Monitoring and Switching of First-line ART in sub-Saharan Africa

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Haas AD[1], Keiser O[1], Dabis F[2], Davies MA[3], Parkes-Ratanshi R[4], Reynolds SJ[5], Wools-Kaloustian K[6], Wandeler G[1] , Egger M[1] for IeDEA collaboration

[1]Institute of Social & Preventive Medicine (ISPM), University of Bern, Switzerland; [2]Université de Bordeaux, ISPED, Centre INSERM U897-Epidemiologie-Biostatistique, Bordeaux, France; [3]Centre for Infectious Disease Epidemiology and Research, University of Cape Town, South Africa; [4]Infectious Diseases Institute, Kampala, Uganda; [5]Rakai Health Sciences Program, Uganda & Division of Intramural Research, NIAID/NIH; [6]Indiana University School of Medicine, Indianapolis, Indiana, USA

Matthias Egger
ISPM, University of Bern
Phone: +41 31 631 35 11
egger@ispm.unibe.ch
www.ispm.ch
www.iedea-sa.org

Objectives

- To describe rates of switching to second-line antiretroviral therapy (ART) in sub-Saharan Africa.
- To examine the impact of routine viral load (VL) monitoring, targeted viral load monitoring, CD4 cell monitoring and clinical monitoring on switching rates.

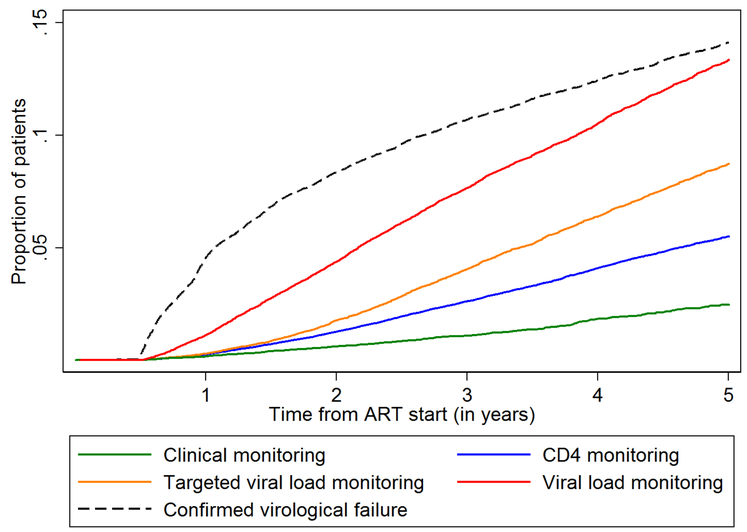
Methods

- Switching was defined as a change from a non-nucleoside reverse-transcriptase inhibitor (NNRTI)-based regimen to a protease inhibitor (PI)-based regimen, with a change of at least one nucleoside reverse-transcriptase inhibitor (NRTI).
- Monitoring strategies were defined for each programme and calendar year:
  - *Routine VL monitoring (RVL):* >75 VL tests per 100 person-years.
  - *Targeted VL monitoring (TVL):* 5-75 VL tests per 100 person-years and >30% of the measurements with VL >1,000 copies/ml.
  - *CD4 monitoring (CD4):* >75 CD4 counts per 100 person-years, but no routine or targeted VL monitoring.
  - *Clinical monitoring (CM):* Sites who do not meet the criteria for any other monitoring strategy.
- Treatment failure were defined according to WHO criteria as:
  - Confirmed virological failure: two consecutive VL values >1,000 copies/ml within 12 months.
  - Confirmed immunologic failure: two consecutive CD4 counts within 12 months <100 cells/ µl, below baseline, or 50% decline from on-treatment peak CD4 value.
- We included treatment naïve HIV-1 infected adults (age >16 years), who initiated ART between 2004 and 2013 in a program participating in the International epidemiologic Databases to Evaluate AIDS (IeDEA) East Africa, West Africa or Southern Africa.
- We used Cox regression models with shared frailty on country to identify determinants of switching and calculate cumulative incidence functions of switching and virological failure.
- We used Kaplan-Meier methods to estimate the probability of switching after failure.
- We modelled the relationship between switching rates and viral load testing using weighted nonlinear least-squares regression to fit a logistic function to the rate of switching and viral load testing in a given calendar year.

Results

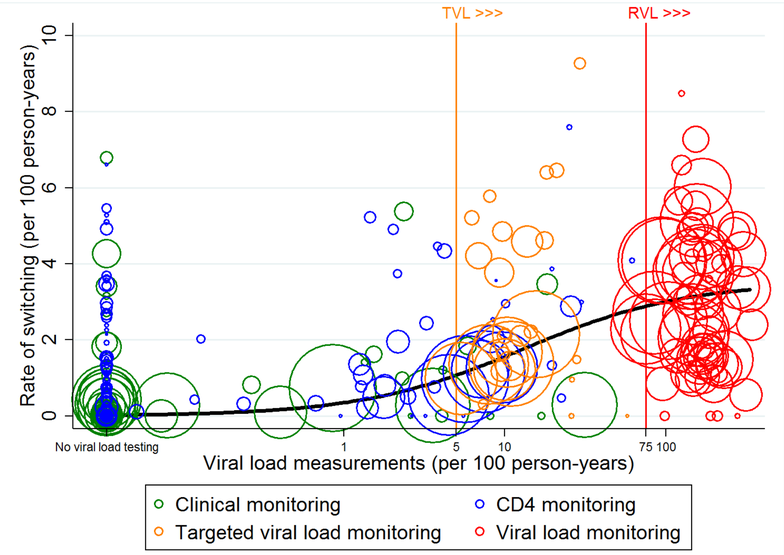
- 323,590 patients from 37 programmes from 16 countries were included: 37,712 (12%) initiated ART in a site with CM, 176,548 (55%) with CD4, 47,975 (15%) with TVL and 61,355 with RVL.
- Overall 11,075 patients (3.4%) switched, for a rate of 1.57 per 100 person-years (95% CI 1.54-1.60).
- The cumulative probability of switching at five years was 7.5% overall, and 2.5% with clinical, 5.5% with immunological, 8.7% with targeted VL and 13.4% with routine VL monitoring (Figure 1).

Figure 1: Cumulative probability of switching to second-line antiretroviral therapy according to monitoring strategy.



- Compared to sites with CM adjusted hazard ratios for switching were 2.56 (95%-CI 1.98-3.31) for sites with RVL, 1.81 (95% CI 1.53-2.13) for sites with TVL testing, and 1.47 (1.27-1.71) with CD4.
- Heterogeneity between clinics and calendar years was large (Figure 2). Switching rates ranged from no switches under CM and CD4 to 9 per 100 person-years with TVL. Switching increased with more TVL, but did not increase further with RVL testing.
- 51.9% of patients with confirmed virological and 15.8% of patients with confirmed immunological failure switched within 2 years.
- Among patients who switched the percentage with evidence of treatment failure based on a single CD4 or VL measurement ranged from 31·0% with clinical to 86.2% with targeted VL monitoring.
- Median CD4 counts at switching were 212 cells/µl under RVL monitoring but lower with other monitoring (120-139 cells/µl).

Figure 2: Bubble plot of annual viral load testing and switching rates in treatment programmes according to monitoring strategy.



Conclusion

- Overall few patients switched to second-line ART and switching occurred late. Switching was more common and occurred earlier with targeted or routine viral load testing.

Project teams

IeDEA Southern Africa

Participating sites: Frank Tanser, Africa Centre for Health and Population Studies, University of Kwazulu-Natal, Somkhele, South Africa; Christopher Hoffmann, Aurum Institute for Health Research, Johannesburg, South Africa; Benjamin Chi, Centre for Infectious Disease Research in Zambia, Lusaka, Zambia; Denise Naniche, Centro de Investigação em Saúde de Manhiça, Manhiça, Mozambique; Robin Wood, Desmond Tutu HIV Centre (Gugulethu and Masiphumelele clinics), Cape Town, South Africa; Kathryn Stinson, Khayelitsha ART Programme and Médecins Sans Frontières, Cape Town, South Africa; Geoffrey Fatti, Kheth'Impilo Programme, South Africa; Sam Phiri, Lighthouse Trust Clinic, Lilongwe, Malawi; Janet Giddy, McCord Hospital, Durban, South Africa; Cleophas Chimbetete, Newlands Clinic, Harare, Zimbabwe; Kennedy Malisita, Queen Elizabeth Hospital, Blantyre, Malawi; Brian Eley, Red Cross War Memorial Children's Hospital and Department of Paediatrics and Child Health, University of Cape Town, Cape Town, South Africa; Michael Hobbins, SolidarMed SMART Programme, Pemba Region, Mozambique; Kamelia Kamenova, SolidarMed SMART Programme, Masvingo, Zimbabwe; Olatunbosun Faturiyele , SolidarMed SMART Programme, Maseru, Lesotho; Matthew Fox, Themba Lethu Clinic, Johannesburg, South Africa; Hans Prozesky, Tygerberg Academic Hospital, Stellenbosch, South Africa; Karl Technau, Empilweni Clinic, Rahima Moosa Mother and Child Hospital, Johannesburg, South Africa; Shobna Sawry, Harriet Shezi Children's Clinic, Chris Hani Baragwanath Hospital, Soweto, South Africa.
Regional Data Centres: Matthias Egger (Principal Investigator), Julia Bohlius, Nello Blaser, Janne Estill, Olivia Keiser, Gilles Wandeler, Luisa Salazar-Vizcaya, Andreas Haas, Marie Ballif, Eliane Rohner, Natascha Wyss, Zofia Baranczuk, Kelly Goodwin, Cam Ha Dao Ostinelli, Institute of Social and Preventative Medicine, University of Bern, Switzerland; Mary-Ann Davies (Principal Investigator), Andrew Boulle, Lucy Campbell, Morna Cornell, Leigh Johnson, Nicola Maxwell, Landon Myer, Michael Schomaker, Mireille Porter, Centre for Infectious Disease Epidemiology and Research, University of Cape Town, South Africa.

IeDEA East Africa

Participating sites: Samuel Ayaya, Lameck Diero, Edwin Sang, Elyne Rotich, AMPATH, Eldoret, Kenya; Elizabeth Bukusi, Medical Research Institute, Kisumu, Kenya; Geoffrey R. Somi, National AIDS Control Program, Dar es Salaam, Tanzania; Rita Lyamuya, Morogoro Regional Hospital, Morogoro, Tanzania; Edward Lugina, Ocean Road Cancer Institute, Dar es Salaam, Tanzania; Mark Urassa, Denna Michael Mkwasa, Kapella Ngonyani, National Institute for Medical Research, Dar es Salaam, Tanzania; Andrew Kambugu, Tumbi Regional Hospital, Kibaha, Tanzania; Philippa Easterbrook, Marion Achieng-Kariuki, Infectious Diseases Institute, Kampala, Uganda; Fred Nalugoda, Rakai Health Sciences Program, Kalisizo, Uganda; John Ssali, Masaka Regional Referral Hospital, Masaka, Uganda; Mwebesa Bosco Bwana, Winnie Muyindike, Mbarara University of Science and Technology, Mbarara, Uganda.
Regional Data Centres: Constantin T. Yiannoutsos (Principle Investigator), Beverly S. Musick, Yee Yee H. Kuhn, Indiana University, Indianapolis, Indiana, United States of America.

IeDEA West Africa

Participating sites: Djimon Marcel Zannou, CNHU Hubert Maga, Cotonou, Benin; Joseph Drabo, CHU Yalgado, Ouagadougou, Burkina Faso; Adrien Bruno Sawadogo, CHU Souro Sanou, Bobo Dioulasso, Burkina Faso; Eugène Messou, ACONDA-CePReF, Abidjan, Cote d'Ivoire; Clarisse Amani Bosse, ACONDA-MTCT-Plus, Abidjan, Cote d'Ivoire; Henri Chenal, CIRBA, Abidjan, Cote d'Ivoire ; Albert Minga, CMSDS/CNTS, Abidjan, Cote d'Ivoire; Aristophane Koffi Tanon, SMIT, CHU de Treichville, Abidjan, Cote d'Ivoire, Serge Olivier Koule, USAC, CHU de Treichville, Abidjan, Cote d'Ivoire; Christian Wejse, Bandim Health Project, Bissau, Guinea-Bissau; David Leuenberger, Jean Hebelamou, Centre Medical Macenta, Macenta, Guinea; Moussa Y Maiga, CH Gabriel Toure, Bamako, Mali; Hamar Alassane Traore, Daouda Minta, CH Point G, Bamako, Mali; Vivian Kwaghe, UATH, Abuja, Nigeria; Festus Igbinoba, National Hospital Abuja, Nigeria; Okwara Benson, Clément Adebamowo, UBTH, Benin City, Nigeria; Moussa Seydi, SMIT, CHU Fann, Dakar, Senegal; Akessiwe Patassi, CHU Tokoin/Sylvanus Olympio, Lome, Togo.
Regional Data Centres: François Dabis (Principal Investigator), Elise Arrivé, Nathalie de Rekeneire, Antoine Jaquet, Valériane Leroy, Charlotte Lewden & Annie Sasco, Bordeaux, France ; Emmanuel Bissagnene (Co-Principal Investigator), Patrick Coffie & Didier Ekouevi (Abidjan, Cote d'Ivoire) ; Man Charurat, UMB/IHV, Abuja, Nigeria.

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