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Prevalence of detected drug resistance across different regions of Europe: Data from EuroSIDA 1997-2012

Anna Schultze, AN Phillips, R Paredes, M Battegay, J Rockstroh, L Machala, J Tomazic, O Kirk, J Lundgren and A Cozzi-Lepri

on behalf of EuroSIDA in EuroCoord

Background

- cART has brought considerable benefits, but if viral suppression is incomplete resistance can develop.
- The presence of drug resistance at virological failure:
  - Limits treatment options.
  - May impact negatively on clinical endpoints.
  - Contributes to potential spread of transmitted drug resistance.
- Trends in resistance testing are important for interpreting resistance prevalence estimates.

Aims

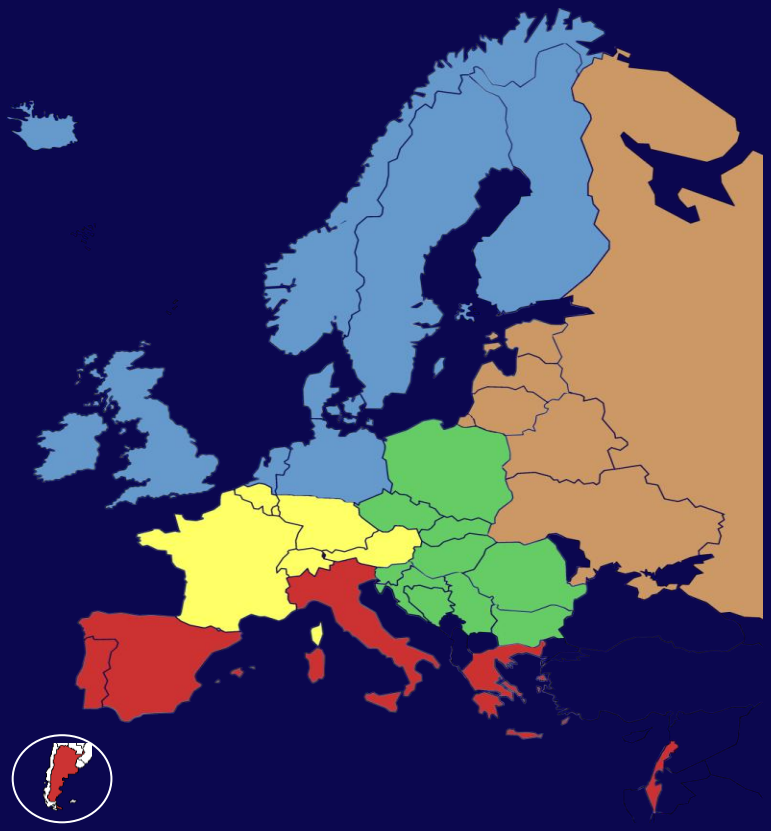
Aim 1: Describe trends in resistance testing among individuals with virological failure (VF).

Aim 2: Describe trends in and factors associated with detecting resistance among those who had a resistance test.

- Focus on geographical differences and changes over time.

Methods - EuroSIDA

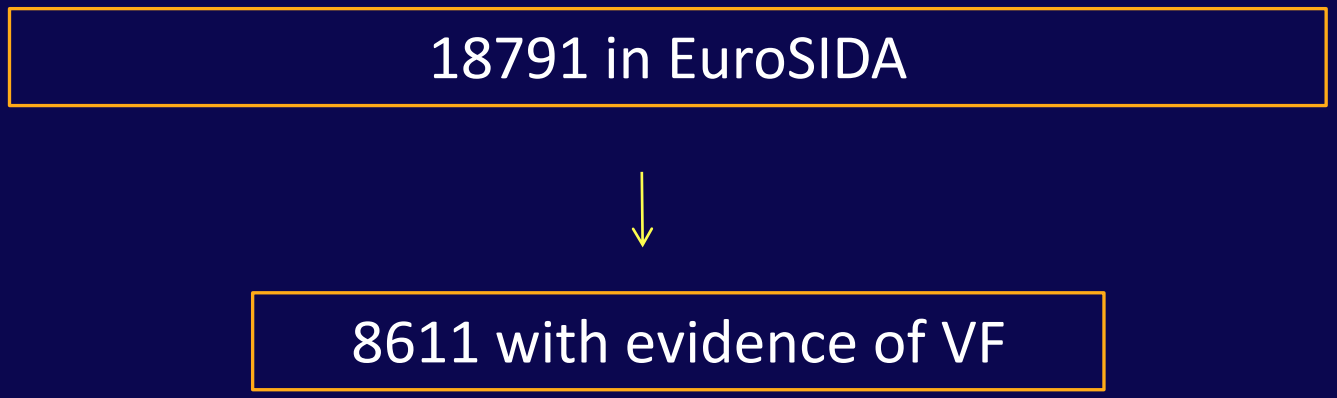
EuroSIDA is a large prospective cohort with 18,791 patients from 108 clinics in 34 European countries, Israel and Argentina.
Regularly collecting:



- Demographic information
- CD4 counts, HIV viral loads
- All treatment start/stop dates
- Routine resistance tests
  - On patient case report form (CRF)
  - Submitted to central resistance laboratory

5 different geographical regions

Inclusion Criteria: Flowchart

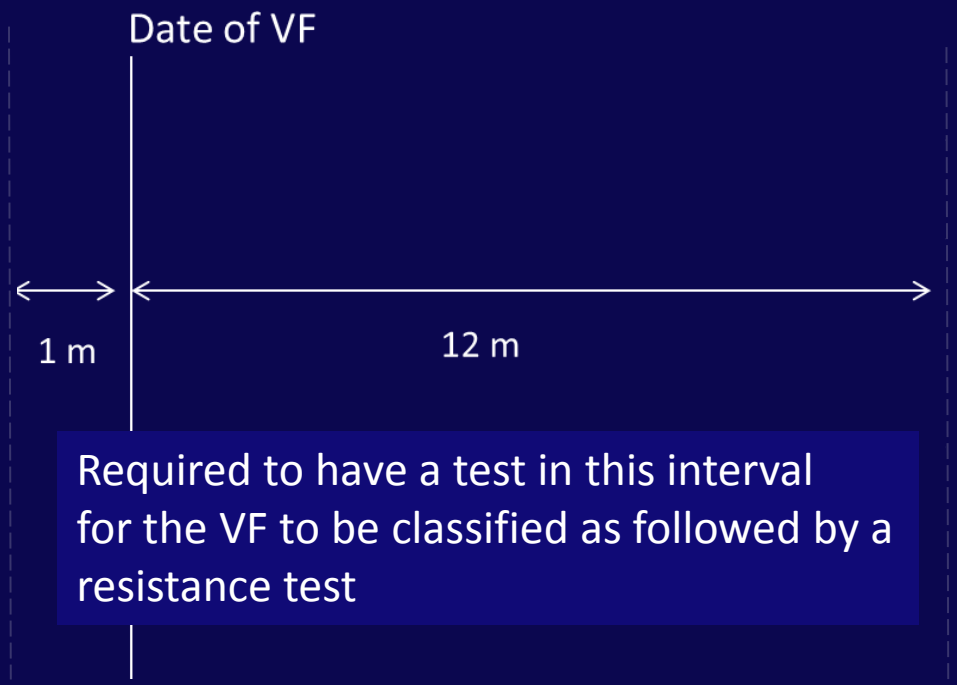


- **VF:** ≥1 RNA measurement >500 on ART after > 4 months of ART exposure.

Inclusion Criteria: Outcome Definitions

Aim 1

- **Having a resistance test:** Test occurring between -1 month and +12 months of the date of VF.



Inclusion Criteria: Outcome Definitions

Aim 1

- **Having a resistance test:** Test occurring between -1 month and +12 months of the date of VF.
- Example: An individual with a date of VF on 1/1 August 2001 was considered having a test following VF in 2001 if the test occurred any time between 1/1 July 2001 and 1/1 August 2002.
- Individuals contributed data for each year in which they experienced a new VF.
- Individuals could contribute data to several calendar years.

Inclusion Criteria: Outcome Definitions

Aim 2

- **Mutations:** Identified using the IAS-US guidelines[1].
    - PI mutations refers only to major PI mutations
    - Characterized in a non-cumulative manner

1. Victoria A. Johnson, MD; Vincent Calvez, MD, PhD; Huldrych F. Günthard, MD; Roger Paredes, MD, PhD; Deenan Pillay, MD, PhD; Robert W. Shafer, MD; Annemarie Wensing, MD, PhD; Douglas D. Richman, MD, '

Update of the Drug Resistance Mutations in HIV-1: March 2013', ***Topics in Antiviral Medicine*****, 21 (2013), 6–14.**

Methods: Statistical Methods

- Logistic regression with generalized estimating equations.
- Baseline date was defined as the time an individual first experienced virological failure.
- Sensitivity Analyses:
  - VF: ≥1 RNA measurement >1000 while on ART+ 4 months of previous ART exposure.
  - VF: ≥1 RNA measurement >500 while on ART followed by a switch in drug regimen.

Baseline Characteristics

		N	%
TOTAL		***8611***	***100***
Gender	*Male*	6438	*75*
Ethnicity	*White*	7433	*86*
Risk Group	*MSM*	3450	*40*
	IDU	2096	*24*
	Heterosexual	2435	*28*
Region	*Southern*	2661	*31*
	Central	2197	*26*
	Northern	2116	*25*
	Central East	771	*9*
	East	644	*8*
Age (years)	Median *(IQR)*	38	*33-45*
CD4 (cells/mm3)	Median *(IQR)*	286	*164-442*
RNA (cp/ml)	Median *(IQR)*	4100	*1176-23971*

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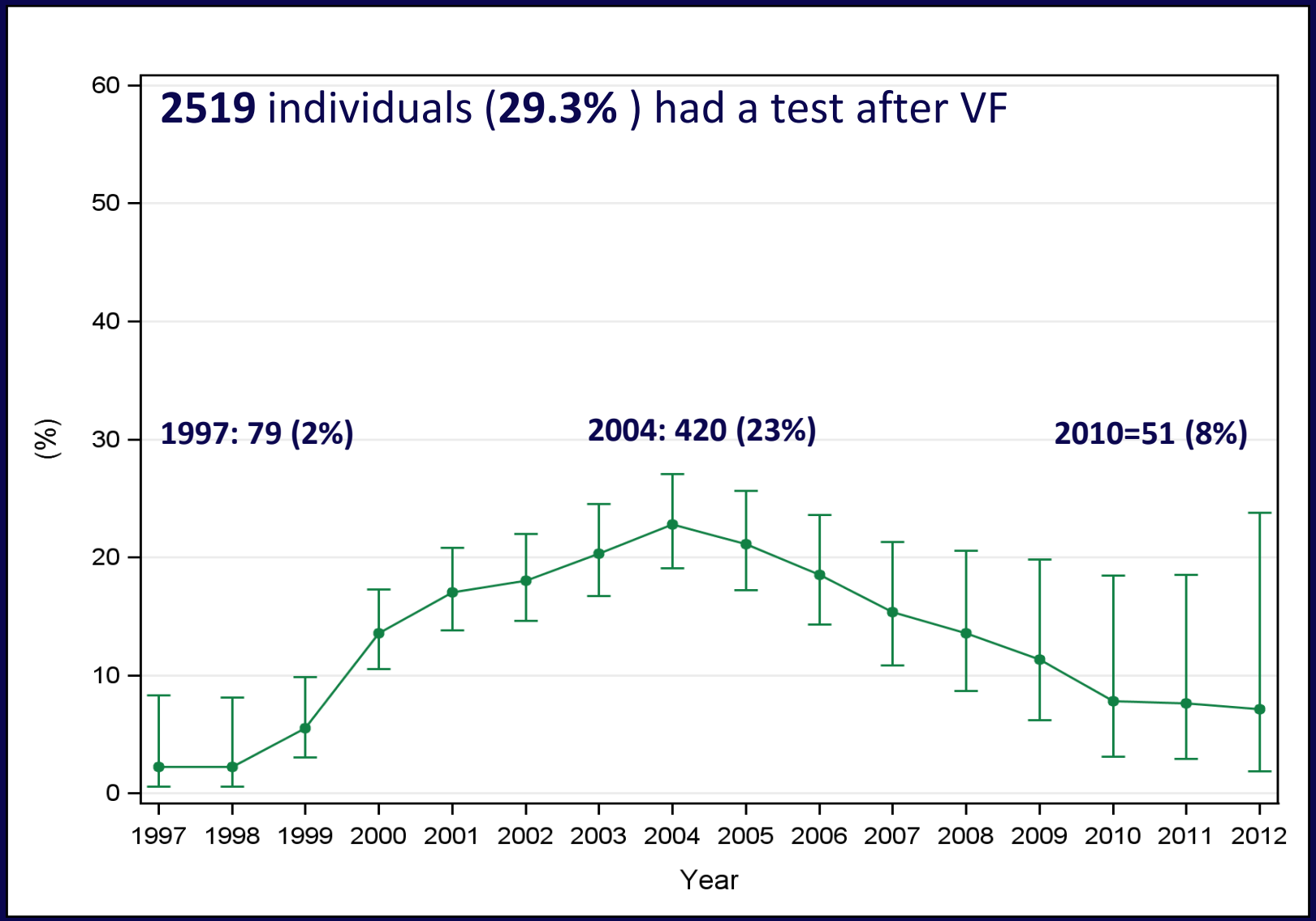
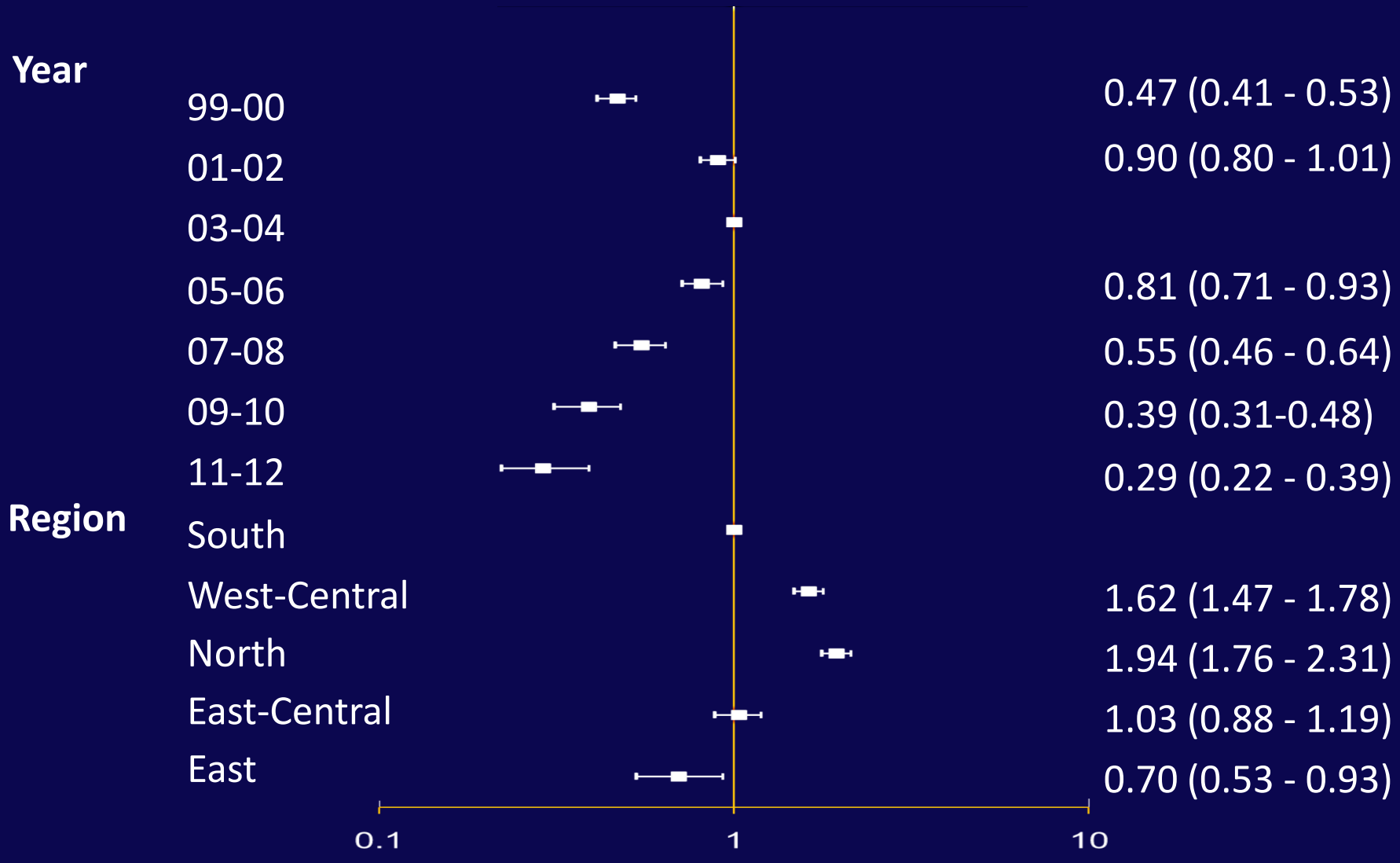
Proportion tested after failure over time



Adjusted odds ratios of resistance testing



1. Additionally adjusted for gender, age, risk group, ethnicity, VL, previous failure, previous resistance test, history of ART exposure and CD4 count.
2. Results from 97-98 not shown because of small numbers

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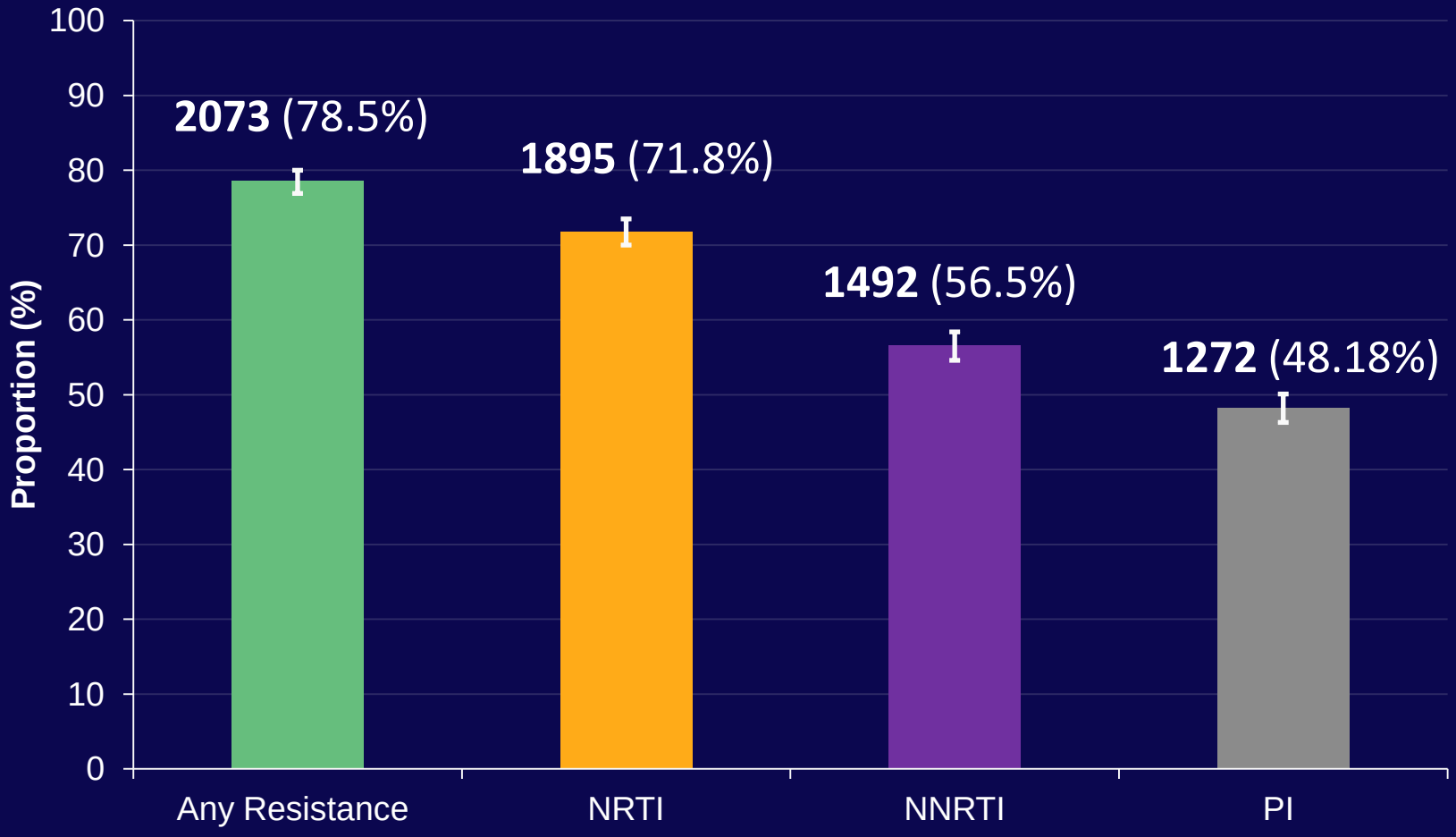
Proportion of tests detecting resistance



Most common:	M184V/I	1419 (53.75%)	(Reverse Transcriptase)
	I54VTALM	764 (28.94%)	(Protease)

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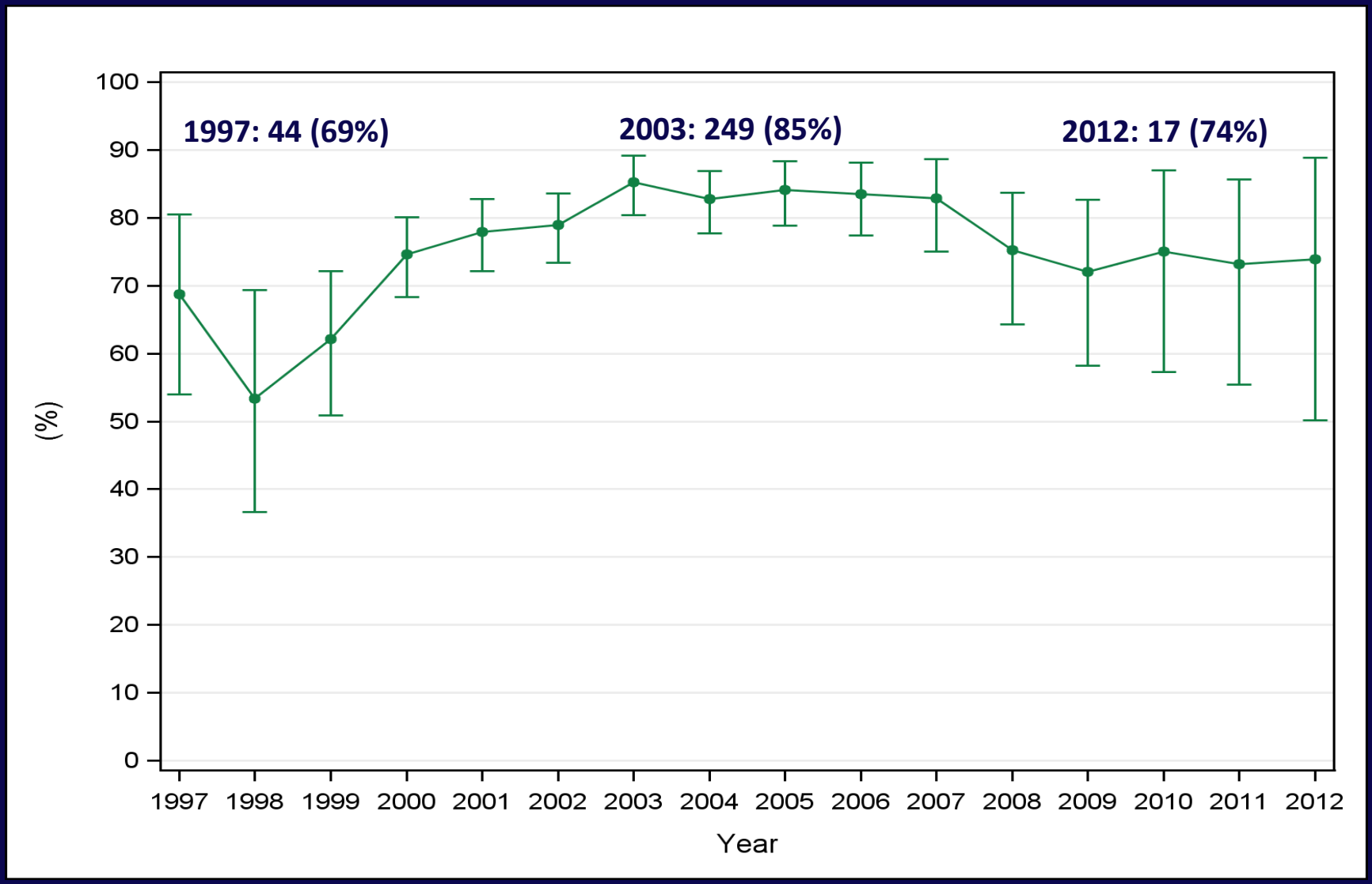
Prevalence of detected resistance over time



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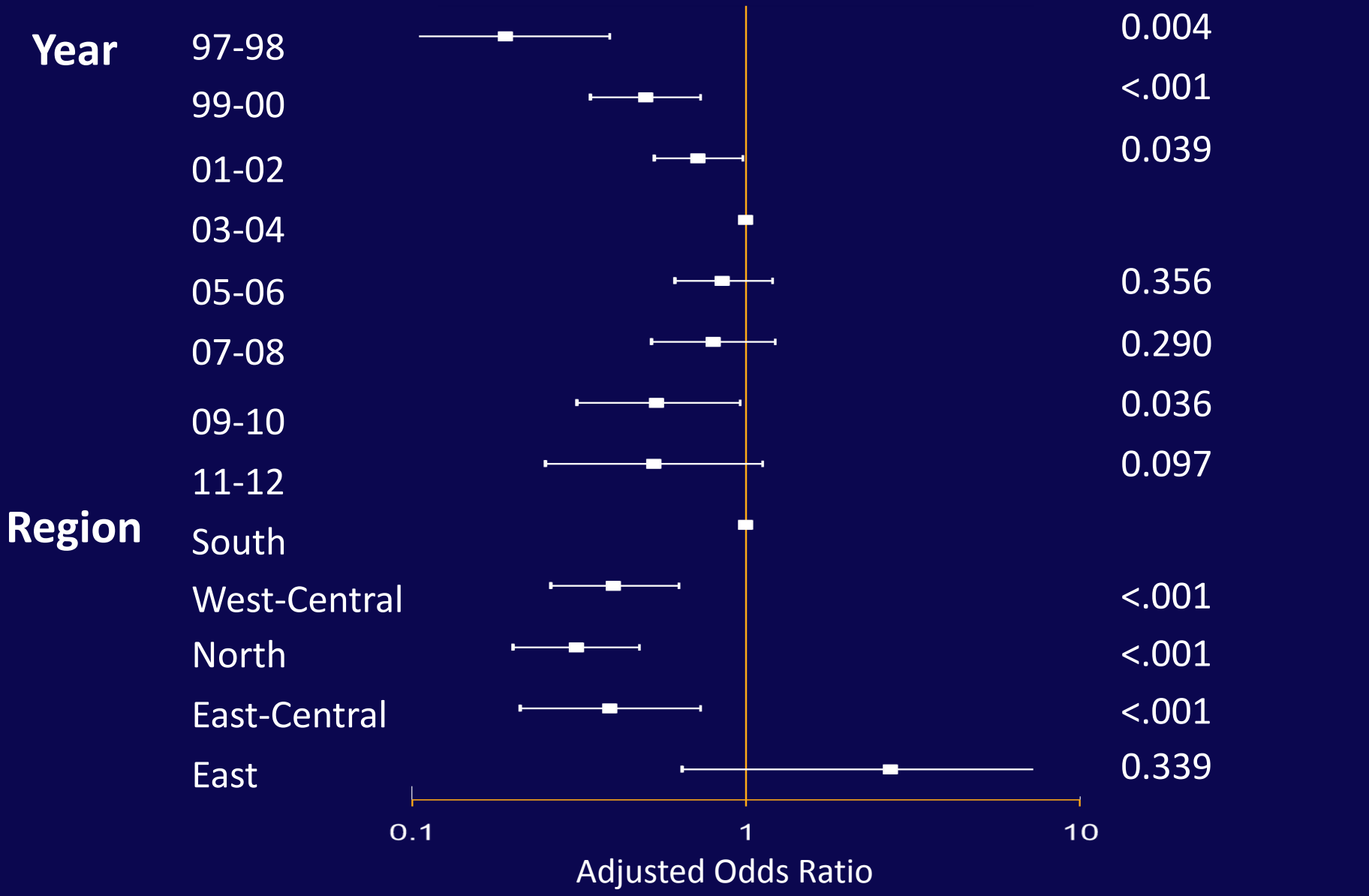
Factors associated with detecting any resistance



Additionally adjusted for gender, age, risk group, ethnicity, VL, previous failure, previous resistance test, history of ART exposure and CD4 count.

Limitations

- Inclusive definition of VF, could underestimate the proportion with a resistance test.

  Sensitivity analyses with stricter criteria were consistent.

- Small number of tests, particularly in recent years. Resulted in uncertainty surrounding prevalence estimates and limited statistical power.

- Cannot exclude under-ascertainment of resistance tests.

Concluding Remarks

- The proportion of individuals who are tested for resistance following VF is lower than expected, and has decreased over time in our study population.
- Despite this, a high proportion of tests detected resistance, and this proportion has remained high over time.
- This may indicate a selective approach to resistance testing in some geographical regions.
- Regional differences observed here could reflect differences in clinical practice and/or resistance testing availability.

The EuroSIDA Study Group

The multi-centre study group of 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; O Suetnov, 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:** (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, 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), 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; P Vanhems, University Claude Bernard, Lyon; C Pradier, 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; M Bickel, JW Goethe University Hospital, Frankfurt; J Bogner, Medizinische Poliklinik, Munich; G. Fätkenheuer, Universität Köln, Cologne. **Greece:** (J Kosmidis), P Gargalianos, G Xylomenos, J Perdios, Athens General Hospital; H Sambatakou, Ippokration Genereal 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; S Pollack, G Hassoun, Rambam Medical Center, Haifa; H Elinav, M Haouzi, Hadassah University Hospital, Jerusalem. **Italy:** (A D'Arminio Monforte), Istituto Di Clinica Malattie Infettive e Tropicale, Milan; 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 Chirianni, E Montesarchio, M Gargiulo, Presidio Ospedaliero AD Cotugno, Monaldi Hospital, Napoli; G D`Offizi, C Taibi , A Antinori, 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), I Zeltina, Infectology Centre of Latvia, Riga. **Lithuania:** (S Chaplinskas), Lithuanian AIDS Centre, 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, Medical University, Wroclaw; A Horban, E Bakowska, Centrum Diagnostyki i Terapii AIDS, Warsaw; A Grzeszczuk, R Flisiak, Medical University, Bialystok; A Boron-Kaczmarska, M Pynka, M Parczewski, Medical Univesity, Szczecin; M Beniowski, E Mularska, Osrodek Diagnostyki i Terapii AIDS, Chorzow; H Trocha, Medical University, Gdansk; E Jablonowska, E Malolepsza, K Wojcik, Wojewodzki Szpital Specjalistyczny, Lodz. **Portugal:** (M Doroana), 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; A Rakhmanova, St Petersburg AIDS Centre, St Peterburg; S Buzunova, 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:** (M Mokráš), D Staneková, Dérer Hospital, Bratislava. **Slovenia:** (J Tomazic), University Clinical Centre Ljubljana, Ljubljana. **Spain:** (J González-Lahoz), V Soriano, P Labarga, 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; J Medrano, Hospital Universitario de Alava, Vitoria-Gasteiz. **Sweden:** (A Blaxhult), Venhaelsan-Sodersjukhuset, Stockholm; L Flamholc, Malmö University Hospital, Malmö, A Thalme, A Sonnerborg, Karolinska University Hospital, Stockholm. **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; P Vernazza, Kantonsspital, St. Gallen. **Ukraine:** (E Kravchenko), N Chentsova, Kiev Centre for AIDS, Kiev; V Frolov, G Kutsyna, Luhansk State Medical University; Luhansk; S Servitskiy, Odessa Region AIDS Center, Odessa; 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, 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; M Fisher, Royal Sussex County Hospital, Brighton; C Leen, Western General Hospital, Edinburgh.

Steering Committee: J Gatell, B Gazzard, A Horban, I Karpov, B Ledergerber, M Losso, A D'Arminio Monforte, C Pedersen, A Rakhmanova, M Ristola, J Rockstroh (Chair), S De Wit t(Vice-Chair)

Additional voting members: J Lundgren, A Phillips, P Reiss

Coordinating Centre Staff: O Kirk, A Mocroft, A Cozzi-Lepri, D Grint, A Schultze, L Shepherd, D Raben, D Podlekareva, J Kjær, L Peters, J E Nielsen, C Matthews, A H Fischer, A Bojesen

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

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