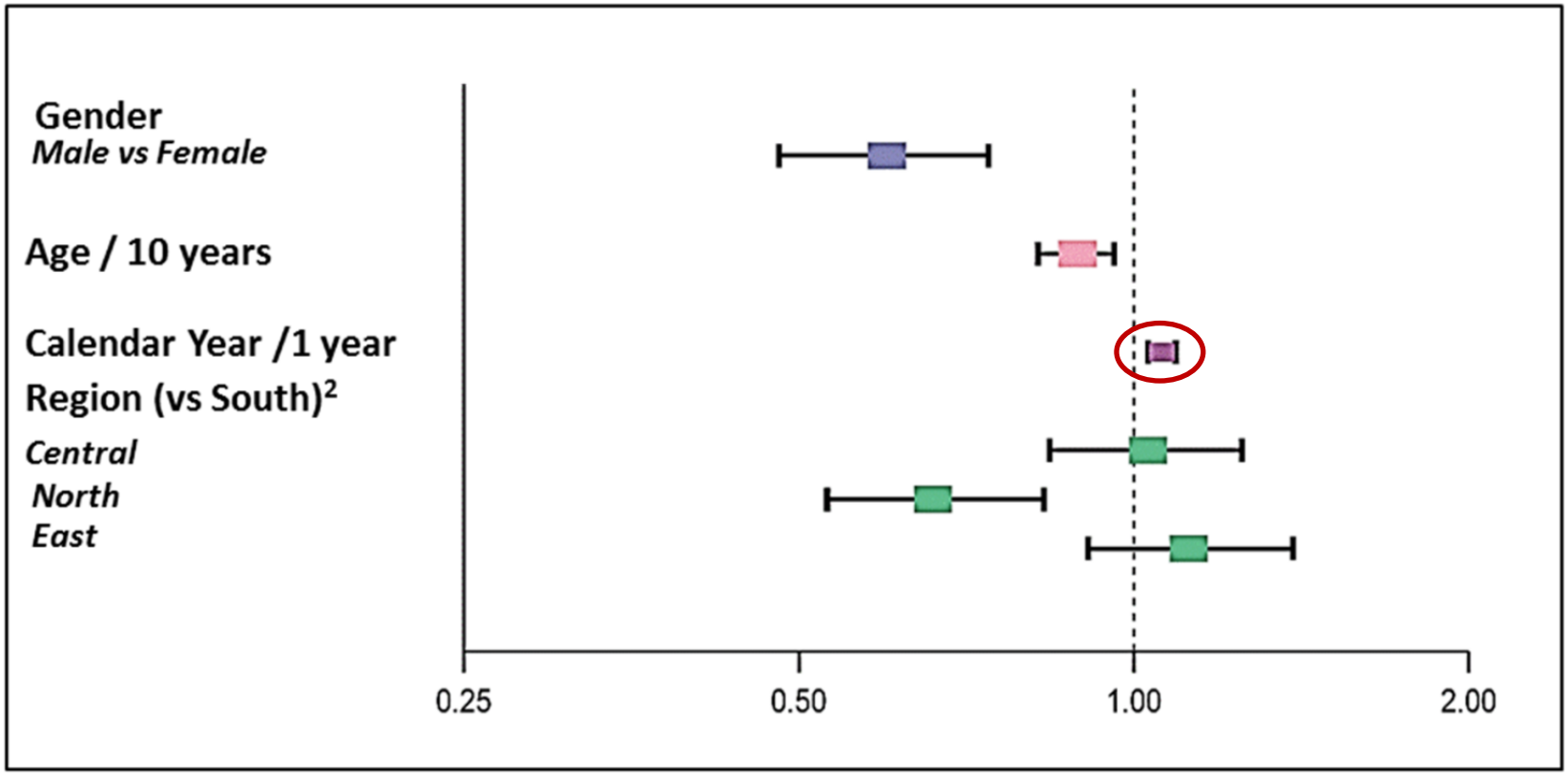
Adjusted Rate Ratios[1] for the modification of blood pressure



1. *Adjusted for age, gender, calendar year, ethnicity, mode of infection, geographical region, CD4 count, CD4 nadir, Undetectable VL, Prior AIDS diagnosis, Prior non-AIDS event, cumulative cART exposure, hepatitis B + C, prior CVD event, family history of CVD and diabetes, BP at baseline, overweight, lipid-lowering drugs, high cholesterol and smoking status;*
2. *Patients from Argentina considered separately.*

Adjusted Rate Ratios for risk modification

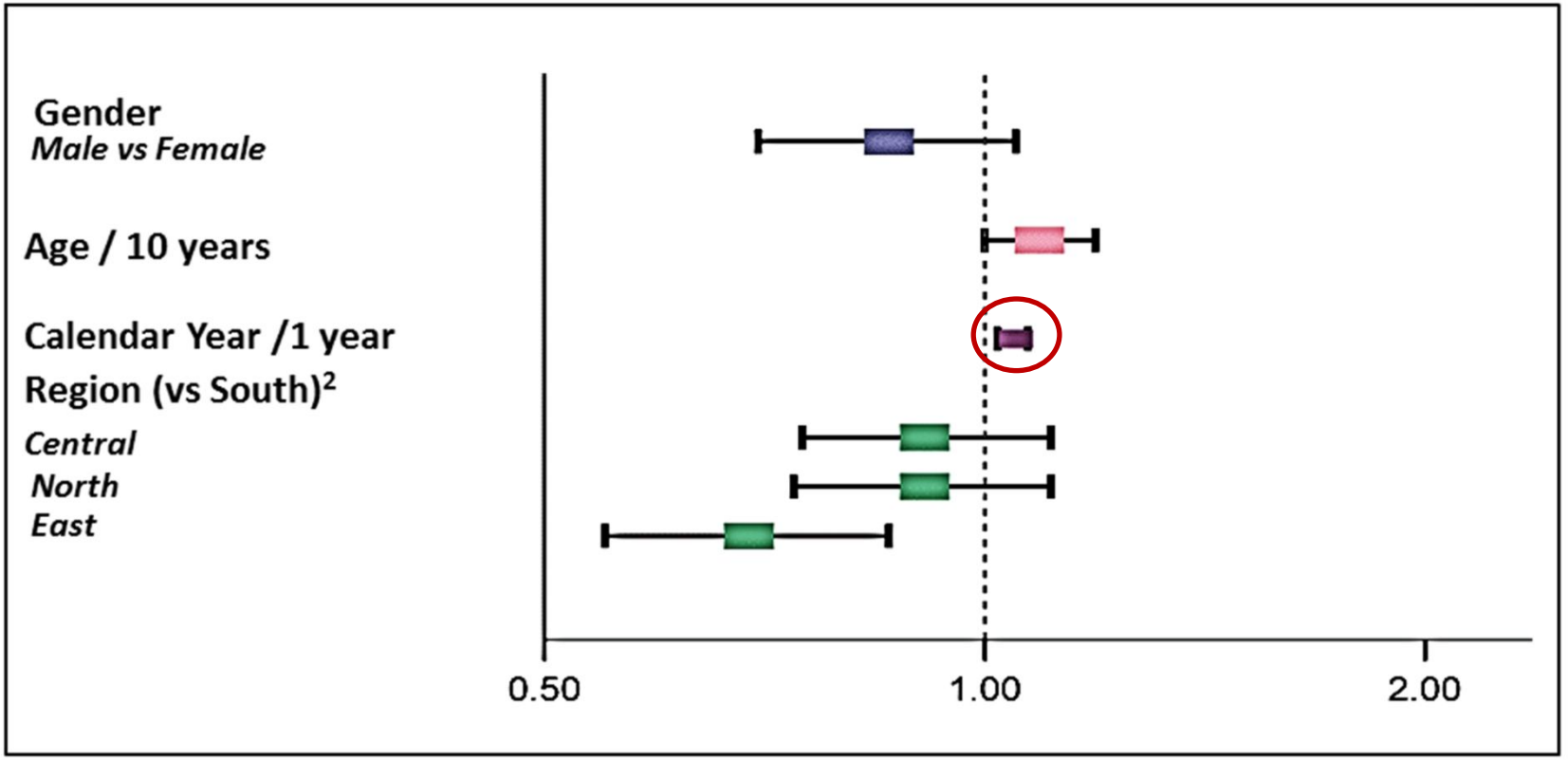
Adjusted Rate Ratios[1] for the modification of blood pressure



1. *Adjusted for age, gender, calendar year, ethnicity, mode of infection, geographical region, CD4 count, CD4 nadir, Undetectable VL, Prior AIDS diagnosis, Prior non-AIDS event, cumulative cART exposure, hepatitis B + C, prior CVD event, family history of CVD and diabetes, BP at baseline, overweight, lipid-lowering drugs, high cholesterol and smoking status;*
2. *Patients from Argentina considered separately.*

Adjusted Rate Ratios for risk modification

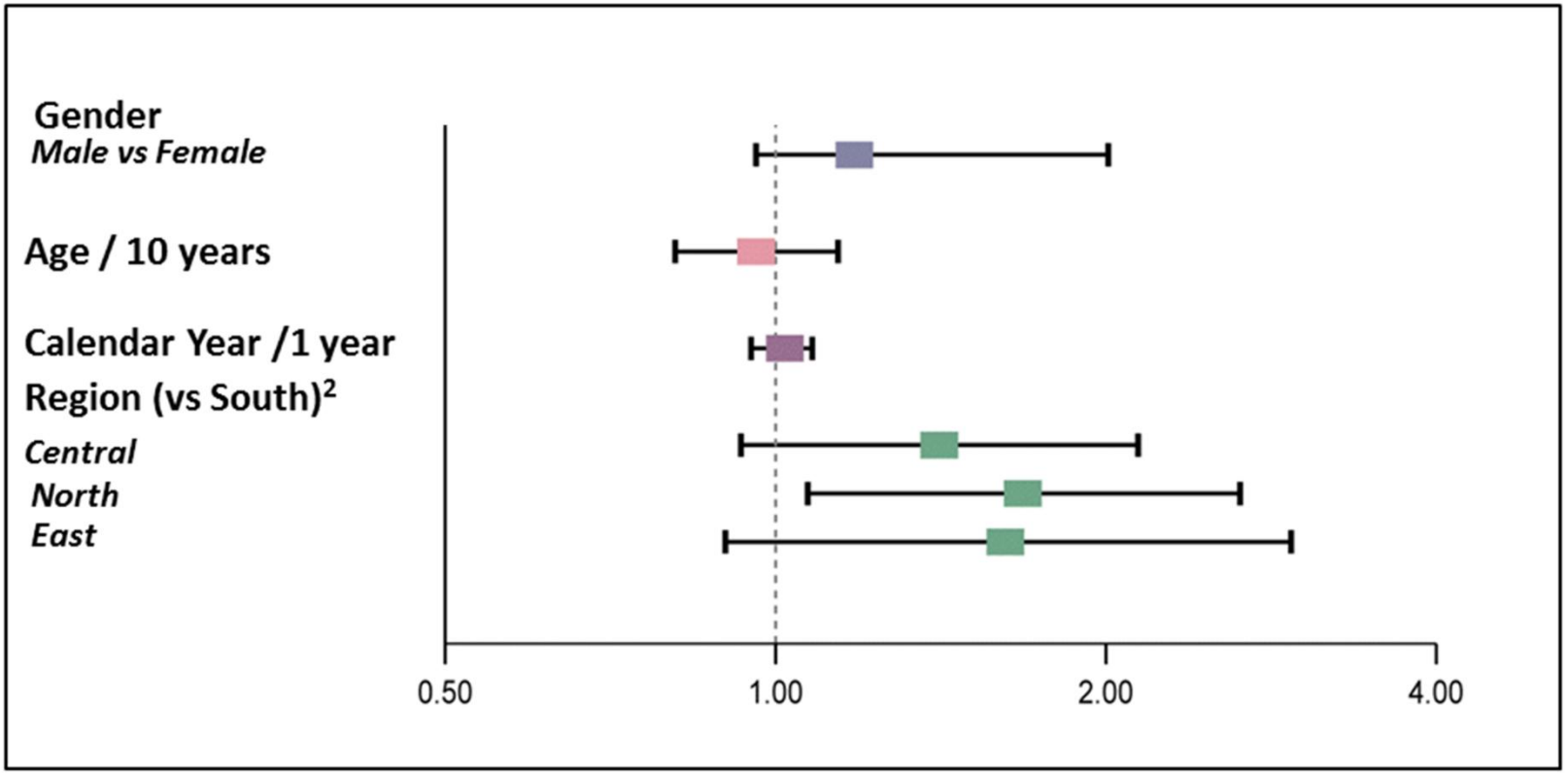
Adjusted Rate Ratios[1] for stopping smoking



1. *Adjusted for age, gender, calendar year, ethnicity, mode of infection, geographical region, CD4 count, CD4 nadir, Undetectable VL, Prior AIDS diagnosis, Prior non-AIDS event, cumulative cART exposure, hepatitis B + C, prior CVD event, family history of CVD and diabetes, BMI and cholesterol at baseline, antihypertensive drugs, smoking status, hypertension*
2. *Patients from Argentina considered separately.*

Adjusted Rate Ratios for risk modification

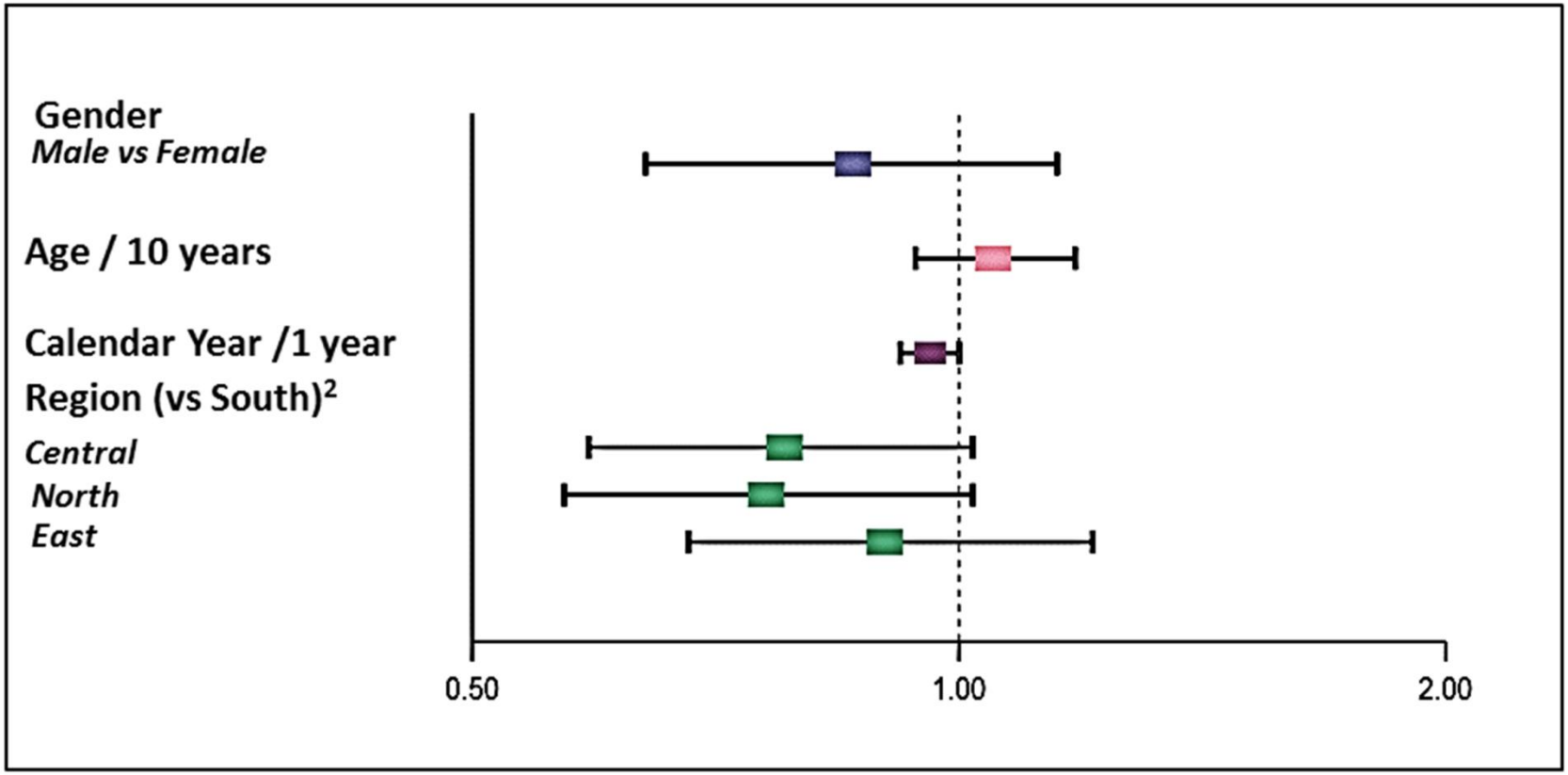
Adjusted Rate Ratios[1] for the modification of cholesterol



1. *Adjusted for age, gender, calendar year, ethnicity, mode of infection, geographical region, CD4 count, CD4 nadir, Undetectable VL, Prior AIDS diagnosis, Prior non-AIDS event, cumulative cART exposure, hepatitis B + C, prior CVD event, family history of CVD and diabetes, BMI and cholesterol at baseline, antihypertensive drugs, smoking status, hypertension*
2. *Patients from Argentina considered separately.*

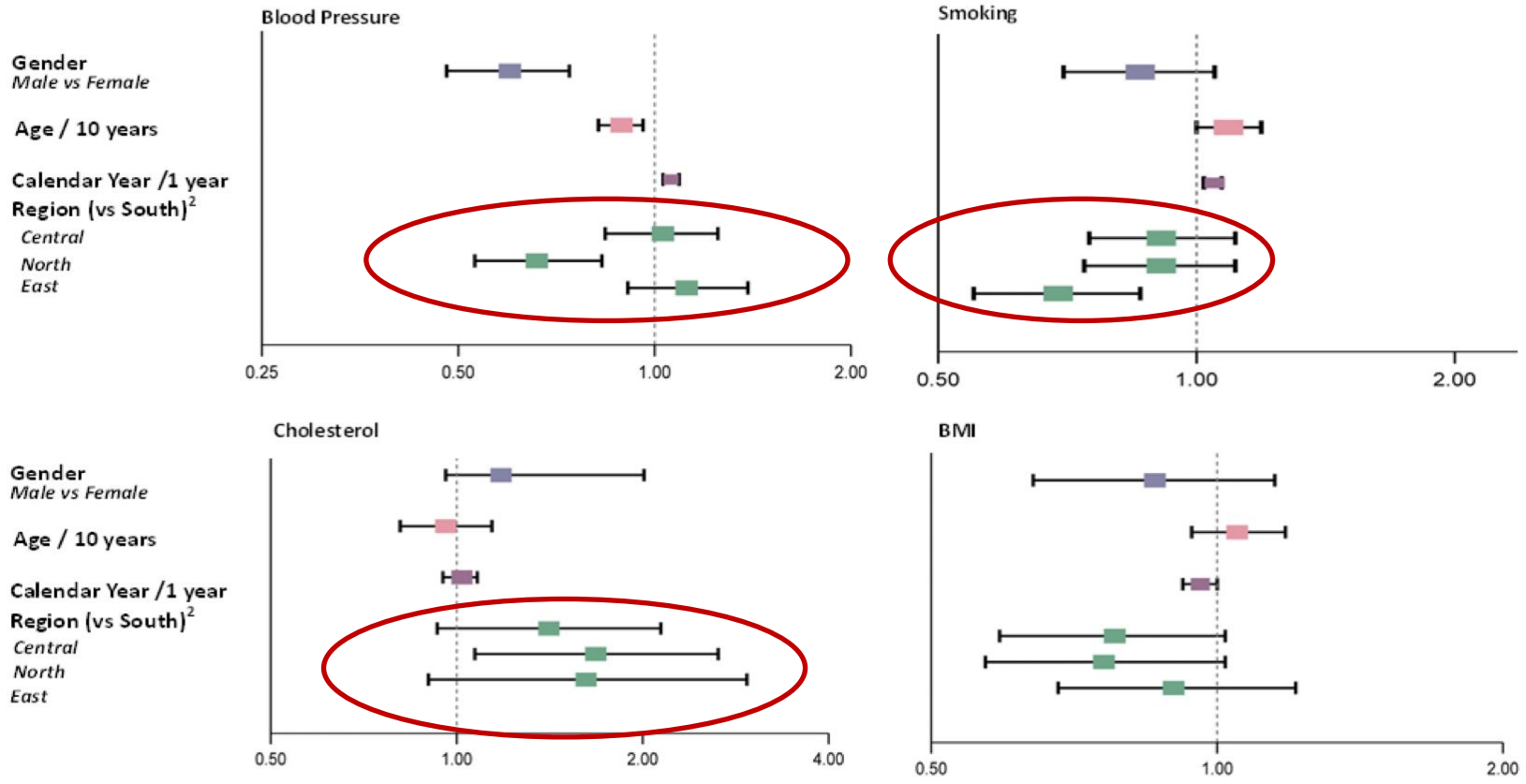
Adjusted Rate Ratios for risk modification

Adjusted Rate Ratios[1] for the modification of BMI



1. *Adjusted for age, gender, calendar year, ethnicity, mode of infection, geographical region, CD4 count, CD4 nadir, Undetectable VL, Prior AIDS diagnosis, Prior non-AIDS event, cumulative cART exposure, hepatitis B + C, prior CVD event, family history of CVD and diabetes, cholesterol and BMI at baseline, antihypertensive drugs, smoking status, hypertension.*
2. *Patients from Argentina considered separately.*

Adjusted Rate Ratios for risk modification



1. *All adjusted for age, gender, calendar year, ethnicity, mode of infection, geographical region, CD4 count, CD4 nadir, Undetectable VL, Prior AIDS diagnosis, Prior non-AIDS event, cumulativ cART exposure, hepatitis B + C, prior CVD event, family history of CVD and diabetes. Adjustments per figure: 2) BP at baseline, overweight, lipid-lowering drugs, high cholesterol and smoking status; 3) BMI and cholesterol at baseline, antihypertensive drugs, smoking status, hypertension; 4) BMI, high cholesterol, antihypertensive drugs, lipid lowering drugs, hypertension, overweight; 5) cholesterol and BMI at baseline, antihypertensive drugs, smoking status, hypertension.*
2. *Patients from Argentina considered separately.*

Limitations

- Conservative definition of high risk
- D.A.D. CV risk prediction is short follow-up
  - DAD versus Framingham's prediction of CV event
    - Medium (5-10%) risk aRR of 11 versus 4
    - High (>10%) risk aRR of 20 versus 8
    - The findings were similar with Framingham
- Channeling bias, higher risk people more CV risk assessment
    - Almost everyone had one CV risk assessment
    - Those with one CV risk assessment were higher risk than those with two

Conclusion

- Prevalence and incidence of CV risk is high
- Over 50% modified some of CV risk
- CV risk modification improved over time
  - smoking and hypertension
- Management of hypertension was more successful in younger people and women
- Geographical variation

Implications

- Modifying CV risk is necessary to sustain the health improvements in HIV
  - Improve the screen and treat cascade for CV risk
  - Reduce geographical and age heterogeneity

- Develop Innovative models of integrated HIV and CV risk Management
  - Test effectiveness on both HIV and CV outcomes in rigorous trials

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The multi-centre study group of EuroSIDA (national coordinators in parenthesis).

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