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Where is the greatest impact of uncontrolled HIV infection on clinical disease progression?

A Mocroft, K Laut, P Reiss, J Gatell, V Ormaasen, M Cavassini, V Hadziosmanovic, K Mansinho, C Katlama, R Chkhetiani, V Mitsura, J Lundgren for EuroSIDA in EuroCoord

Background

- CD4 and HIV-VL are well known predictors of clinical events (AIDS, non-AIDS and deaths) in HIV infection [1-4]
- Unknown whether this relationship varies over time, with age, or in regions of Europe
- Different patterns of clinical events could identify those groups for earlier intervention or closer monitoring

[1]Mocroft et al, Lancet 2000; [2]Monforte et al, AIDS 2008;
[3]Ferry et al, JAIDS 2009, [4]Baker et al, AIDS 2008

Background: An example

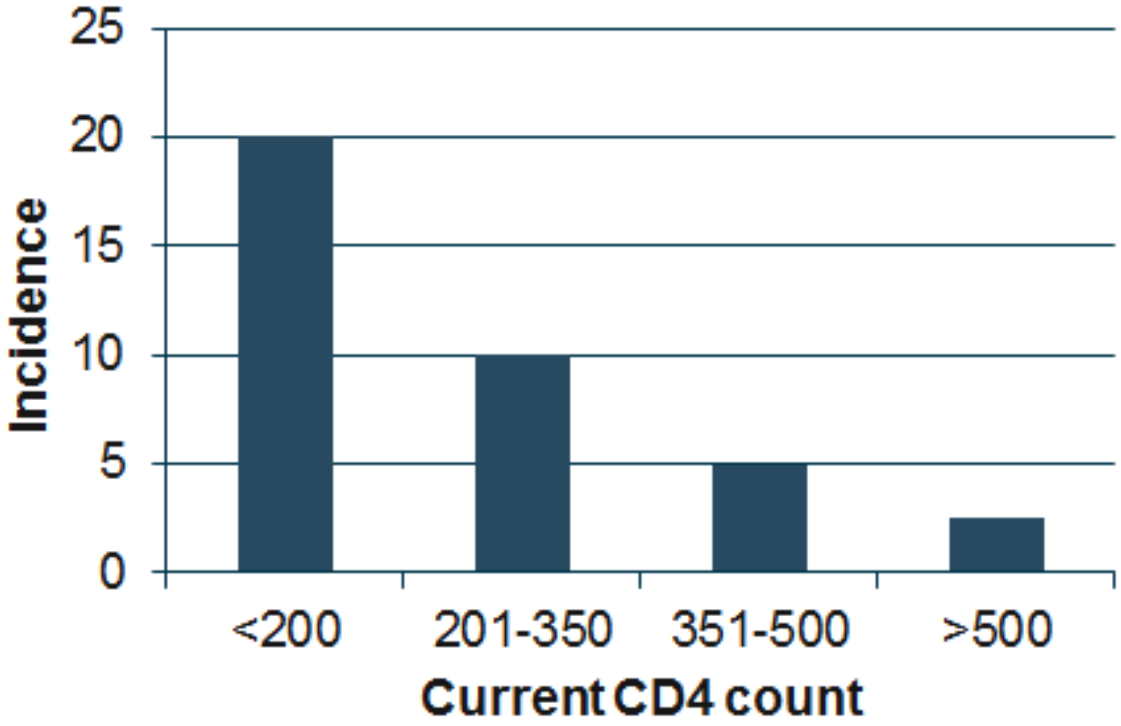

Figure shows an illustration of the incidence of clinical events (fatal/non-fatal AIDS or non-AIDS) / 1000 PYFU stratified by current CD4 count in HIV cohort (fictitious data)

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Background: Is the pattern different in younger vs. older persons?

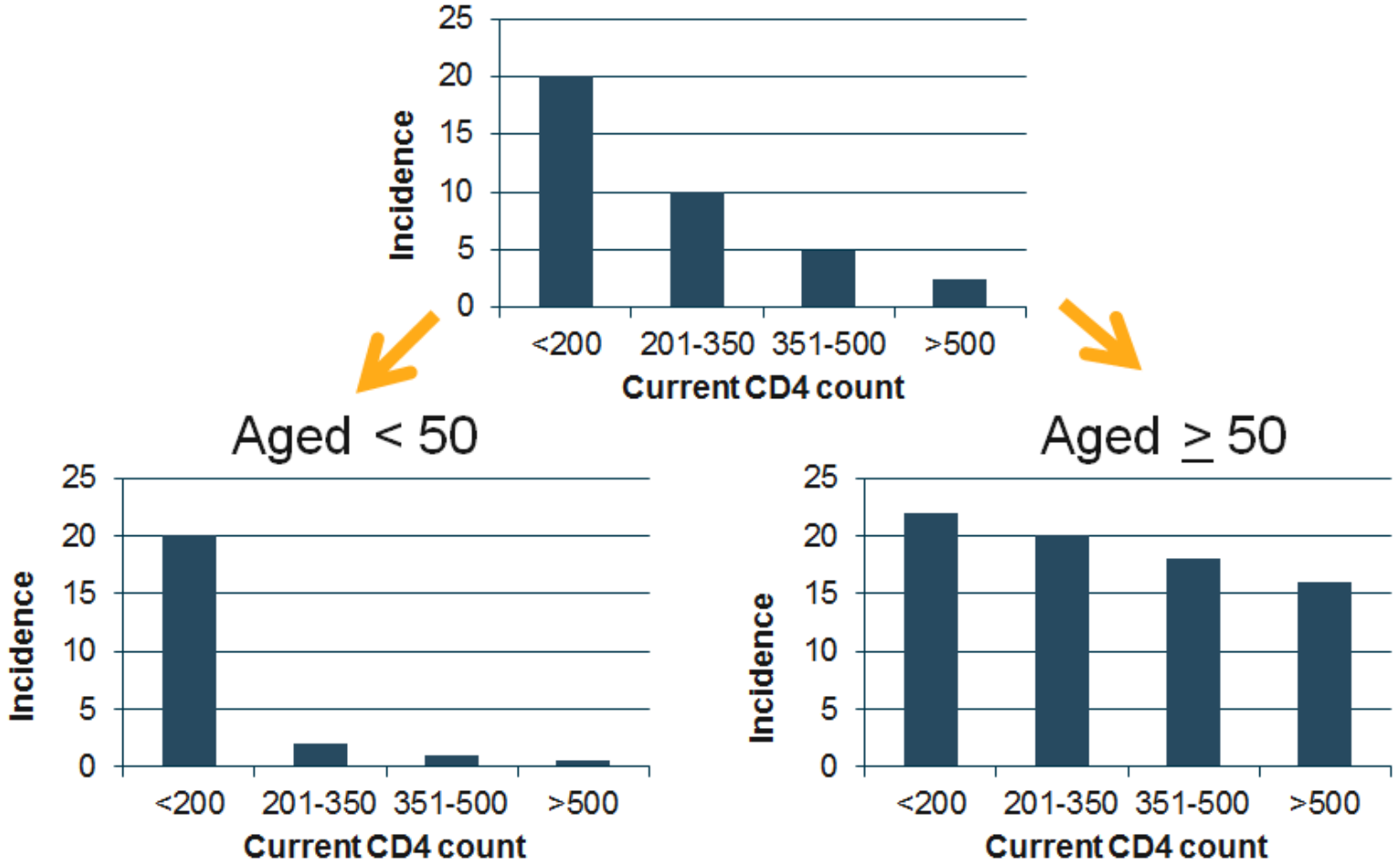

Figure shows an illustration of the theoretical incidence of clinical events (fatal/non-fatal AIDS or non-AIDS) / 1000 PYFU stratified by current CD4 count in HIV cohort

Questions to consider?

- Improvements over time may be better in those at high or low risk of disease progression
- Differences between those at high or low risk likely to vary in different regions due to patient management
- Effect of uncontrolled viremia greater at younger or older ages?

Aims

- Does the risk of HIV disease progression for controlled or uncontrolled HIV differ according to age, year of follow-up or region of Europe?

Methods

- Included EuroSIDA participants with follow-up after 1/1/2001
- Baseline defined as latest of 1/1/2001 or recruitment to EuroSIDA
- Incidence and risk of clinical events assessed using incidence rates and Poisson regression
  - Fatal/non-fatal AIDS
  - Fatal/non-fatal non-AIDS[1]
- Risk of clinical disease categorised as high, medium or low, updated over time, allowing persons to swap over time

Low risk	Medium risk	High risk
CD4 ≥ 500 and VL < 50	*Any other CD4 / VL*	*CD4 < 350 and VL > 10,000*

[1]Mocroft et al, JAIDS 2010; includes non-AIDS malignancies, ESRD, ESLD, CVD, and pancreatitis

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Patient characteristics at baseline

	Low risk *CD4 ≥ 500 and VL < 50*		Medium risk *Any other CD4 / VL*		High risk *CD4 < 350 and VL > 10,000*	
	N	%	N	%	N	%
All	2790	20.2	9437	68.4	1573	11.4
Male	2137	76.6	6983	74.0	1121	71.3
White race	2369	84.9	8247	87.6	1362	86.6
HIV risk : MSM	1399	50.1	3773	40.0	536	34.1
HIV risk : IDU	360	12.4	1971	20.9	390	24.8
Prior AIDS	609	21.8	2676	28.4	520	33.1
Started cART	2699	96.7	7691	81.5	1088	69.2
	Median	IQR	Median	IQR	Median	IQR
Age	41	35 – 49	47	39 – 55	38	33 – 44
Nadir CD4	240	145 – 333	165	35 – 291	125	47 - 225

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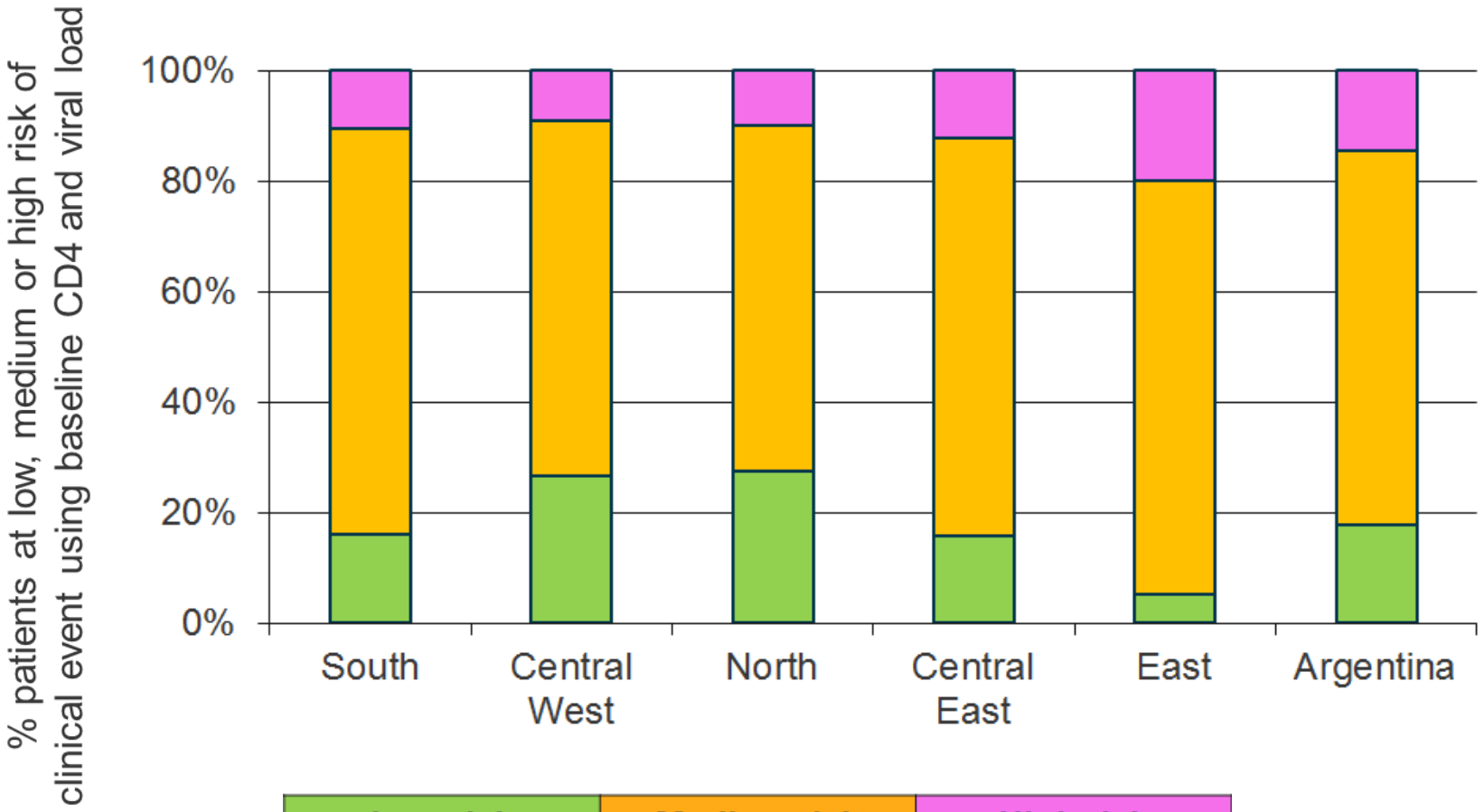
Heterogeneity across Europe:

Baseline risk of clinical event



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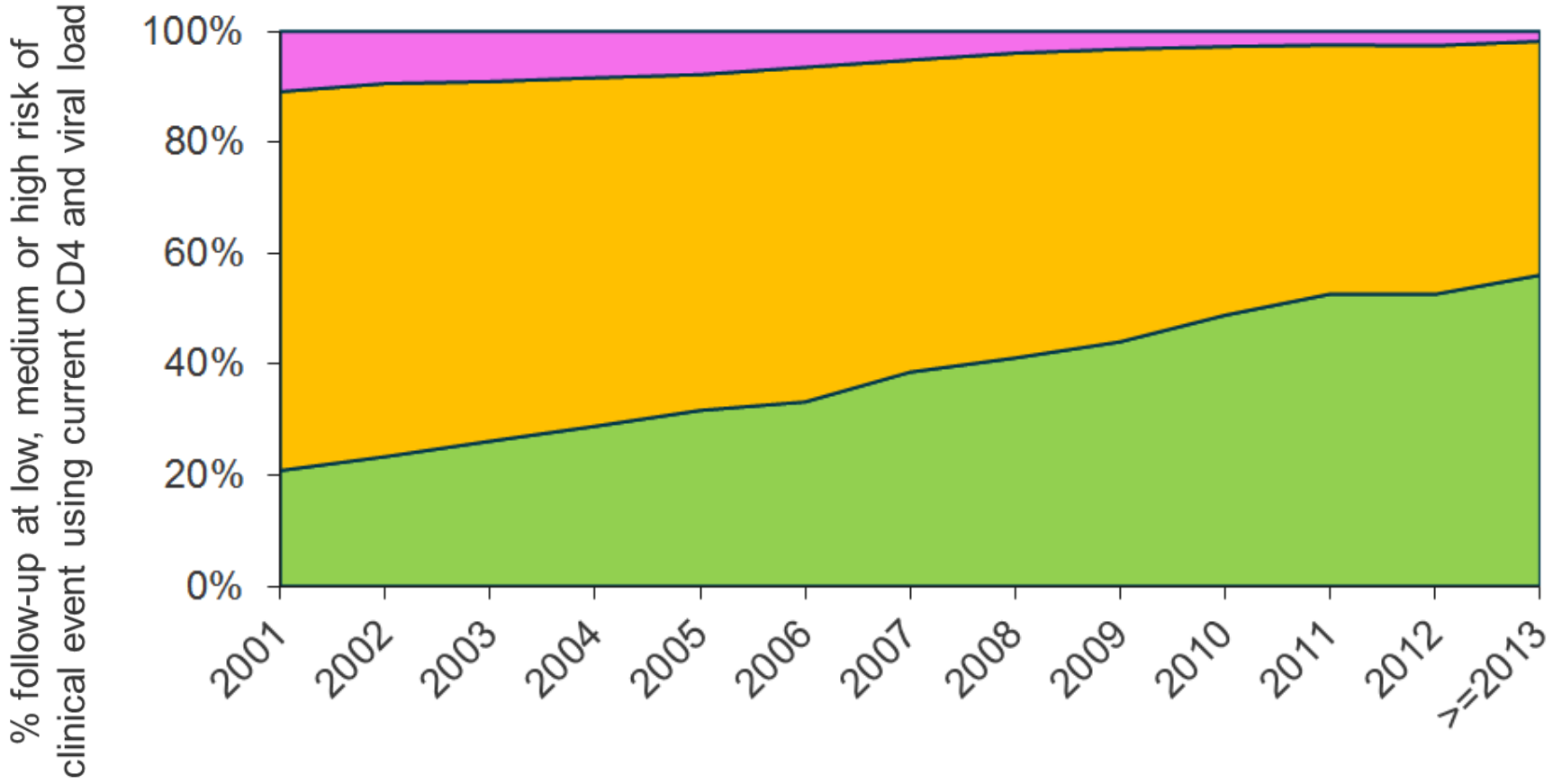
Improvements over calendar time:

Risk of clinical event



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Incidence of clinical events

(per 100 PYFU)

	Events	PYFU	Incidence	95% CI
AIDS	***1521***	***104758***	***1.45***	***1.38 – 1.52***
Low	134	42351	0.32	0.26 – 0.37
Medium	764	57038	1.34	1.24 – 1.43
High	623	5369	11.60	10.69 – 12.52
Non-AIDS	***2631***	***104758***	***2.51***	***2.42 – 2.61***
Low	726	42351	1.71	1.59 – 1.84
Medium	1618	57038	2.84	2.70 – 2.98
High	287	5369	5.35	4.73 – 5.96

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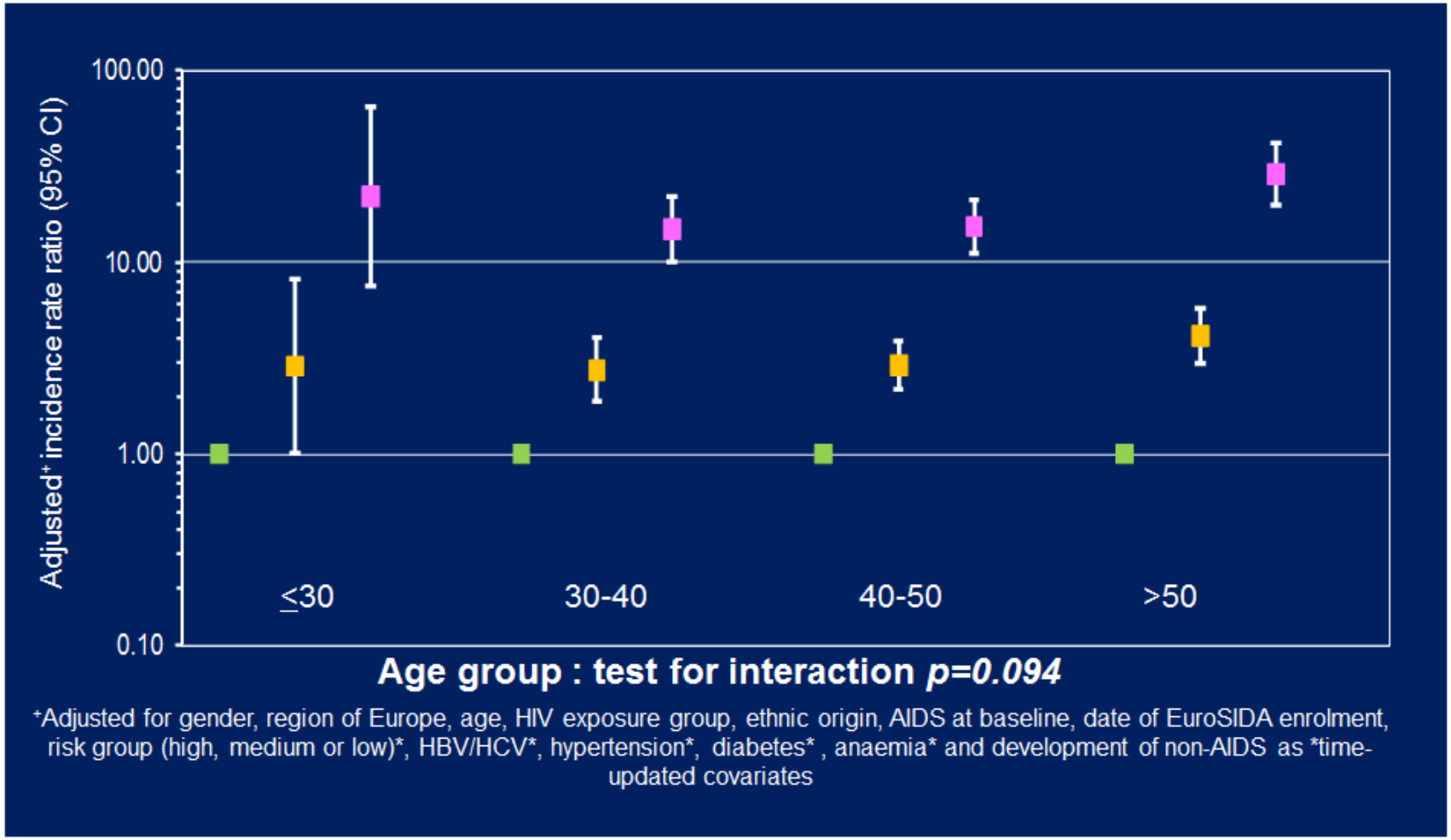
Adjusted⁺ incidence rate ratio: ***AIDS***

Age



⁺Adjusted for gender, region of Europe, age, HIV exposure group, ethnic origin, AIDS at baseline, date of EuroSIDA enrolment, risk group (high, medium or low)*, HBV/HCV*, hypertension*, diabetes* , anaemia* and development of non-AIDS as *time-updated covariates

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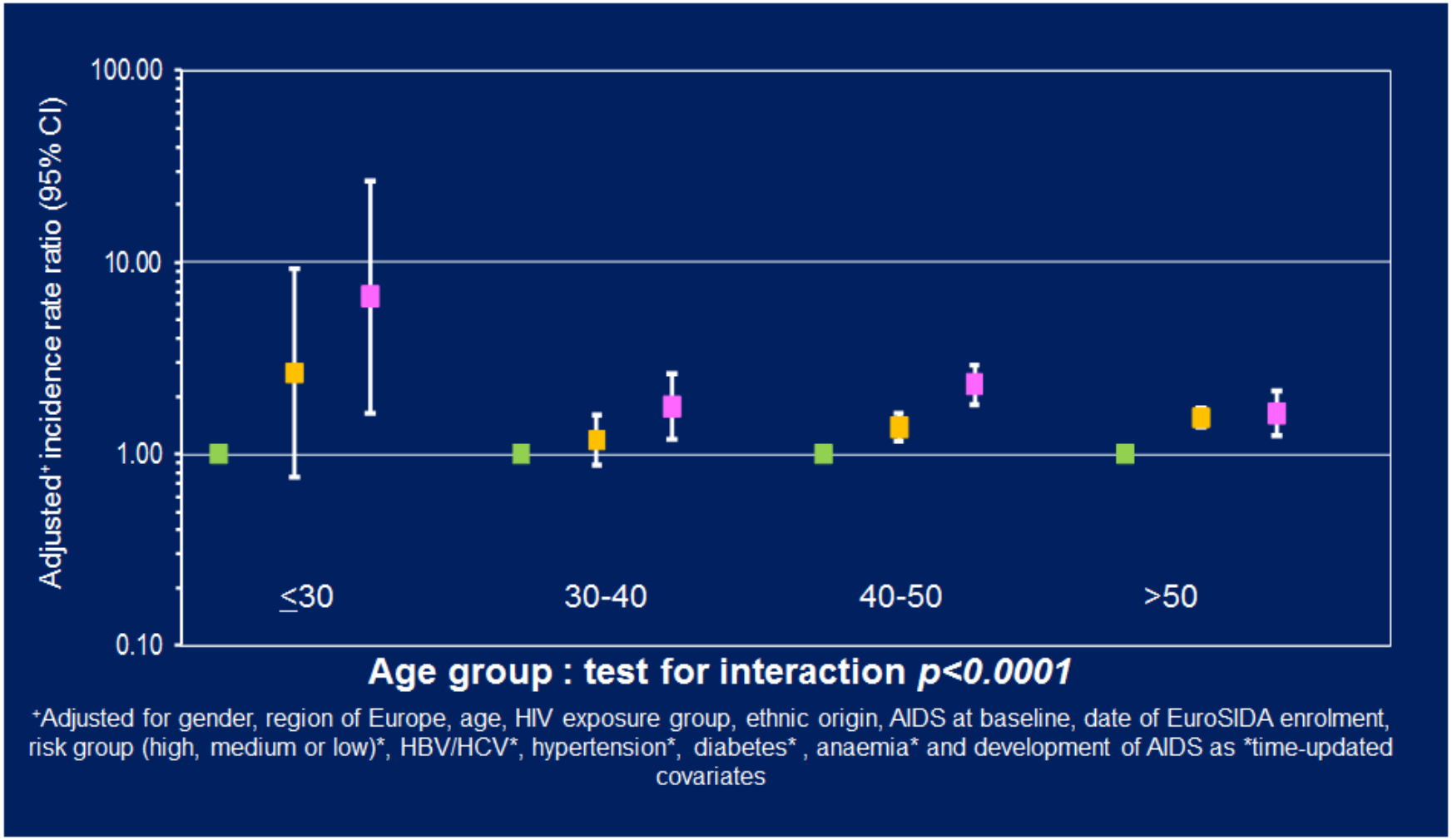
Adjusted+ incidence rate ratio: ***non-AIDS***

Age



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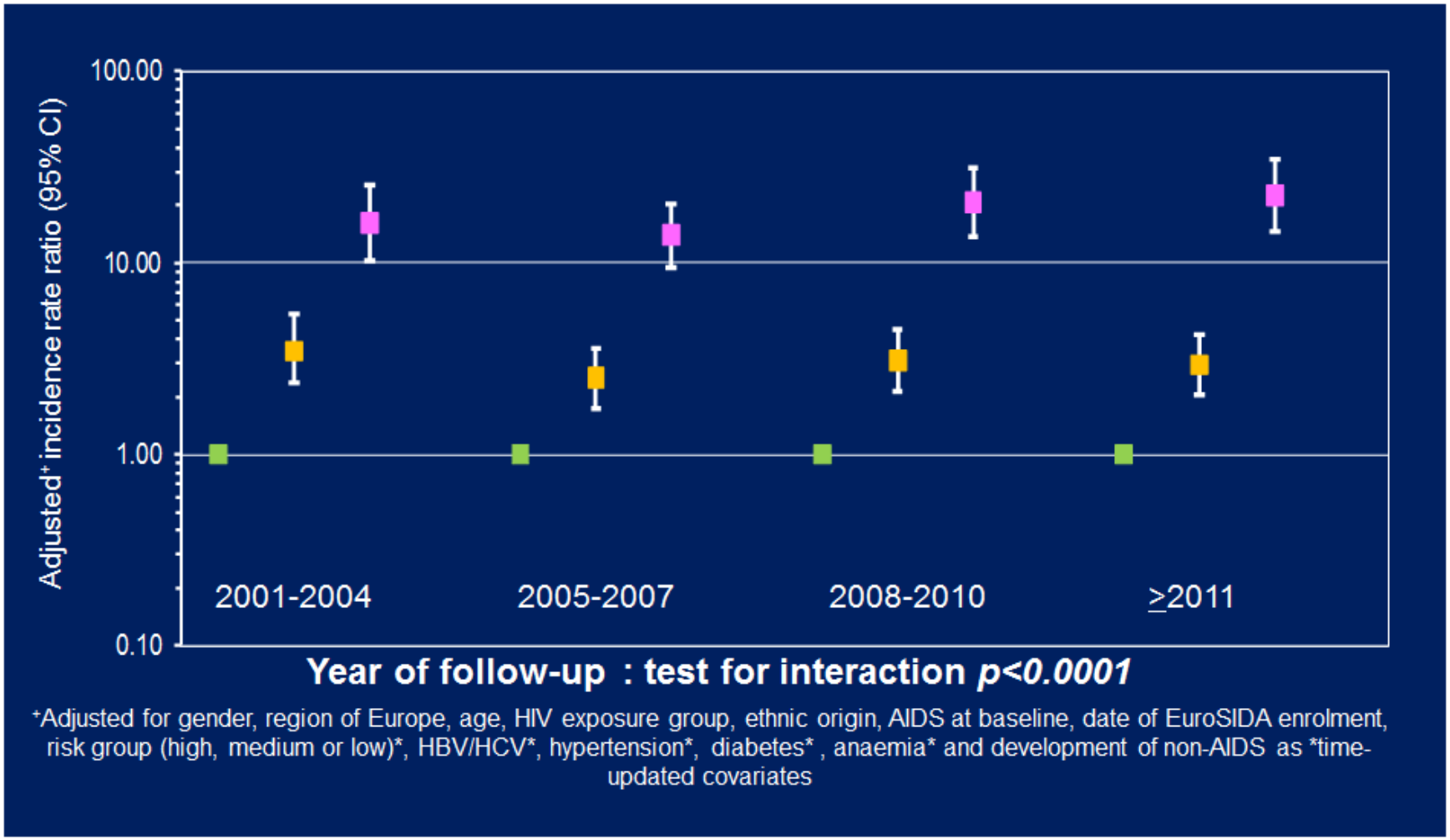
Adjusted⁺ incidence rate ratio: ***AIDS***

Year of follow-up



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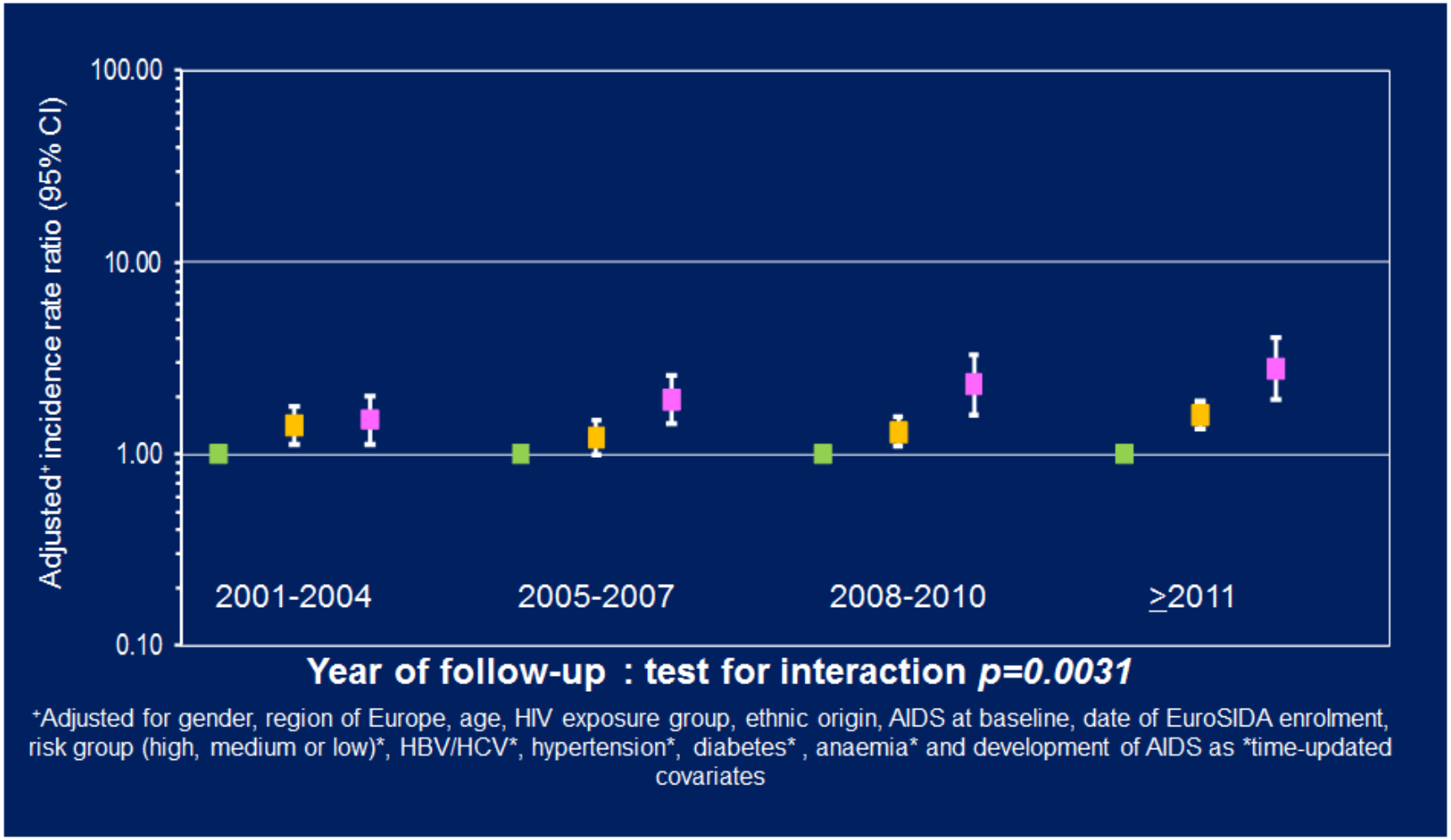

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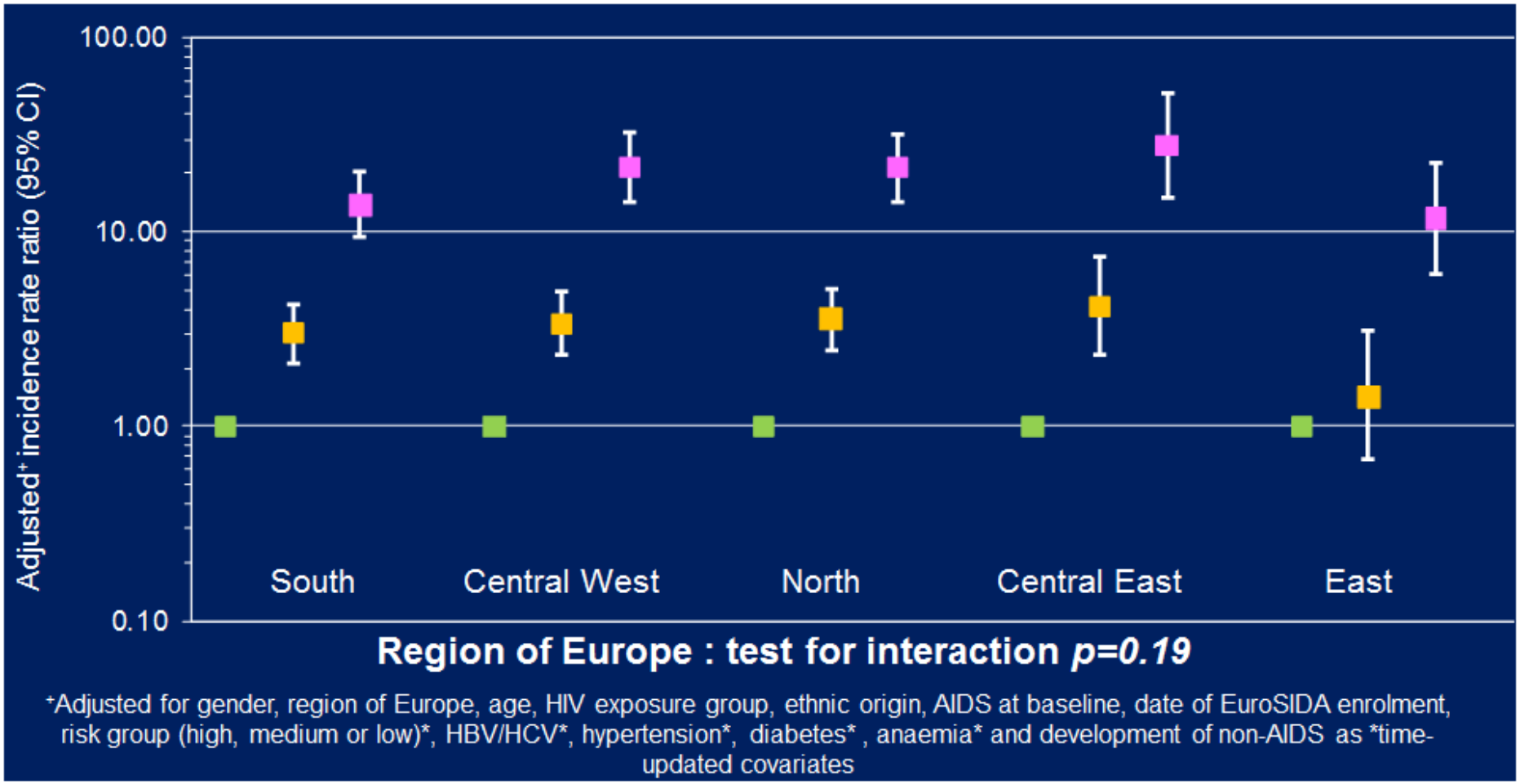
Adjusted incidence rate ratio: ***AIDS***

Region



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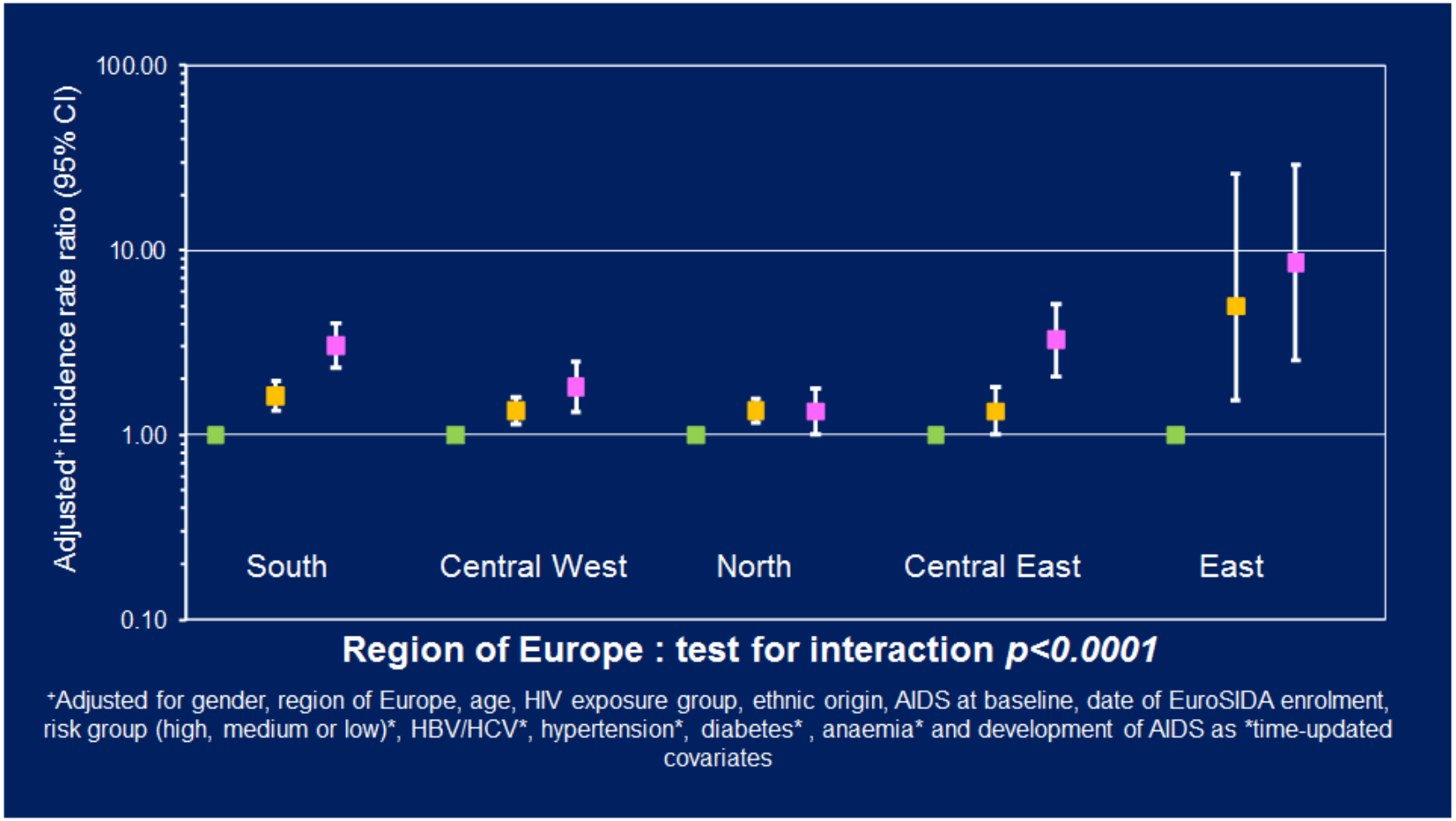
Adjusted⁺ incidence rate ratio: ***non-AIDS***

Region



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Summary

		Difference between high and low risk
Age	AIDS	Similar across age groups
Age	Non-AIDS	Decreases as patients age
Year of follow-up	AIDS	Increases in later calendar years
Year of follow-up	Non-AIDS	Increases in later calendar years
Region	AIDS	Similar across regions
Region	Non-AIDS	Highest in Central East and Eastern Europe, lowest in Central West and Northern Europe

Low risk	Medium risk	High risk
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Sensitivity analyses and limitation

- Considered fatal and non-fatal events separately
- Used LLOD for VL for low risk of 500 cp/ml

- Centres included in EuroSIDA may not be representative of European HIV care
- Persons included required CD4 and viral counts measured; some variability in frequency of measurements

Conclusions

- Difference in risk between those at high and low risk was
  - Widest for non-AIDS for those aged <30; *other factors become more important than HIV control as persons age*
  - Increasing over time for AIDS and non-AIDS; *improvements in care for those at low risk and better management required for those at high risk*
  - Largest for non-AIDS in CE and E regions, lowest in N and CW; *differences in patient management and underlying socioeconomic differences*[1]

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[1]Mackenbach et al, Lancet 2013

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Implications

- Start ART as soon as HIV is diagnosed
- Important to get all patients to as low a risk of clinical progression as quickly as possible
- Retain patients in care and at low risk of clinical progression
- Monitoring and managing comorbidities in all patients

The EuroSIDA Study Group

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

Argentina: (M Losso), M Kundro, Hospital JM Ramos Mejia, Buenos Aires. **Austria**: (N Vetter), Pulmologisches Zentrum der Stadt Wien, Vienna; R Zangerle, Medical University Innsbruck, Innsbruck. **Belarus**: (I Karpov), A Vassilenko, Belarus State Medical University, Minsk, VM Mitsura, Gomel State Medical University, Gomel; D Paduto, Regional AIDS Centre, Svetlogorsk. **Belgium**: (N Clumeck), S De Wit, M Delforge, Saint-Pierre Hospital, Brussels; E Florence, Institute of Tropical Medicine, Antwerp; L Vandekerckhove, University Ziekenhuis Gent, Gent. **Bosnia-Herzegovina**: (V Hadziosmanovic), Klinicki Centar Univerziteta Sarajevo, Sarajevo. **Bulgaria**: (K Kostov), Infectious Diseases Hospital, Sofia. **Croatia**: (J Begovac), University Hospital of Infectious Diseases, Zagreb. **Czech Republic**: (L Machala), D Jilich, Faculty Hospital Bulovka, Prague; D Sedlacek, Charles University Hospital, Plzen. **Denmark**: G Kronborg,T Benfield, Hvidovre Hospital, Copenhagen; J Gerstoft, T Katzenstein, A-B E Hansen, Rigshospitalet, Copenhagen; C Pedersen, NF Møller, Odense University Hospital, Odense; L Ostergaard, Skejby Hospital, Aarhus, U B Dragsted, Roskilde Hospital, Roskilde; L N Nielsen, Hillerod Hospital, Hillerod. **Estonia**: (K Zilmer), West-Tallinn Central Hospital, Tallinn; Jelena Smidt, Nakkusosakond Siseklinik, Kohtla-Järve. **Finland**: (M Ristola), I Aho, Helsinki University Central Hospital, Helsinki. **France**: (C Katlama), Hôpital de la Pitié-Salpétière, Paris; J-P Viard, Hôtel-Dieu, Paris; P-M Girard, Hospital Saint-Antoine, Paris; L Cotte, Hôpital de la Croix Rousse, Lyon; C Pradier, E Fontas, Hôpital de l'Archet, Nice; F Dabis, D Neau, Unité INSERM, Bordeaux, C Duvivier, Hôpital Necker-Enfants Malades, Paris. **Germany**: (J Rockstroh), Universitäts Klinik Bonn; R Schmidt, Medizinische Hochschule Hannover; J van Lunzen, O Degen, University Medical Center Hamburg-Eppendorf, Infectious Diseases Unit, Hamburg; HJ Stellbrink, IPM Study Center, Hamburg; C Stefan, JW Goethe University Hospital, Frankfurt; J Bogner, Medizinische Poliklinik, Munich; G. Fätkenheuer, Universität Köln, Cologne. **Georgia**: (N Chkhartishvili) Infectious Diseases, AIDS & Clinical Immunology Research Center, Tbilisi. **Greece**: (J Kosmidis), P Gargalianos, G Xylomenos, P Lourida, Athens General Hospital; H Sambatakou, Ippokration General Hospital, Athens. **Hungary**: (D Banhegyi), Szent Lásló Hospital, Budapest. **Iceland**: (M Gottfredsson), Landspitali University Hospital, Reykjavik. **Ireland**: (F Mulcahy), St. James's Hospital, Dublin. **Israel**: (I Yust), D Turner, M Burke, Ichilov Hospital, Tel Aviv; E Shahar, G Hassoun, Rambam Medical Center, Haifa; H Elinav, M Haouzi, Hadassah University Hospital, Jerusalem; ZM Sthoeger, AIDS Center (Neve Or), Jerusalem. **Italy**: (A D'Arminio Monforte), Istituto Di Clinica Malattie Infettive e Tropicale, Milan; R Esposito, I Mazeu, C Mussini, Università Modena, Modena; F Mazzotta, A Gabbuti, Ospedale S Maria Annunziata, Firenze; V Vullo, M Lichtner, University di Roma la Sapienza, Rome; M Zaccarelli, A Antinori, R Acinapura, G D'Offizi, Istituto Nazionale Malattie Infettive Lazzaro Spallanzani, Rome; A Lazzarin, A Castagna, N Gianotti, Ospedale San Raffaele, Milan; M Galli, A Ridolfo, Osp. L. Sacco, Milan. **Latvia**: (B Rozentale), Infectology Centre of Latvia, Riga. **Lithuania**: (V Uzdaviniene) Vilnius University Hospital Santariskiu Klinikos, Vilnius; R Matulionyte, Center of Infectious Diseases, Vilnius University Hospital Santariskiu Klinikos, Vilnius. **Luxembourg**: (T Staub), R Hemmer, Centre Hospitalier, Luxembourg. **Netherlands**: (P Reiss), Academisch Medisch Centrum bij de Universiteit van Amsterdam, Amsterdam. **Norway**: (V Ormaasen), A Maeland, J Bruun, Ullevål Hospital, Oslo. **Poland**: (B Knysz), J Gasiorowski, M Inglot, Medical University, Wroclaw; A Horban, E Bakowska, Centrum Diagnostyki i Terapii AIDS, Warsaw; A Grzeszczuk, R Flisiak, Medical University, Bialystok; M Parczewski, M Pynka, K Maciejewska, Medical Univesity, Szczecin; M Beniowski, E Mularska, Osrodek Diagnostyki i Terapii AIDS, Chorzow; T Smiatacz, M Gensing, Medical University, Gdansk; E Jablonowska, E Malolepsza, K Wojcik, Wojewodzki Szpital Specjalistyczny, Lodz; I Mozer-Lisewska, Poznan University of Medical Sciences, Poznan. **Portugal**: (M Doroana), L Caldeira, Hospital Santa Maria, Lisbon; K Mansinho, Hospital de Egas Moniz, Lisbon; F Maltez, Hospital Curry Cabral, Lisbon. **Romania**: (R Radoi), C Oprea, Spitalul de Boli Infectioase si Tropicale: Dr. Victor Babes, Bucarest. **Russia**: (A Rakhmanova), Medical Academy Botkin Hospital, St Petersburg; A Rakhmanova, St Petersburg AIDS Centre, St Peterburg; T Trofimora, Novgorod Centre for AIDS, Novgorod, I Khromova, Centre for HIV/AIDS & and Infectious Diseases, Kaliningrad; E Kuzovatova, Nizhny Novgorod Scientific and Research Institute, Nizhny Novogrod. **Serbia**: (D Jevtovic), The Institute for Infectious and Tropical Diseases, Belgrade. **Slovakia**: A Shunnar, D Staneková, Dérer Hospital, Bratislava. **Slovenia**: (J Tomazic), University Clinical Centre Ljubljana, Ljubljana. **Spain**: (JM Gatell), JM Miró, Hospital Clinic Universitari de Barcelona, Barcelona; S Moreno, J. M. Rodriguez, Hospital Ramon y Cajal, Madrid; B Clotet, A Jou, R Paredes, C Tural, J Puig, I Bravo, Hospital Germans Trias i Pujol, Badalona; P Domingo, M Gutierrez, G Mateo, MA Sambeat, Hospital Sant Pau, Barcelona; JM Laporte, Hospital Universitario de Alava, Vitoria-Gasteiz. **Sweden**: (A Blaxhult), Venhaelsan-Sodersjukhuset, Stockholm; L Flamholc, Malmö University Hospital, Malmö, K Falconer, A Thalme, A Sonnerborg, Karolinska University Hospital, Stockholm. **Switzerland**: (B Ledergerber), R Weber, University Hospital Zurich; M Cavassini, University Hospital Lausanne; A Calmy, University Hospital Geneva; H Furrer, University Hospital Bern; M Battegay, L Elzi, University Hospital Basel; P Schmid, Cantonal Hospital St. Gallen. **Ukraine**: (E Kravchenko), N Chentsova (deceased), Kiev Centre for AIDS, Kiev; V Frolov, G Kutsyna, I Baskakov, Luhansk State Medical University, Luhansk; A Kuznetsova, Kharkov State Medical University, Kharkov; G Kyselyova, Crimean Republican AIDS centre, Simferopol. **United Kingdom**: (B Gazzard), St. Stephen's Clinic, Chelsea and Westminster Hospital, London; AM Johnson, E Simons, S Edwards, Mortimer Market Centre, London; A Phillips, MA Johnson, A Mocroft, Royal Free and University College Medical School, London (Royal Free Campus); C Orkin, Royal London Hospital, London; J Weber, G Scullard, Imperial College School of Medicine at St. Mary's, London; A Clarke, Royal Sussex County Hospital, Brighton; C Leen, Western General Hospital, Edinburgh. **The following centers have previously contributed data to EuroSIDA**: Bernhard Nocht Institut für Tropenmedizin, Hamburg, Germany; 1st I.K.A Hospital of Athens, Athens, Greece; Ospedale Riuniti, Divisione Malattie Infettive, Bergamo, Italy
Ospedale di Bolzano, Divisione Malattie Infettive, Bolzano, Italy; Ospedale Cotugno, III Divisione Malattie Infettive, Napoli, Italy; Hospital Carlos III, Departamento de Enfermedades Infecciosas, Madrid, Spain; Odessa Region AIDS Center, Odessa, Ukraine.

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