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Effect of ART, immunologic-virologic status and prior tuberculosis on mortality among people with HIV in Europe

Christian Kraef, **Erich Tusch**, Sabine Singh, Lars Østergaard, Gerd Fätkenheuer, Adriano Lazzarin, Santiago Moreno, Katharina Kusejko, Brygida Knysz, Anastasiia Kuznetsova, Janez Tomažič, Jovan Ranin, Robert Zangerle, Fredrik Mansson, Giulia Marchetti, Stéphane De Wit, Amanda Clarke, Jan Gerstoft, Daria Podlekareva, Lars Peters, Joanne Reekie, Ole Kirk

Presenter Disclosure Information

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disclosed no conflict of interest.

BACKGROUND

- It is of clinical relevance to examine survival and causes of death among people with HIV
- Especially in terms of
  - Regional differences in Europe[1]
  - Impact of antiretroviral therapy (ART)
  - Tuberculosis (TB)[2]

1. Reekie J, Kowalska JD, Karpov I, Rockstroh J, Karlsson A, Rakhmanova A, et al. Regional differences in AIDS and non-AIDS related mortality in HIV-positive individuals across Europe and Argentina: the EuroSIDA study. PLoS One. 2012;7(7):e41673.
2. Kraef C, Bentzon A, Roen A, Bolokadze N, Thompson M, Azina I, et al. Long-term outcomes after tuberculosis for people with HIV in eastern Europe. AIDS. 2023 Nov 1;37(13):1997–2006.

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METHODS

- People with HIV in EuroSIDA were followed from 2001–2020.
  - Baseline defined as latest of enrollment or 1 Jan 2001
- Cause of death was classified using the Coding Causes of Death in HIV (CoDe) methodology[3]
- Multivariable Poisson regression on all-cause and AIDS mortality, including interactions with region
  - Baseline risk factors: gender, HIV transmission risk, region
  - Time-updated risk factors: age, time period, immunologic-virologic status, ART status, TB history, and smoking history

3. Kowalska JD, Friis-Møller N, Kirk O, Bannister W, Mocroft A, Sabin C, et al. The Coding Causes of Death in HIV (CoDe) Project: Initial Results and Evaluation of Methodology. Epidemiology. 2011 Jul;22(4):516–23.

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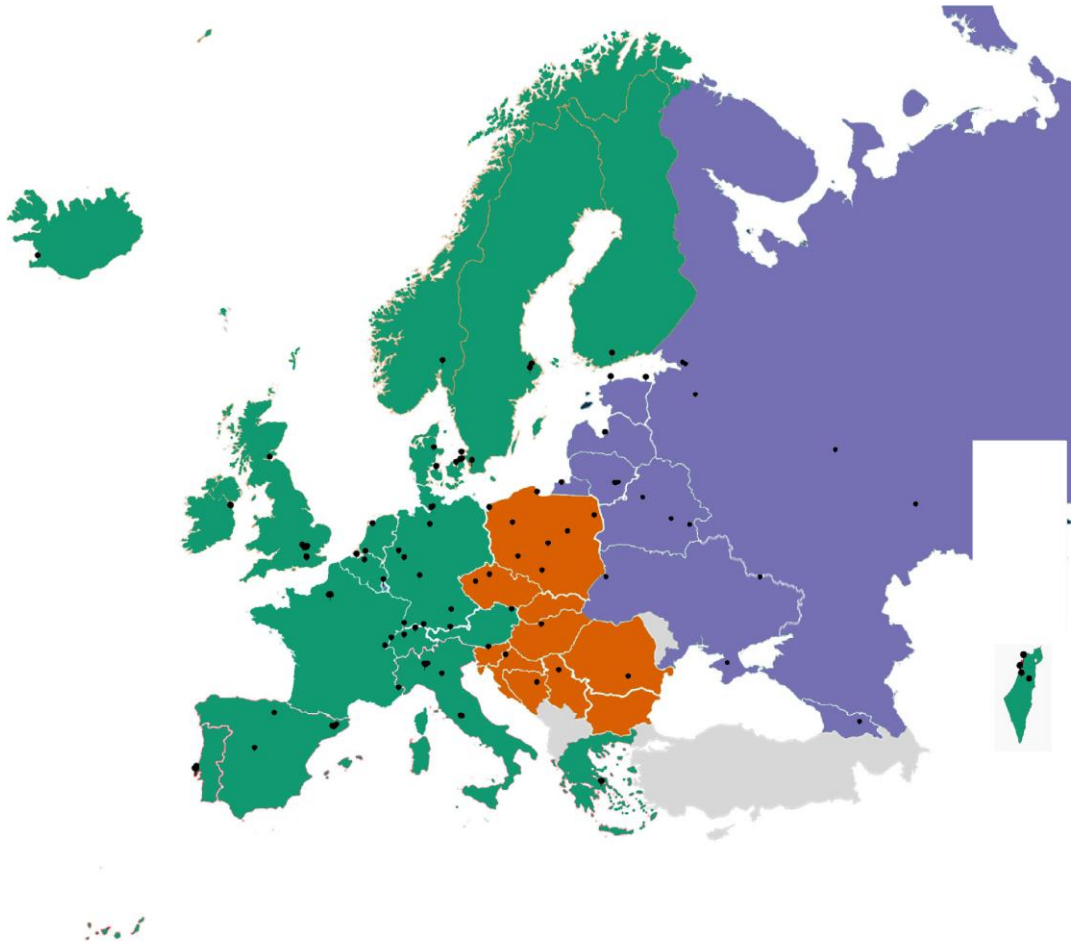
EuroSIDA Regions



- **West:** Austria, Belgium, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, the Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, and the UK
- **Central-East:** Bosnia-Herzegovina, Croatia, Czechia, Hungary, North Macedonia, Poland, Romania, Serbia and Slovenia
- **East:** Belarus, Estonia, Georgia, Latvia, Lithuania, Russia and Ukraine

Participant Characteristics at Baseline

		West n=13715 (67.4%)	Central East n=3020 (14.8%)	East n=3616 (17.8%)
Median baseline date		2004-01-16	2008-07-10	2008-12-16
Median Age (IQR)		42 (36-50)	35 (30-43)	32 (27-39)
Gender	Male	10575 (77.1%)	2326 (77%)	2092 (57.9%)
HIV transmission risk	MSM	5967 (43.5%)	1334 (44.2%)	228 (6.3%)
	Injection drug use	3300 (24.1%)	774 (25.6%)	1743 (48.2%)
	Heterosexual contact	3450 (25.2%)	698 (23.1%)	1513 (41.8%)
	Other/unknown	998 (7.3%)	214 (7.1%)	132 (3.7%)
ART status	On ART	12060 (87.9%)	2550 (84.4%)	1974 (54.6%)
	Off ART, not naive	672 (4.9%)	69 (2.3%)	133 (3.7%)
	ART naive	983 (7.2%)	401 (13.3%)	1509 (41.7%)
Immunologic-virologic status	Poor (CD4≤350 VL>200)	2084 (15.2%)	419 (13.9%)	696 (19.2%)
	Intermediate	6652 (48.5%)	1525 (50.5%)	1400 (38.7%)
	Good (CD4≥500 VL<200)	4717 (34.4%)	917 (30.4%)	494 (13.7%)
	Unknown	262 (1.9%)	159 (5.3%)	1026 (28.4%)
TB pre-baseline		707 (5.2%)	162 (5.4%)	235 (6.5%)

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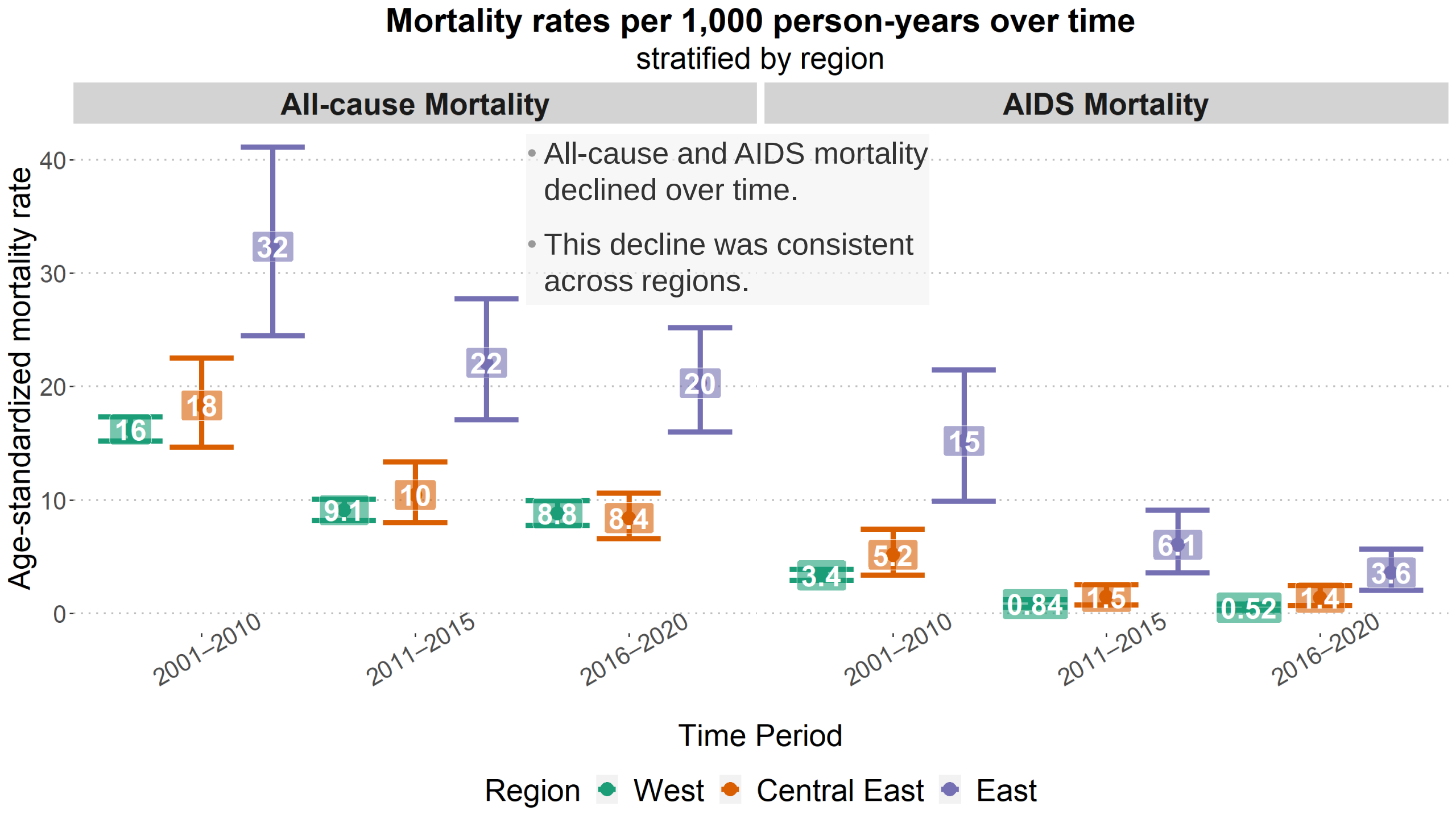
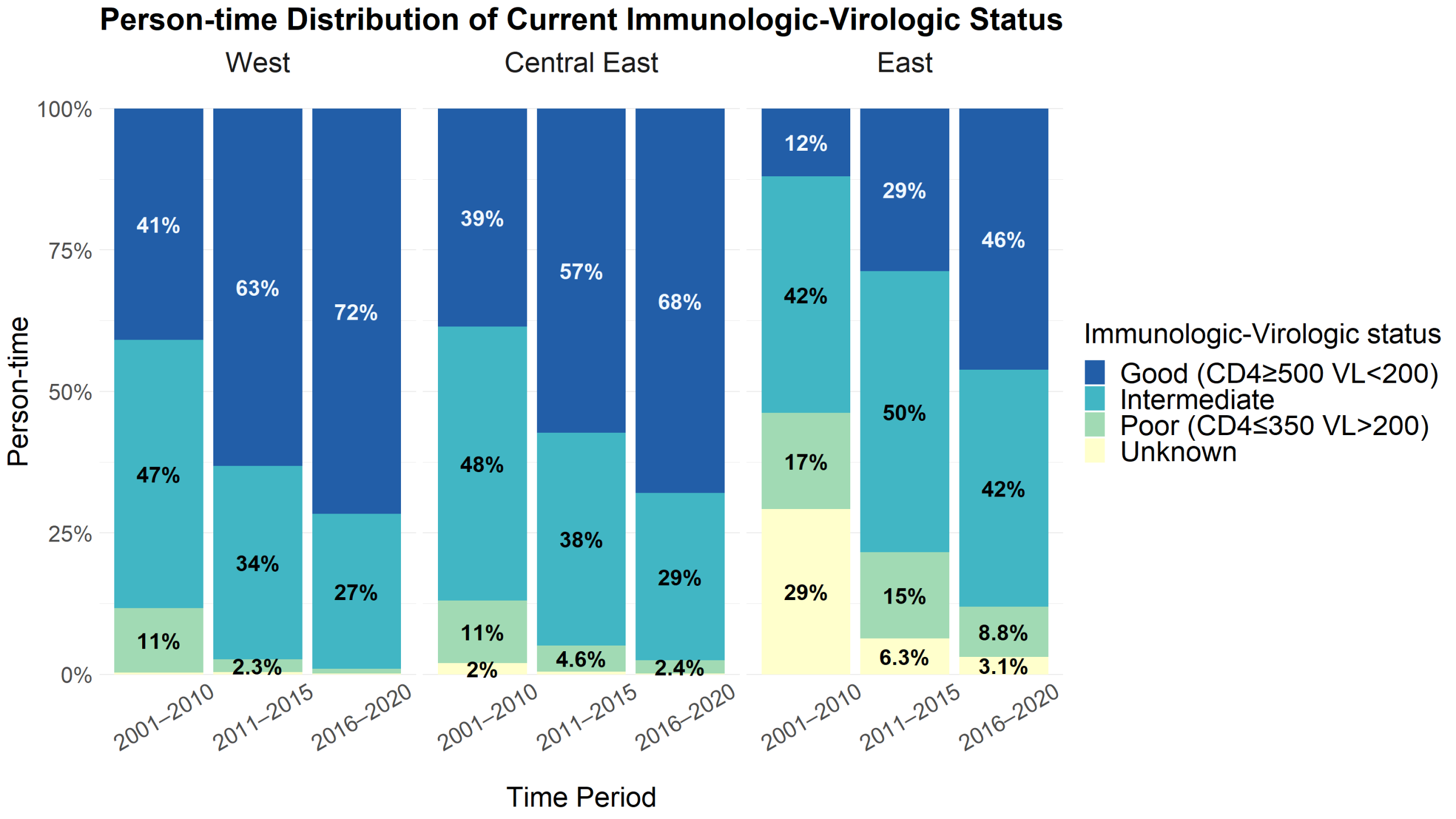
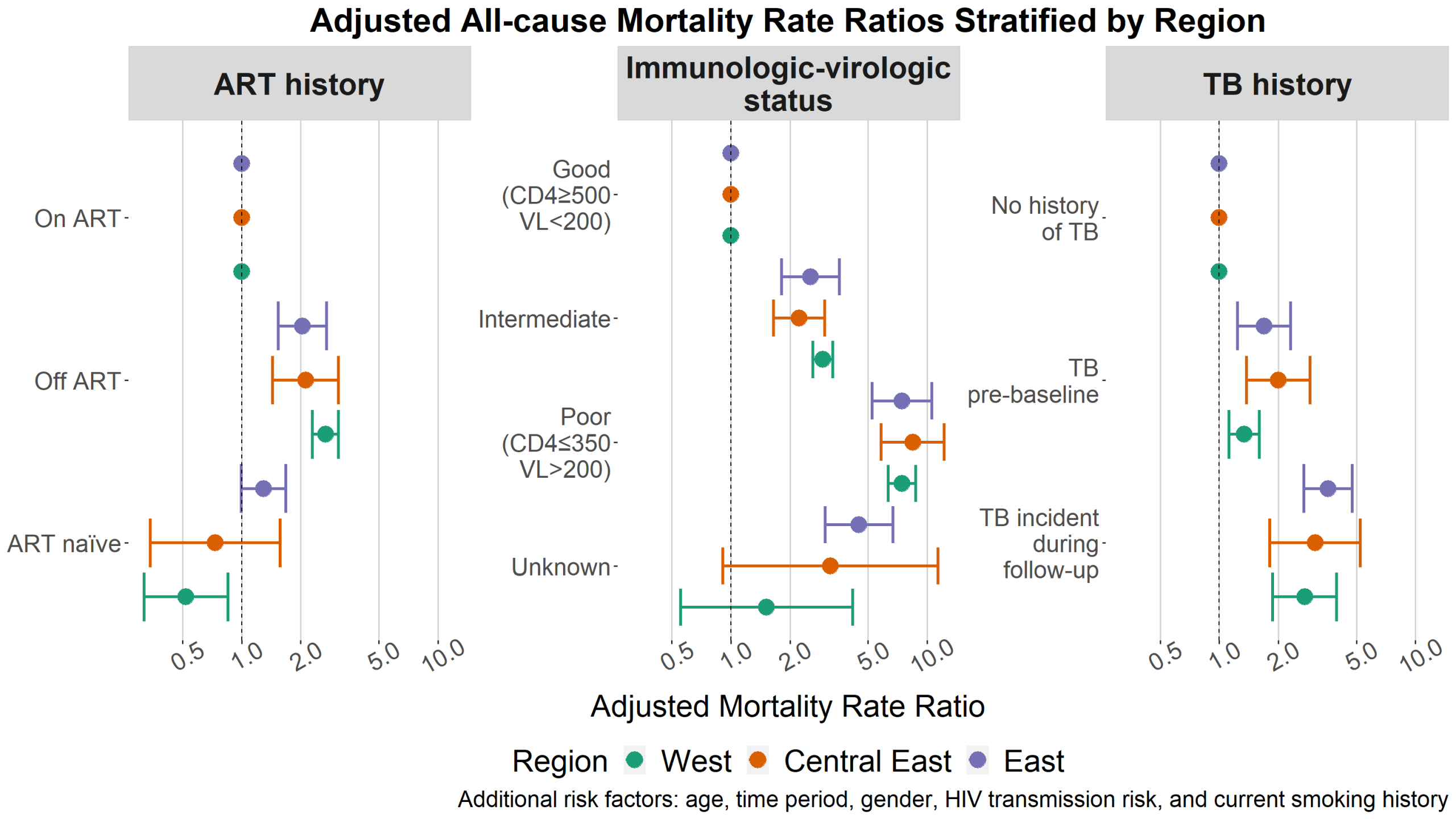
RESULTS

- 20,351 people; 192,544 person-years of follow-up (PYFU)
  - median 8.1 years; IQR 4.4, 15.0
- 2626 died (13.6/1000 PYFU, 95%CI: 13.1–14.2)
- 499 died from AIDS (2.6/1000 PYFU, 95%CI: 2.4–2.8)


Mortality rates per 1,000 person-years over time
stratified by region
All-cause Mortality
AIDS Mortality
All-cause and AIDS mortality declined over time.
This decline was consistent across regions.
Age-standardized mortality rate
40
30
20
10
0
16
18
32
9.1
10
22
8.8
8.4
20
3.4
5.2
15
0.84
1.5
6.1
0.52
1.4
3.6
2001–2010
2011–2015
2016–2020
2001–2010
2011–2015
2016–2020
Time Period
Region
West
Central East
East


Person-time Distribution of Current Immunologic-Virologic Status
West
Central East
East
100%
75%
50%
25%
0%
Person-time
41%
47%
11%
63%
34%
2.3%
72%
27%
39%
48%
11%
2%
57%
38%
4.6%
68%
29%
2.4%
12%
42%
17%
29%
29%
50%
15%
6.3%
46%
42%
8.8%
3.1%
2001–2010
2011–2015
2016–2020
Time Period
Immunologic-Virologic status
Good (CD4≥500 VL<200)
Intermediate
Poor (CD4≤350 VL>200)
Unknown


Adjusted All-cause Mortality Rate Ratios Stratified by Region
ART history
On ART
Off ART
ART naïve
Immunologic-virologic status
Good (CD4≥500 VL<200)
Intermediate
Poor (CD4≤350 VL>200)
Unknown
TB history
No history of TB
TB pre-baseline
TB incident during follow-up
0.5
1.0
2.0
5.0
10.0
Adjusted Mortality Rate Ratio
Region
West
Central East
East
Additional risk factors: age, time period, gender, HIV transmission risk, and current smoking history

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LIMITATIONS

Important mortality predictors not collected, including:

- Socioeconomic status
- Alcohol use
- Current substance use

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CONCLUSIONS

- All-cause and AIDS mortality improved across regions from 2001–2020, but remained higher in Eastern Europe
- Immunologic-virologic status was generally better in West and Central Eastern Europe, whereas Eastern Europe has the highest proportion of people with poor or unknown status
- Being off ART, poorer immunologic-virologic status, and incident TB were associated with higher mortality consistently across regions
- ART-naïve status was associated with higher mortality only in Eastern Europe
- These findings emphasize the need to improve personalized and integrated HIV care, especially in Eastern Europe

The EuroSIDA Study Group

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

Albania: (A Harxhi), University Hospital Center of Tirana, Tirana. **Argentina:** (M Losso), M Kundro, Hospital JM Ramos Mejia, Buenos Aires. **Austria:** (B Schmied), Klinik Penzing, Vienna; R Zangerle, Medical University Innsbruck, Innsbruck. **Belarus:** (I Karpov), A Vassilenko, Belarusian State Medical University, Minsk; VM Mitsura, Gomel State Medical University, Gomel; D Paduto, Regional AIDS Centre, Svetlogorsk. **Belgium:** 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. **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:** T Benfield, Hvidovre Hospital, Copenhagen; J Gerstoft, O Kirk, Rigshospitalet, Copenhagen; C Pedersen, IS Johansen, Odense University Hospital, Odense; L Ostergaard, Skejby Hospital, Aarhus, L Wiese, Sjællands Universitetshospital, Roskilde; L N Nielsen, Hillerod Hospital, Hillerod. **Estonia:** (K Zilmer), West-Tallinn Central Hospital, Tallinn; Jelena Smidt, Nakkusosakond Siseklinik, Kohtla-Järve. **Finland:** (I Aho), Helsinki University Hospital, Helsinki. **France:** (J-P Viard), Hôtel-Dieu, Paris; K Lacombe, Hospital Saint-Antoine, Paris; C Pradier, E Fontas, Hôpital de l'Archet, Nice; C Duvivier, Hôpital Necker-Enfants Malades, Paris. **Germany:** (J Rockstroh), Universitäts Klinik Bonn; O Degen, University Medical Center Hamburg-Eppendorf, Infectious Diseases Unit, Hamburg; C Hoffmann, HJ Stellbrink, ICH Study Center GmbH & Co. KG , 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:** (H Sambatakou), Ippokration General Hospital, Athens; G Adamis, N Paissios, Athens General Hospital "G Gennimatas", Athens. **Hungary:** (J Szlávik), South-Pest Hospital Centre – National Institute for Infectology and Haematology, Budapest.**Iceland:** (M Gottfredsson), Landspitali University Hospital, Reykjavik. **Ireland:** (E Devitt), St. James's Hospital, Dublin. **Israel:** (L Tau), D Turner, M Burke, Ichilov Hospital, Tel Aviv; E Shahar, LM Wattad, Rambam Health Care Campus, Haifa; H Elinav, M Haouzi, Hadassah University Hospital, Jerusalem; D Elbirt, AIDS Center (Neve Or), Rehovot. **Italy:** (A D'Arminio Monforte), Istituto Di Clinica Malattie Infettive e Tropicale, Milan; G Guaraldi, R Esposito, I Mazeu, C Mussini, Università Modena, Modena; F Mazzotta, A Gabbuti, Ospedale S Maria Annunziata, Firenze; A Lazzarin, A Castagna, N Gianotti, Ospedale San Raffaele, Milan; M Galli, A Ridolfo, Osp. L. Sacco, Milan. **Lithuania:** (R Matulionyte) Vilnius University Hospital Santaros Klinikos, Vilnius; R Matulionyte, Vilnius University, Faculty of Medicine, Department of Infectious Diseases and Dermatovenerology, Vilnius. **Luxembourg:** (T Staub), R Hemmer, Centre Hospitalier, Luxembourg. **Netherlands:** (Marc vd Valk), Academisch Medisch Centrum bij de Universiteit van Amsterdam, Amsterdam. **North Macedonia** (J Trajanovska), University Clinic for Infectious Diseases & Febrile Conditions, Mother Teresa 17, Skopje. **Norway:** (DH Reikvam), A Maeland, J Bruun, Oslo University Hospital, Ullevaal. **Poland:** (B Knysz), B Szetela , M Inglot, Medical University, Wroclaw; E Bakowska, Centrum Diagnostyki i Terapii AIDS, Warsaw; R Flisiak, A Grzeszczuk, Medical University, Bialystok; M Parczewski, K Maciejewska, B Aksak-Was, Medical Univesity, Szczecin; M Beniowski, E Mularska, Osrodek Diagnostyki i Terapii AIDS, Chorzow; E Jablonowska, J Kamerys, K Wojcik, Wojewodzki Szpital Specjalistyczny, Lodz; I Mozer-Lisewska, B Rozplochowski,Poznan University of Medical Sciences, Poznan. **Portugal:** (A Zagalo), Hospital Santa Maria, Lisbon; K Mansinho, Hospital de Egas Moniz, Lisbon; F Maltez, Hospital Curry Cabral, Lisbon. **Romania:** (R Radoi), C Oprea, Carol Davila University of Medicine and Pharmacy Bucharest, Victor Babes Clinical Hospital for Infectious and Tropical Diseases, Bucharest. **Russia:** D Gusev, Medical Academy Botkin Hospital, St Petersburg; T Trofimova, Novgorod Centre for AIDS, Novgorod, I Khromova, Centre for HIV/AIDS & and Infectious Diseases, Kaliningrad; E Kuzovatova, Academician I.N.Blokhina Nizhny Novgorod Scientific Research Institute of Epidemiology and Microbiology, Nizhny Novgorod; E Borodulina, E Vdoushkina, Samara State Medical University, Samara. **Serbia:** (J Ranin), The Institute for Infectious and Tropical Diseases, Belgrade. **Slovenia:** (J Tomazic), University Clinical Centre Ljubljana, Ljubljana. **Spain:** (JM Miro), JM Miró, M. Laguno, E. Martinez, F. Garcia, JL Blanco, M. Martinez-Rebollar, J. Mallolas, P Callau, J Rojas, A Inciarta, Hospital Clinic – IDIBAPS University of Barcelona, Barcelona; S Moreno, S. del Campo, Hospital Ramon y Cajal, Madrid; B Clotet, A Jou, R Paredes, J Puig, JM Llibre, JR Santos, Infectious Diseases Unit & IrsiCaixa AIDS Research Institute, 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:** (P Novak), A Thalme, A Sönnerborg, Karolinska University Hospital, Stockholm; J Brännström, Venhälsan-Sodersjukhuset, Stockholm; L Flamholc, Malmö University Hospital, Malmö. **Switzerland:** (K Kusejko), D Braun, University Hospital Zurich; M Cavassini, University Hospital Lausanne; A Calmy, University Hospital Geneva; H Furrer, University Hospital Bern; M Battegay, University Hospital Basel; P Schmid, Cantonal Hospital St. Gallen. **Ukraine:** A Kuznetsova, Kharkov State Medical University, Kharkov. **United Kingdom:** A Milinkovic, St. Stephen's Clinic, Chelsea and Westminster Hospital, London; AM Johnson, 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; A Winston, Imperial College School of Medicine at St. Mary's, London; A Clarke, Royal Sussex County Hospital, Brighton; C. Mackintosh, C Leen, Western General Hospital, Edinburgh.

EuroSIDA Steering Committee: I Karpov, M Losso, J Lundgren, J Rockstroh, I Aho, LD Rasmussen, P Novak, G Wandeler, C Pradier, N Chkhartishvili, R Matulionyte, C Oprea, JD Kowalska, J Begovac, JM Miró, G Guaraldi, R Paredes. **Chair:** G Wandeler. **Co-Chair:** R Paredes. **Study lead:** L Peters. **Coordinating Centre Staff:** L Peters, JF Larsen, M Gardizi, O Fursa, N Jaschinski, B Neesgaard, D Raben, D Kristensen, AH Fischer, TW Elsing. **Statistical Staff:** A Mocroft, J Reekie, A Cozzi-Lepri, A Pelchen-Matthews, A Roen, ES Tusch, W Bannister.

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