

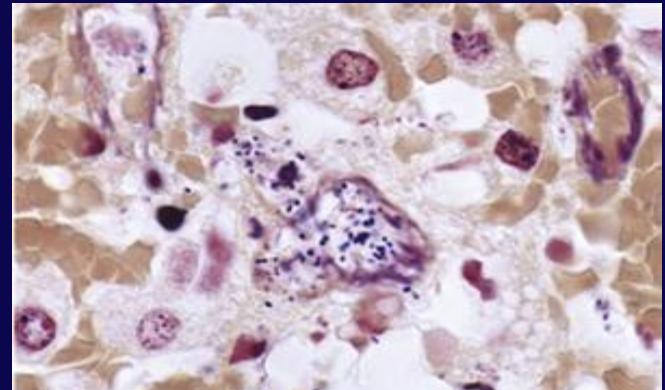
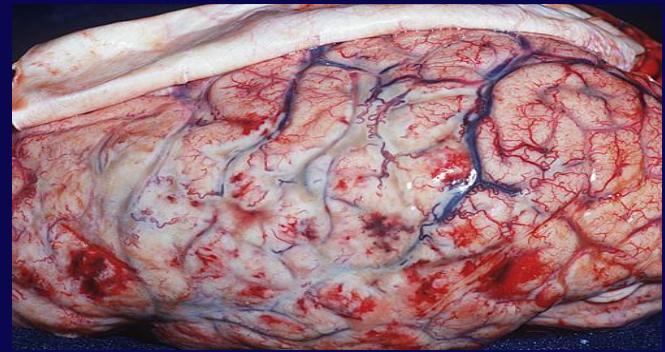


# The incidence of serious non-AIDS bacterial infections in the EuroSIDA cohort

O Søgaard, J Reekie, M Ristola, D Jevtovic, I Karpov, M Beniowski, S Servitskiy, P Domingo, P Reiss, A Mocroft, O Kirk for EuroSIDA in EuroCoord

# Background

- Risk of pneumonia in the cART era remains 6-8 fold higher among persons with HIV than those without HIV<sup>1,2</sup>
- Similar trends have also been reported for bacterial meningitis and invasive pneumococcal disease<sup>3,4</sup>



# Background

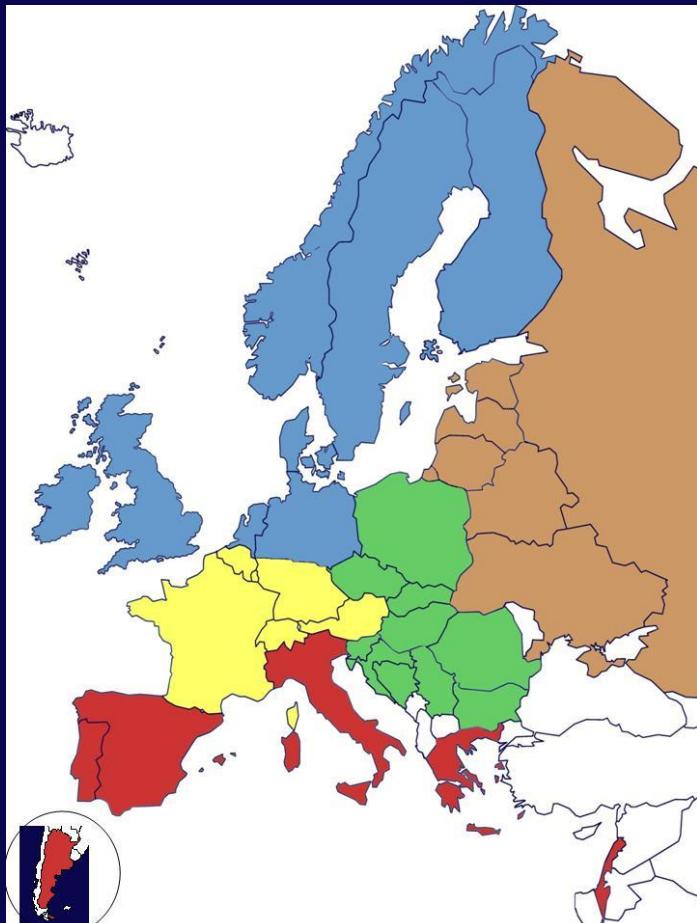
- There is an association between increasing risk of certain non-AIDS defining conditions and decreasing CD4+ count counts<sup>5,6</sup>
- By restoring CD4+ cell counts, cART reduces the risk of some non-AIDS defining diseases
- It has also been suggested that cART may have a protective effect against certain non-AIDS infections that is independent of CD4+ cell count<sup>2</sup>

# Aim

- Estimate incidence rates of serious non-AIDS bacterial infections requiring hospitalization across Europe
- Explore potential risk factors
- Determine the influence of cART on risk of infection at various levels of immune competence defined by CD4+ cell count.

# EuroSIDA

EuroSIDA is a large prospective cohort with 16597 patients from 33 European countries, Israel and Argentina.



- From September 2006 onwards data has been routinely collected on serious non-AIDS infections requiring hospitalization

# Methods

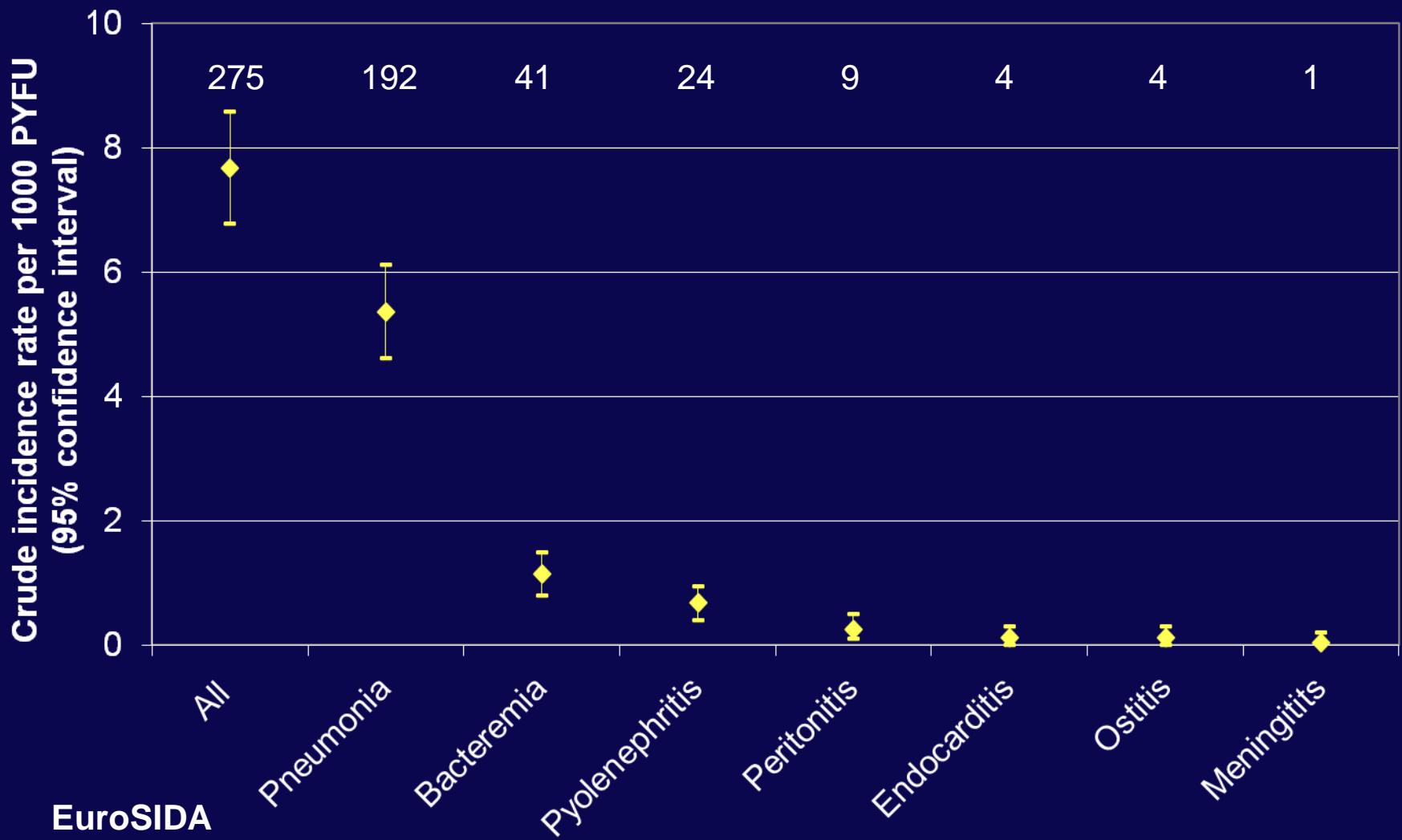
- Inclusion criteria
  - Patients under follow-up after 1 September 2006
  - CD4+ count available at enrolment
- Follow up
  - Patients were followed until their first diagnosis of a non-AIDS bacterial infection or their last visit
- Statistical methods
  - Incidence rate calculated per 1000 PYFU
  - Poisson regression used to investigate factors associated with diagnosis
  - Variables that could change over time were included as time-updated covariates

# Baseline characteristics

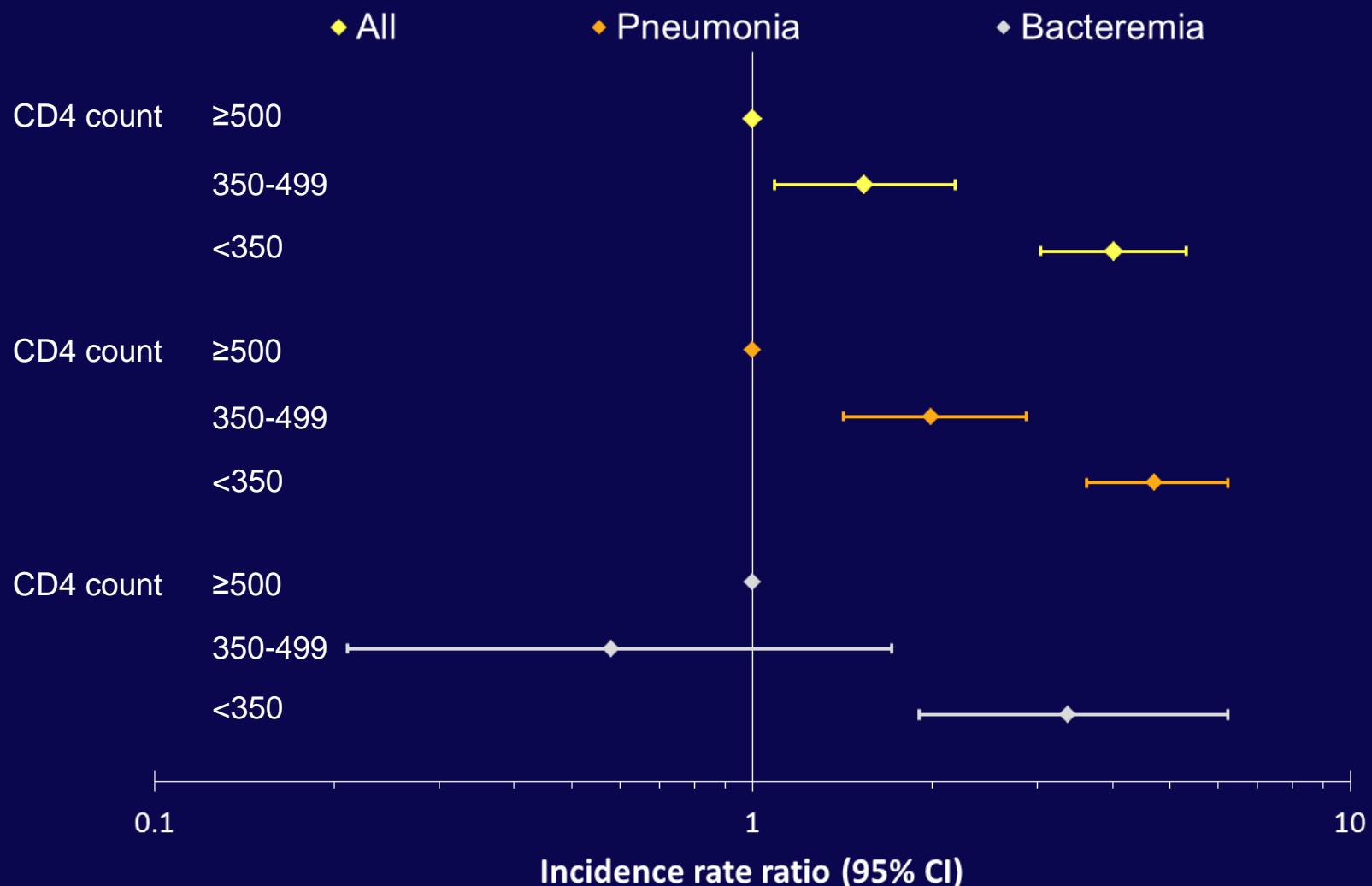
<b>All Patient (N,%)</b>		<b>10851</b>	<b>100</b>
Gender (N,%)	Male	7857	72.4
Ethnic origin (N,%)	White	9562	88.1
Age (median, IQR)		42	35-49
HIV exposure Group (N,%)	Homosexual IDU Heterosexual	4210 2346 3461	38.8 21.6 31.9
Region of Europe (N,%)	South West Central North East Central East Argentina	2517 2484 2369 1489 1546 446	23.2 22.9 21.8 13.7 14.3 4.1
Prior AIDS diagnosis (N,%)		3130	28.9
On cART (N,%)		9110	84.0
CD4 count (median, IQR) cells/mm <sup>3</sup>		458	413-641

# Results

- 10,851 HIV patients
- 275 events occurred during 35,839 PYFU



# Crude incidence rate ratio by CD4 count strata



# All events (n=275)

CD4 count

$\geq 500$

350-499

<350

Gender

Female vs. Male

HIV exposure

group Homosexual

IDU

Heterosexual

Region of Europe

South

West Central

North

East Central

East

Prior AIDS

Yes vs. No

On cART

Yes vs. No

Age

per 10 years older

Smoking

Current vs. never

Diabetic

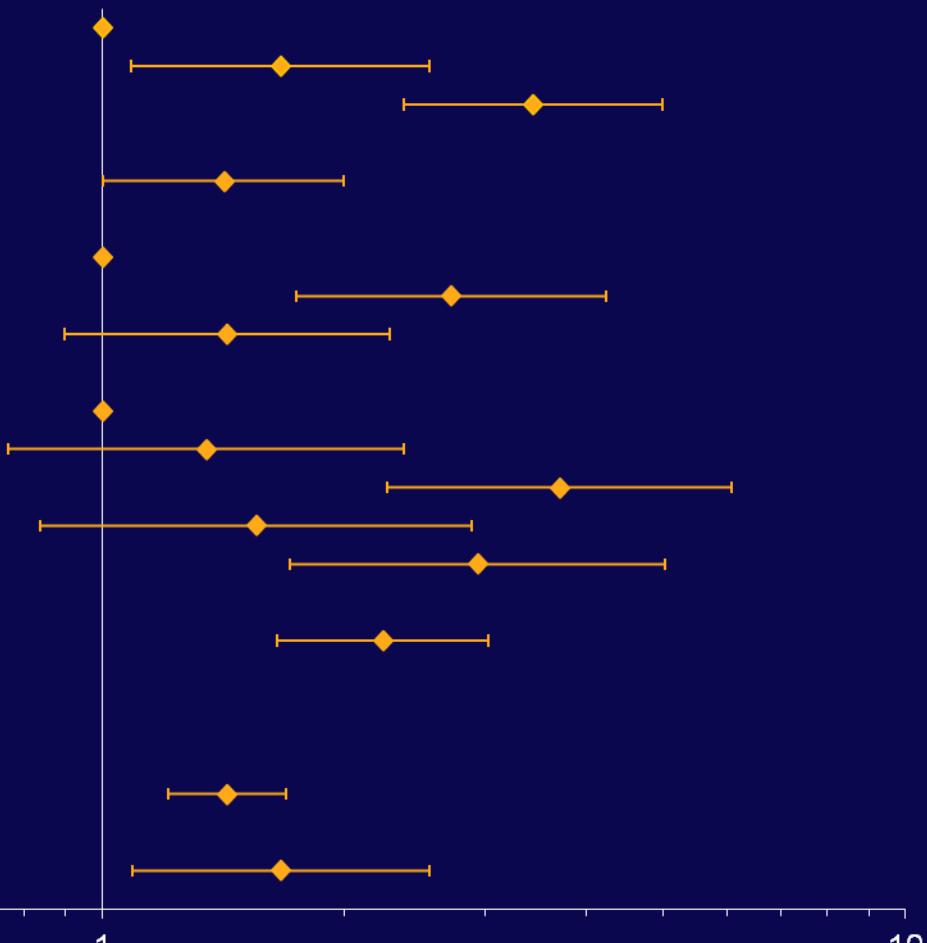
Yes vs. No



Adjusted incidence rate ratio (95% CI)  
Also adjusted for race

# Pneumonia (n=192)

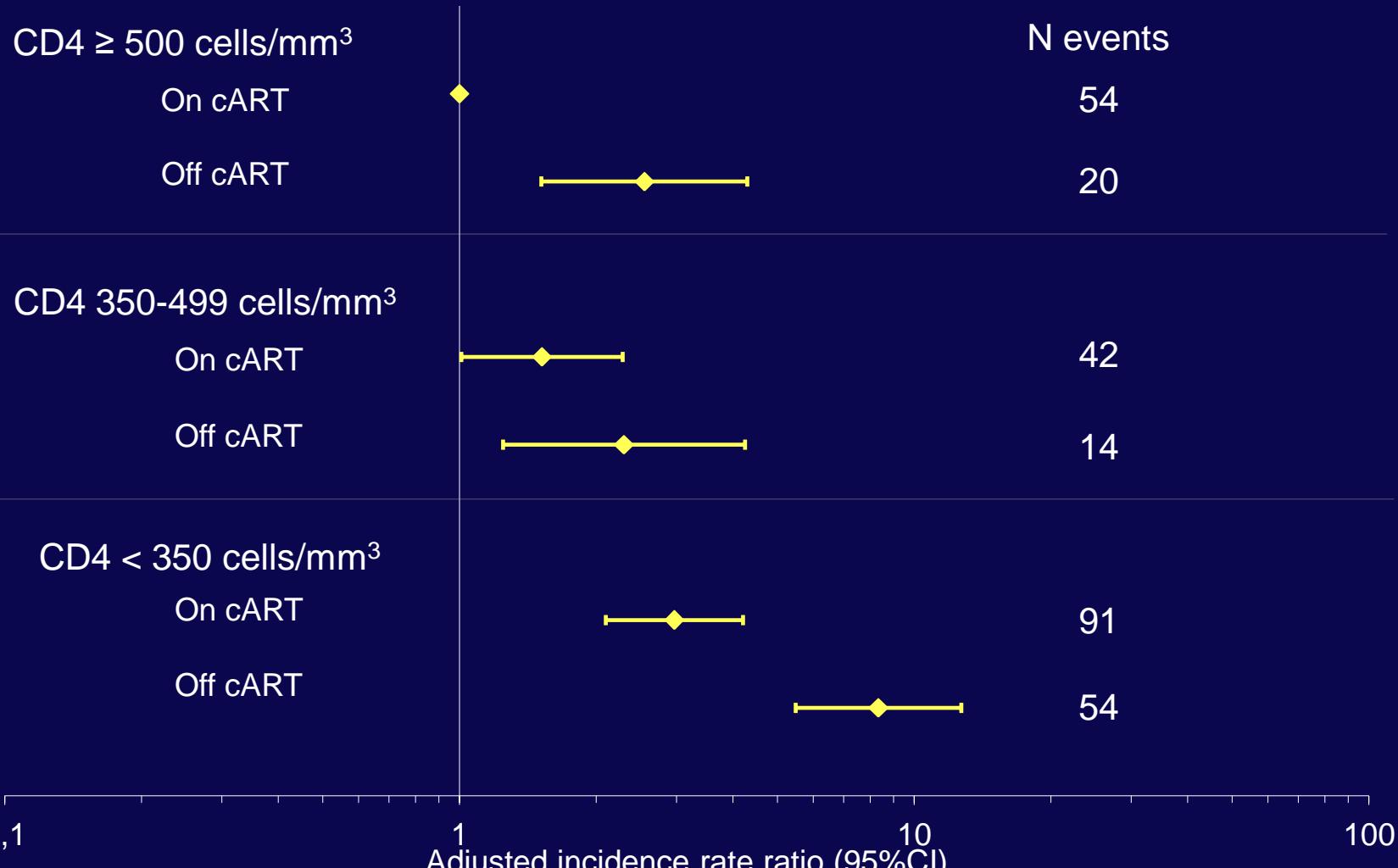
CD4 count	$\geq 500$
	350-499
	<350
Gender	Female vs. Male
HIV exposure group	Homosexual
	IDU
	Heterosexual
Region of Europe	South
	West Central
	North
	East Central
	East
Prior AIDS	Yes vs. No
On cART	Yes vs. No
Age	per 10 years older
Smoking	Current vs. never



**Adjusted incidence rate ratio  
(95% confidence interval)**

Also adjusted for race and diabetes

# Adjusted incidence rate ratio by current CD4 count and use of cART



\*Also adjusted for gender, HIV exposure group, region, prior AIDS, age, smoking, diabetes, and race

# Limitations

- Data collection
- Not all infections analysed separately
- Unable to control for influenza/pneumococcal vaccination
- Outcome after diagnosis
- Unmeasured confounding

# Conclusions

- Non-AIDS bacterial infections remain a significant cause of morbidity
- The risk of bacterial infection was lowest in persons on cART with high CD4+ cell counts
- Timely initiation of cART in treatment naive individuals and adherence to cART is likely to reduce morbidity from non-AIDS infections
- Further investigation of regional differences could contribute to improvement in HIV management across Europe

# The EuroSIDA Study Group

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

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

**Argentina:** (M Losso), C Elias, 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; O Suetnov, Regional AIDS Centre, Svetlogorsk. **Belgium:** (N Clumeck), S De Wit, M Delforge, Saint-Pierre Hospital, Brussels; R Colebunders, 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:** (J Nielsen), G Kronborg, T Benfield, M Larsen, Hvidovre Hospital, Copenhagen; J Gerstoft, T Katzenstein, A-B E Hansen, P Skinhøj, Rigshospitalet, Copenhagen; C Pedersen, Odense University Hospital, Odense; L Ostergaard, Skejby Hospital, Aarhus. **Estonia:** (K Zilmer), West-Tallinn Central Hospital, Tallinn; Jelena Smidt, Nakkusosakond Siseklinik, Kohtla-Järve. **Finland:** (M Ristola), Helsinki University Central Hospital, Helsinki. **France:** (C Katlama), Hôpital de la Pitié-Salpêtrière, Paris; J-P Viard, Hôpital Necker-Enfants Malades, Paris; P-M Girard, Hospital Saint-Antoine, Paris; JM Livrozet, Hôpital Edouard Herriot, Lyon; P Vanhems, University Claude Bernard, Lyon; C Pradier, Hôpital de l'Archet, Nice; F Dabis, D Neau, Unité INSERM, Bordeaux. **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; S Staszewski, JW Goethe University Hospital, Frankfurt; J Bogner, Medizinische Poliklinik, Munich; G. Fätkenheuer, Universität Köln, Cologne. **Greece:** (J Kosmidis), P Gargalianos, G Xyloomenos, J Perdios, Athens General Hospital; G Panos, A Filandras, E Karabatsaki, 1st IKA Hospital; H Sambatakou, Ippokration Genereal Hospital, Athens. **Hungary:** (D Banhegyi), Szent László Hospital, Budapest. **Ireland:** (F Mulcahy), St. James's Hospital, Dublin. **Israel:** (I Yust), D Turner, M Burke, Ichilov Hospital, Tel Aviv; S Pollack, G Hassoun, Rambam Medical Center, Haifa; S Maayan, Hadassah University Hospital, Jerusalem. **Italy:** (S Vella), Istituto Superiore di Sanità, Rome; R Esposito, I Mazeu, C Mussini, Università Modena, Modena; C Arici, Ospedale Riuniti, Bergamo; R Pristera, Ospedale Generale Regionale, Bolzano; F Mazzotta, A Gabbuti, Ospedale S Maria Annunziata, Firenze; V Vullo, M Lichtner, University di Roma la Sapienza, Rome; A Chiriaci, E Montesarchio, M Gargiulo, Presidio Ospedaliero AD Cotugno, Monaldi Hospital, Napoli; G Antonucci, A Testa, P Narciso, C Vlassi, M Zaccarelli, 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; A d'Arminio Monforte, Istituto Di Clinica Malattie Infettive e Tropicale, Milan. **Latvia:** (B Rozentale), I Zeltina, Infectology Centre of Latvia, Riga. **Lithuania:** (S Chaplinskas), Lithuanian AIDS Centre, Vilnius. **Luxembourg:** (R Hemmer), T Staub, 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, Medical University, Wrocław; A Horban, E Bakowska, Centrum Diagnostyki i Terapii AIDS, Warsaw; A Grzeszczuk, R Flisiak, Medical University, Białystok; A Boron-Kaczmarśka, M Pynka, M Parczewski, Medical University, Szczecin; M Beniowski, E Mularska, Osrodek Diagnostyki i Terapii AIDS, Chorzow; H Trocha, Medical University, Gdańsk; E Jabłonowska, E Malolepsza, K Wojcik, Wojewódzki Szpital Specjalistyczny, Łódź. **Portugal:** (F Antunes), M Doroana, L Caldeira, Hospital Santa Maria, Lisbon; K Mansinho, Hospital de Egas Moniz, Lisbon; F Maltez, Hospital Curry Cabral, Lisbon. **Romania:** (D Duiculescu), Spitalul de Boli Infectioase si Tropicale: Dr. Victor Babes, Bucarest. **Russia:** (A Rakhmanova), Medical Academy Botkin Hospital, St Petersburg; N Zakharova, St Petersburg AIDS Centre, St Peterburg; S Buzunova, Novgorod Centre for AIDS, Novgorod. **Serbia:** (D Jevtic), The Institute for Infectious and Tropical Diseases, Belgrade. **Slovakia:** (M Mokráš), D Staneková, Dérer Hospital, Bratislava. **Slovenia:** (J Tomazic), University Clinical Centre Ljubljana, Ljubljana. **Spain:** (J González-Lahoz), V Soriano, P Labarga, J Medrano, Hospital Carlos III, Madrid; 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; JM Gatell, JM Miró, Hospital Clinic i Provincial, Barcelona; P Domingo, M Gutierrez, G Mateo, MA Sambeat, Hospital Sant Pau, Barcelona. **Sweden:** (A Karlsson), Venhaelsing-Södersjukhuset, Stockholm; L Flamholc, Malmö University Hospital, Malmö. **Switzerland:** (B Ledergerber), R Weber, University Hospital, Zürich; P Francioli, M Cavassini, Centre Hospitalier Universitaire Vaudois, Lausanne; B Hirschel, E Boffi, Hospital Cantonal Universitaire de Geneve, Geneve; H Furrer, Inselspital Bern, Bern; M Battegay, L Elzi, University Hospital Basel. **Ukraine:** (E Kravchenko), N Chentsova, Kiev Centre for AIDS, Kiev; V Frolov, G Kutysna, Luhansk State Medical University; Luhansk; S Servitskiy, Odessa Region AIDS Center, Odessa; M Krasnov, Kharkov State Medical University, Kharkov. **United Kingdom:** (S Barton), St. Stephen's Clinic, Chelsea and Westminster Hospital, London; AM Johnson, D Mercey, Royal Free and University College London Medical School, London (University College Campus); A Phillips, MA Johnson, A Mocroft, Royal Free and University College Medical School, London (Royal Free Campus); M Murphy, Medical College of Saint Bartholomew's Hospital, London; J Weber, G Scullard, Imperial College School of Medicine at St. Mary's, London; M Fisher, Royal Sussex County Hospital, Brighton; C Leen, Western General Hospital, Edinburgh.

**Steering Committee:** J Gatell, B Gazzard, A Horban, J Lundgren, I Karpov, B Ledergerber, M Losso, A D'Arminio Monforte, C Pedersen, , A Phillips, A Rakhmanova, M Ristola, P Reiss, J Rockstroh (Chair), S De Wit (Vice-Chair)

**Coordinating Centre Staff:** O Kirk, A Mocroft, A Cozzi-Lepri, D Grint, M Ellefson, D Podlekareva, J Kjær, L Peters, J Reekie, J Kowalska, J Nielsen, J Tverland, A H Fischer

**EuroSIDA representatives to EuroCoord:** O. Kirk, A. Mocroft, J. Grarup, S. deWitt, P. Reiss, A. Cozzi-Lepri, R. Thiebaut, J. Rockstroh, D. Burger, R. Paredes, J. Kjær

## Statement of Funding:

Primary support for EuroSIDA is provided by the European Commission BIOMED 1 (CT94-1637), BIOMED 2 (CT97-2713), the 5th Framework (QLK2-2000-00773), the 6th Framework (LSHP-CT-2006-018632), and the 7th Framework (FP7/2007-2013, EuroCoord n° 260694) programmes. Current support also includes unrestricted grants by Gilead, Pfizer, and Merck and Co. The participation of centres from Switzerland was supported by The Swiss National Science Foundation (Grant 108787).