

Regional differences in hepatitis testing, vaccination and treatment in the EuroSIDA study

Jeffrey V Lazarus¹, Lars Peters¹, Kamilla Grønberg Laut¹, Jens D Lundgren¹, Ole Kirk¹, Amanda Mocroft² on behalf of the EuroSIDA study in EuroCOORD

¹CHIP – Centre for Health and Infectious Disease Research, Rigshospitalet, University of Copenhagen, Denmark
²Department Infection and Population Health, University College London, London, United Kingdom

BACKGROUND

Hepatitis screening is a crucial step to timely care. We explored regional variability in self-reported hepatitis B and C management and linked it to liver fibrosis across Europe.

METHODS

A survey was conducted in 2014 in active EuroSIDA clinics. Separate HBV and HCV scores (**Table 1**) were developed based on screening, vaccination and treatment and linked to the clinical database to determine the odds of HBV or HCV score of 3 and of liver fibrosis (≥F2).

RESULTS

80/97 (82%) clinics completed the survey. There were no differences between eastern European (EE) and non-EE for routine screening of HBV or HCV but HBV vaccination (**Figure 1**) and HCV treatment with DAAs (**Figure 2**) varied significantly (**Table 2**). 9,304 patients were enrolled in EuroSIDA from clinics participating in the survey. Among these, those from EE had lower odds of an HBV or HCV score of 3 (aOR 0.21 [95% CI 0.18–0.56 and 0.65; 0.55–0.77 respectively]). Patients from larger clinics (n>200) were more likely to have an HBV score of 3 (aOR 1.38 [1.23–1.55]) but less likely to have an HCV score of 3 (aOR 0.86 [0.79–0.94]) .

Among 7,976 patients with fibrosis data, 498 (6.2%) had ≥F2 fibrosis. Gradually lower HBV scores related to a gradually higher risk of ≥F2 fibrosis; this trend was not observed for HCV (**Figure 3**). The relationship between HBV or HCV score for developing ≥F2 fibrosis was similar between regions.

CONCLUSIONS

This study found that EuroSIDA clinics outside of EE were more likely to vaccinate for HBV than those in EE and to use DAAs to treat HCV. Also, a novel simple measure of quality of HBV care at the clinics was found to be inversely correlated with fibrosis-staging among patients followed in the clinic, suggesting concrete steps to improve care in clinics with a low HBV score. However, a high hepatitis management score for both HBV and HCV would always be something to aim for.

The EuroSIDA Study Group

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 Jlich, 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 Skinhej, Rigshospitalet, Copenhagen; C Pedersen, Odense University Hospital, Odense; L Ostergaard, Skejby Hospital, Aarhus, U B Dragsted, Roskilde Hospital, Roskilde; L N Nielsen, Hillerød Hospital, Hillerød. **Estonia:** (K Zilmer), West-Tallinn Central Hospital, Tallinn; Jelena Smidt, Nakkusosakond Sisekliinik, Kohtla-Järve. **Finland:** (M Ristola), Helsinki University Central Hospital, Helsinki. **France:** (C Katlama), Hôpital de la Pitié-Salpêtrière, 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 Duvvier, 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 Falkenheuer, Universität Köln, Cologne. **Georgia:** (N Chkharitishvili), Infectious Diseases, AIDS & Clinical Immunology Research Center, Tbilisi. **Greece:** (J Kosmidis), P Gargalianos, G Xylomenos, J Perdikis, Athens General Hospital; H Sambatakou, Ippokraton General Hospital, Athens. **Hungary:** (D Banhegyi), Szent László Hospital, Budapest. **Iceland:** (M Gottfredsson), Landspítali 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 Shoguer, AIDS Center (Neve Or), Jerusalem. **Italy:** (A D'Arminio Monforte), Istituto Di Clinica Malattie Infettive e Tropicale, Milan; R Esposito, I Mazzei, C Mussini, Università Modena, Modena; 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; 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 Rozentalis), Infectology Centre of Latvia, Riga. **Lithuania:** V Uzdavinienė, 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, M Inglot, Medical University, Wrocław; A Horban, E Bakowska, Centrum Diagnostyki i Terapii AIDS, Warsaw; A Grzeszczuk, R Flisiak, Medical University, Białystok; M Parczewski, M Pynka, K Maciejewska, Medical University, Szczecin; M Beniowski, E Mularska, Ośrodek Diagnostyki i Terapii AIDS, Chorzów; T Smiatczak, R Flisiak, Medical University, Gdansk; E Jablonowska, E Malolepsza, K Wojcik, Wojewodzki Szpital Specjalistyczny, Łódź; I Mozer-Lisewska, Poznan University of Medical Sciences, Poznań. **Portugal:** (M Doraño), 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, Bucharest. **Russia:** (A Rakhmanova), Medical Academy Botkin Hospital, St Petersburg; A Rakhmanova, St Petersburg AIDS Centre, St Petersburg; T Trofimova, Novgorod Centre for AIDS, Novgorod, I Khromova, Centre for HIV/AIDS & Infectious Diseases, Kaliningrad; E Kuzovatova, Nizhny Novgorod Scientific and Research Institute, Nizhny Novgorod. **Serbia:** (D Jevtic), The Institute for Infectious and Tropical Diseases, Belgrade. **Slovakia:** A Shurnar, D Stanekova, Dér Hospital, Bratislava. **Slovenia:** (J Tomazic), University Clinical Centre Ljubljana, Ljubljana. **Spain:** (J González-Lahoz) S Moreno, J. M. Rodríguez, 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 Universitari de Barcelona, Barcelona; P Domingo, M Gutierrez, G Mateo, MA Sarmat, Hospital Sant Pau, Barcelona; JM Laporte, Hospital Universitario de Alava, Vitoria-Gasteiz. **Sweden:** (A Blaxhult), Venhaalsan-Sodersjukhuset, Stockholm; L Flaholm, Malmö University Hospital, Malmö; A Thälme, A Sonnenberg, Karolinska University Hospital, Stockholm. **Switzerland:** (B Ledergerber), R Weber, University Hospital, Zürich; M Cavassini, Centre Hospitalier Universitaire Vaudois, Lausanne; A Calmy, Hospital Cantonal Universitaire de Geneve, Geneve; H Furrer, Inselspital Bern, Bern; M Battegay, L Elzi, University Hospital Basel; P Schmid, Kantonsspital, St. Gallen. **Ukraine:** (E Kravchenko), N Chentsova, Kiev Centre for AIDS, Kiev; V Frolov, G Kutsyna, I Baskakov, Luhansk State Medical University, Luhansk; S Servitskiy, Odessa Region AIDS Center, Odessa; A Kuznetsova, Kharkov State Medical University, Kharkov; G Kyselova, 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; M Fisher, 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 Cotugno, III Divisione Malattie Infettive, Napoli, Italy; Hospital Carlos III, Departamento de Enfermedades Infecciosas, Madrid, Spain; EuroSIDA Steering Committee: J Gatell, B Gazzard, A Horban, I Karpov, B Ledergerber, M Losso, A d'Arminio Monforte, C Pedersen, A Rakhmanova, M Ristola, A Phillips, P Reiss, J Lundgren, J Rockstroh, S De Wit. Chair: J Rockstroh. Vice-chair: S De Wit. Study Co-leads: A Mocroft, O Kirk. EuroSIDA Representatives to EuroCoord: O Kirk, A Mocroft, J Grup, P Reiss, A Cozzi-Lepri, R Thiebaut, J Rockstroh, D Burger, R Paredes, L Peters, EuroSIDA staff Coordinating Centre Staff: D Podlekareva, L Peters, JE Nielsen, C Matthews, AH Fischer, A Bojesen, D Raben, D Kristensen, K Grønberg Laut, JF Larsen. Statistical Staff: A Mocroft, A Phillips, A Cozzi-Lepri, D Grint, L Shepherd, A Schultze. 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 Janssen R&D, Merck and Co. Inc., Pfizer Inc., GlaxoSmithKline LLC. The participation of centres from Switzerland was supported by The Swiss National Science Foundation (Grant 108787).

Table 1

Methods: HBV and HCV Scoring

The score from the clinic survey was derived as follows:

HBV	HCV
Add 1 if routinely screened for HBV (yes or sometimes)	Add 1 if routinely screened for HCV (yes or sometimes)
Add 1 if routinely vaccinated for HBV (yes or sometimes)	Add 1 if it performs a fibroscan or biopsy (yes or sometimes for either)
Add 1 if it performs a fibroscan or biopsy (yes or sometimes for either)	Maximum 1 point from 3 treatment components, weighted equally (1/3 of a point each): - Add 1/3 if treated for HCV (sometimes or yes); - Add 1/3 if treatment is free; - Add 1/3 if access to and use DAAs.
Note: Both HBV and HCV can therefore have a score of between 0 and 3. Due to small numbers, the score for both HBV and HCV was categorised as 1, 2 or 3.	

Table 2

Results

Summary of HBV and HCV screening, vaccination and treatment questions from the EuroSIDA clinic survey

		All of Europe		Western Europe ²		East Europe ³		
		N centres	%	N centres	%	N centres	%	p-value
N		80	100	68	85.0	12	15.0	
N patients	Total	133,532	100	102,794	77.0	30,738	23.0	
HBV routine screening	No	5	6.2	5	7.4	0	0	
	Yes/sometimes	75	93.8	63	92.7	12	100	0.99
HCV routine screening	No	12	15.0	10	14.7	2	16.7	
	Yes	67	83.8	57	83.8	10	83.3	0.99
	Do not know	1	1.2	1	1.5	0	0	
HBV vaccination	No	16	20.0	8	11.8	8	66.7	
	Yes/sometimes	64	80.0	60	88.2	4	33.3	<0.0001
HCV treatment	No	4	5.0	2	2.9	2	16.7	
	Yes/sometimes	76	95.0	66	97.1	10	83.3	0.10
HCV treatment with direct acting antivirals ⁴	No	14	18.0	8	12.1	6	50.0	
	Yes/sometimes	63	80.8	57	86.4	6	50.0	0.0090
	Don't know	1	1.3	1	1.5	0	0	

1. N=78 responses; 66 from non-east Europe and 12 from east Europe.
2. Austria, Belgium, Croatia, the Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Israel, Italy, Luxembourg, the Netherlands, Norway, Poland, Portugal, Romania, Serbia, Slovakia, Spain, Sweden, Switzerland, the United Kingdom.
3. Belarus, Estonia, Lithuania, Ukraine, the Russian Federation.

Results

HBV vaccination and HCV treatment with DAA

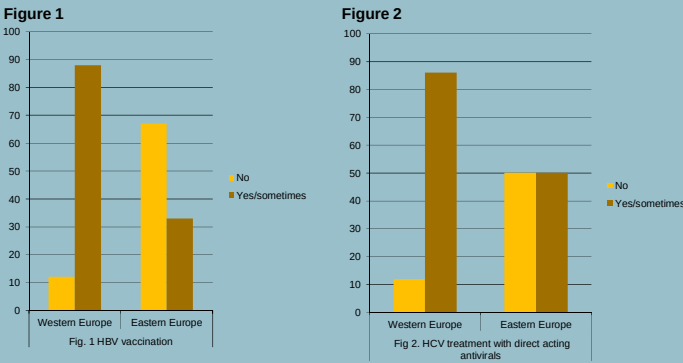
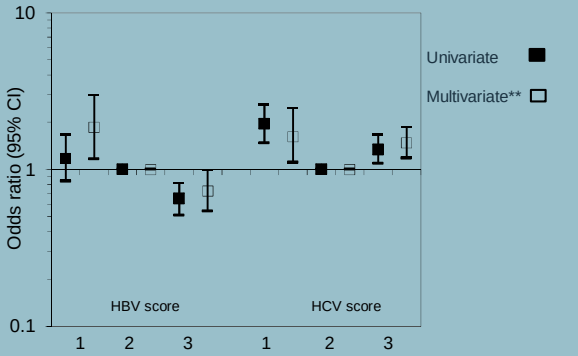


Figure 3

Results

Odds of liver fibrosis (≥F2), according to the EuroSIDA clinic's HBV score and HCV score



**Adjusted for gender, ethnicity, HIV risk group, region, prior AIDS or non-AIDS, hepatitis B or C status, use of cART, VL < 500, CD4 + age, CD4 nadir, time in EuroSIDA, size of centre, anaemia, hypertension, diabetes and smoking status