Model to Eliminate Viral Hepatitis Infection in Migrants: A Prospective Multicenter Study in Southern Italy

Mariantonietta Pisaturo (University of Campania Luigi Vanvitelli, Italy)

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- Migration data In Italy
- Chronic viral hepatitis prevalence in general population in Italy
- Chronic viral hepatitis prevalence in migrants in Italy
- Our model to eliminate Viral Hepatitis Infection in Migrants

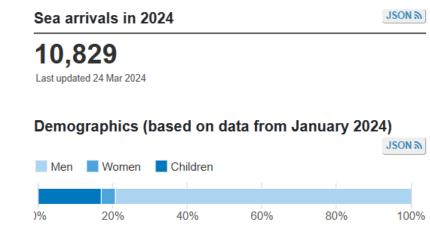
...Burden of migrants in Italy...



...Burden of migrants in ITALY



The boundaries and names shown and the designations used on this map do not imply official endorsement or acceptance by the United Nations



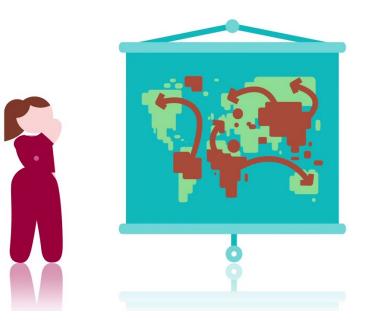
• Migration of subjects coming from countries

high or intermediate endemicity for

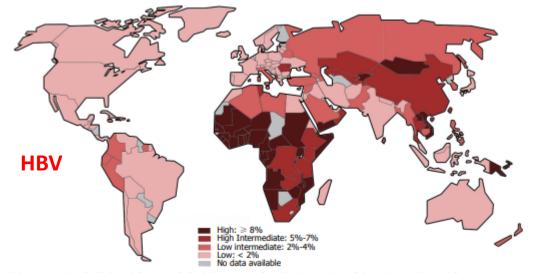
HBV, HCV and HIV infections

...Burden of viral hepatitis worldwide...

- Viral hepatitis are the most common cause of liver diseases and continue to constitute a global public health challenge.
- The different viruses are present worldwide, but their spread varies from country to country



Burden of chronic viral hepatitis worldwide...

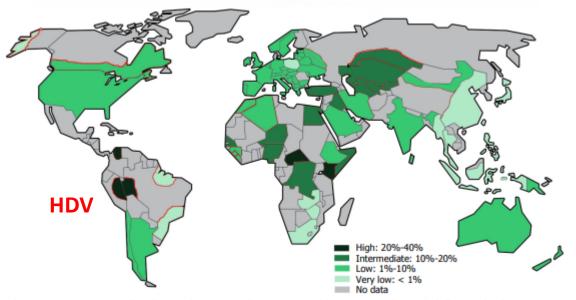


Source: Schweitzer A, Horn J, Mikolajczyk R, Krause G, Ott J. Estimations of worldwide prevalence of chronic heptitis B virus infection: a systematic review of data published between 1965 and 2013. The Lancet. 2015 Jul 28; 386(10003): 1546-1555.

Hepatitis B prevalence



	HBsAg	anti-HVC
Low	<2%	<1%
Intermediate	<2-7%	n.a.
High	>=8%	>=1%





Source: Gower et al. Global epidemiology and genotype distribution of the hepatitis C virus infection. J Hepatol. 2014 Nov; 61(1 Suppl): S45-57. DOI: 10.1016/j.jhep.2014.07.027. Epub 2014 Jul 30

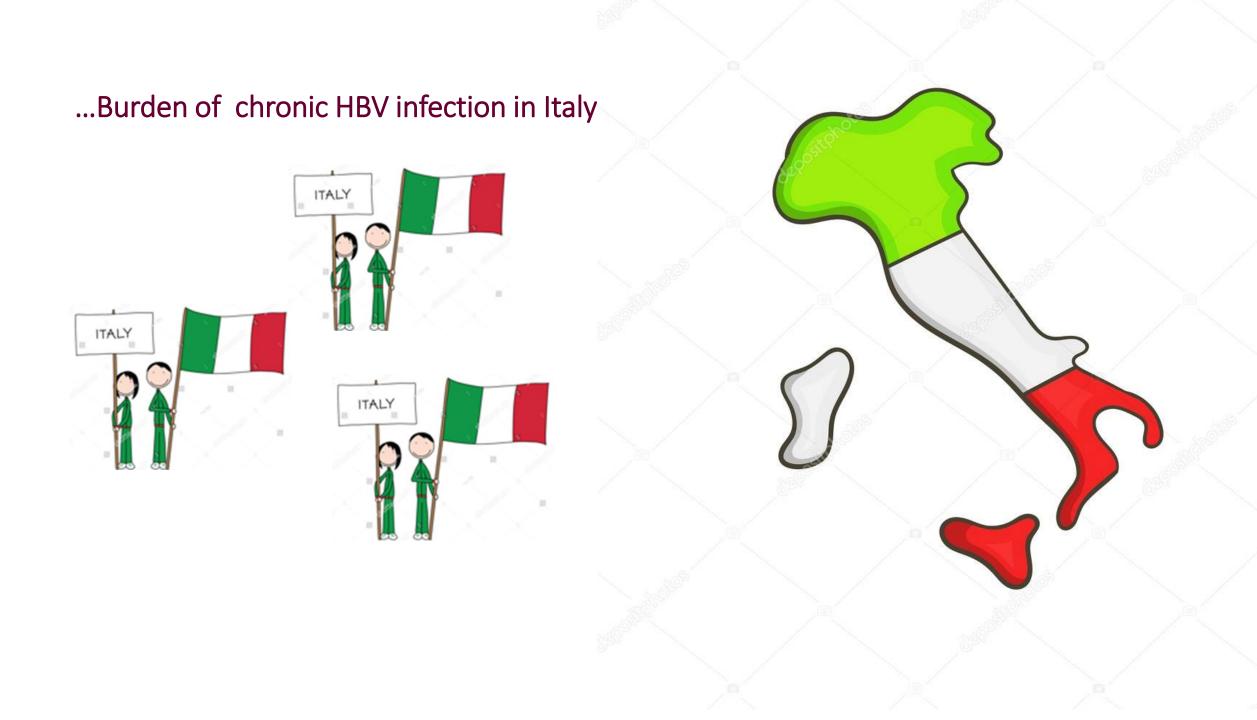


0.0-< 0.6%

0.6-< 0.8% 0.8-< 1.3%

1.3-2.9% 2.9-6.7%

HCV





Liver, Pancreas and Biliary Tract

Low prevalence of hepatitis B and hepatitis C virus serum markers in a cohort of pregnant women from Southern Italy

Tindaro Lembo^{a,b,1}, Francesca Saffioti^{a,1}, Benito Chiofalo^{c,d}, Roberta Granese^{c,d}, Roberto Filomia^b, Roberta Grasso^{c,d}, Onofrio Triolo^{c,d}, Giovanni Raimondo^{a,b,*}

a total of 7558 pregnant

women were admitted

latalian data HBV and HCV prevalence

a cohort of pregnant women consecutively admitted to the Division of Obstetrics and Gynecology of the University Hospital of Messina, Italy, from January 2010 to December 2015

Yearly number of individuals tested, missing data, and prevalence of HBsAg and anti-HCV positive cases in a cohort of Italian and non-Italian pregnant women.

Year	Pregnant women, n. (%)		HBsAg		Anti-HCV	
			Missing n. (%)	Pos./tested n. (%)	Missing n. (%)	Pos./tested n. (%
2010	Total	1258	45 (4)	5/1213 (0.4)	705 (56)	0/553 (0)
	IT	1176 (93)	42 (4)	2/1134 (0.2)	662 (56)	0/514(0)
	n-IT	82(7)	3 (4)	3/79 (3.8)	43 (52)	0/39(0)
2011	Total	1449	264 (18)	6/1185 (0.5)	324 (22)	7/1125 (0.6)
	IT	1306 (90)	244 (19)	3/1062 (0.3)	298 (23)	7/1008 (0.7)
	n-IT	143 (10)	20 (14)	3/123 (2.4)	26 (18)	0/117 (0)
2012	Total	1451	290 (20)	5/1161 (0.4)	340 (23)	0/1111(0)
	IT	1291 (89)	259 (20)	3/1032 (0.3)	301 (23)	0/990(0)
	n-IT	160 (11)	31 (19)	2/129 (1.6)	39 (24)	0/121 (0)
2013	Total	1332	310 (23)	4/1022 (0.4)	345 (26)	1/987 (0.1)
	IT	1203 (90)	274 (23)	0/929(0)	306 (25)	1/897 (0.1)
	n-IT	129 (10)	36 (28)	4/93 (4.3)	39 (30)	0/90 (0)
2014	Total	799	138 (17)	5/661 (0.7)	245 (31)	1/554 (0.2)
	IT	751 (94)	130 (17)	4/621 (0.6)	228 (30)	1/523 (0.2)
	n-IT	48 (6)	8 (17)	1/40 (2.5)	17 (35)	0/31 (0)
2015	Total	1269	383 (30)	4/886 (0.5)	415 (33)	1/854 (0.1)
	IT	1120 (88)	339 (30)	1/781 (0.1)	365 (33)	1/755 (0.1)
	n-IT	149 (12)	44 (30)	3/105 (2.9)	50 (34)	0/99 (0)
2010-2015	Total	7558	1430 (19)	29/6128 (0.5)	2374 (31)	10/5184 (02)
	IT	6847 (91)	1288 (19)	12/5559 (0.2)	2160 (32)	10/4687 (0.2) ^a
	n-IT	711 (9)	142 (20)	17/559 (3	214 (30)	0/497 (0)" <

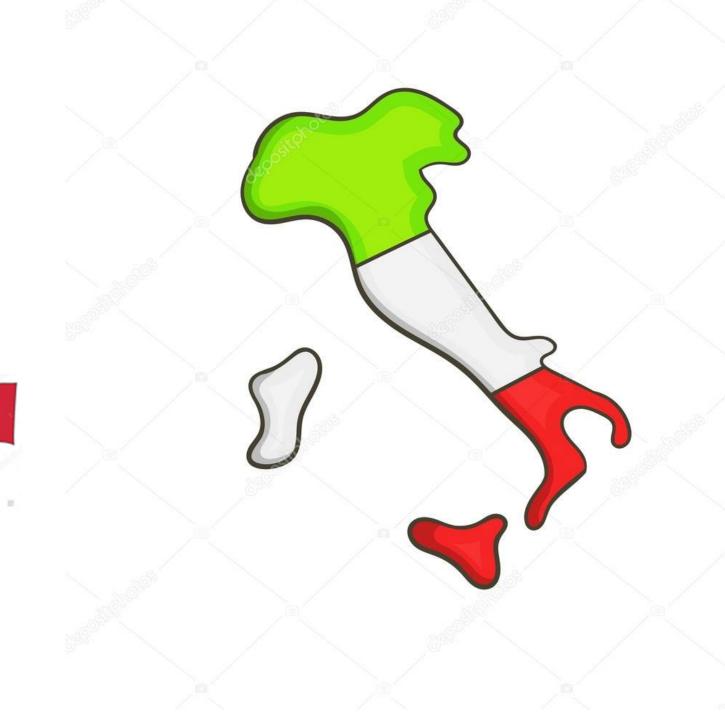
Abbreviations: HBsAg, Hepatitis B surface antigen; Anti-HCV, anti-Hepatitis C virus antibodies; IT, Italians; n-IT, non-Italians; Pos., positive. Values are expressed as numbers (%).

* P<0.001.

^a P=n.s.







FULL PAPER

Prevalence of hepatitis C virus estimates of undiagnosed individuals in different Italian regions: a mathematical modelling approach by route of transmission and fibrosis progression with results up to January 2021

Loreta A. Kondili¹, Massimo Andreoni², Alessio Aghemo^{3,4}, Claudio Maria Mastroianni⁵, Rocco Merolla⁶, Valentina Gallinaro⁶, Antonio Craxi⁷ ¹Center for Global Health, Istituto Stuperiore di Sanità, Rome, Italy: ²Diviersity of Tor Vergata, Rome, Italy: ³Division of Internal Medicine and Hepatology. Department of Gastroenterology, IRCCS Humanitas Research Hospital, Rozzano, Italy; ⁴Department of Infectious Diseases, Azienda Policlinico Umberio I, Rome, Italy; ⁴Medical Department of Materia Diseases, Azienda Policlinico Umberio I, Rome, Italy; ⁴Medical Department AbbVe Italy, Rome Italy; ⁵Gastroenterology and Liver Unit, DiBIMS, University of Palermo, Italy

Map showing the estimated prevalence of active HCV infection in the 4 macroareas of Italy up to January 2021.



...Burden of chronic viral hepatitis in migrants in Italy...



Epidemiology of viral hepatitis in migrants in Italy

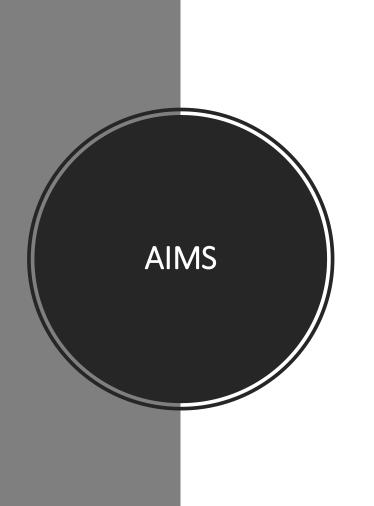
- Fragmented data
- Research group initiatives
- There is a lack of structured surveillance data

Authors	Period of enrollment	Geographical area of study	Sample size	HBV prevalence	HCV	HDV
					prevalence	prevalence
Colucci et al	2019-2020	Milano	362	2%	1.7%	
SSA-AL-	2006-2010	Brescia	3720	6%	3.6%	
lammal						
Piffer et al	2099-2018	Trento	45000		6%	
Cuomo et al	March-December 2016	Modena	304	12.2%	3.3%	
Donisi	Jan December 2015	Piacenza	316	5.3%	1.9%	
Majori et al	March december 2005	Verona	182	9.3%		
Del Pinto et al	July december 2015			22%	20%	
Buonfrate	2015	HBV: 2-409		11.6%	0.8%	
Donisi et al	2020	1100.2-40		5.3%	1.9%	
Malagnino et al	2013-2015		00/	15%	2.2%	
Mazzitelli et al	2015-2018	HCV: 0,8-2	0%	7%		
cotto et al.	Jan december 2015			11.2%	3.9%	
Prestileo et al	2015-2017	Agrigento, Palermo, Trapani	2639	9,7%	0.9%	
Prestileo	200-2015	Palermo	133	40%	9.8%	
Stroffolini	Jan-June 2019	Nord-Centro-Sud	140			23%
Quaranta et al	Coorte Piter	Coorte Piter Nord-Centro- Sud	301	3.8%		
rotalo et al	Jan 2020-Jan 2021	Puglia	309		2.9%	
Zermiani et al	2012	North East Italy	345	3.5%	0.9%	
Coppola et al	Jan-June 2013	Napoli Caserta	882	8.8%	4%	
Coppola et al	Jan 2012-June 2018	Campania Puglia Calabria	3839	10%	3.5%	
Marrone et al	2020	Roma	836	10.8	1.1%	
Pisaturo et al	Jan2012- February 2020	Napoli, Caserta. Foggia	319			2.5%
Colucci et al	March 2019 February 2020	Milan	362	2.0	1.7%	0
afuri et al	May-June 2008	Bari	529	9.7%	2.2%	
Scotto et al	Jan 2003-March 2009	Foggia	1623	11%		

HBV, HCV and HDV prevalence in migrants in Italy Data on the prevalence of hepatitis C virus (HCV) and hepatitis B virus (HBV) in migrants living in Italy are scanty and there are few screening and linkage-to-care programs for this target.





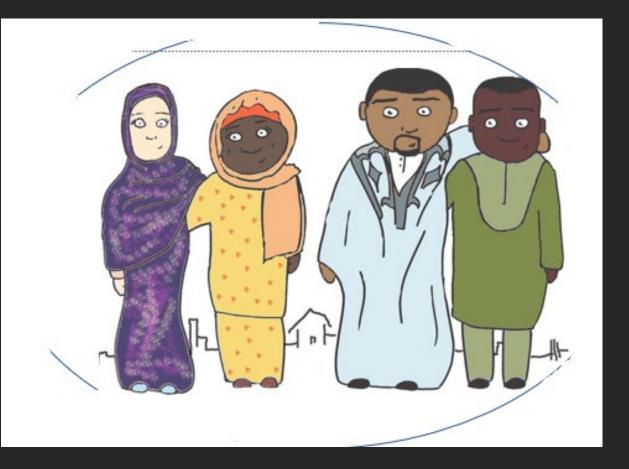


To validate an innovative elimination model for diagnosis and treatment of viral hepatitis in migrants in Italy

Study design

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A prospective, multicenter, collaborative study based on the long-term active cooperation between 2 third-level units of infectious diseases and 4 first-level clinical centers in southern Italy was designed.



TARGET POPULATION

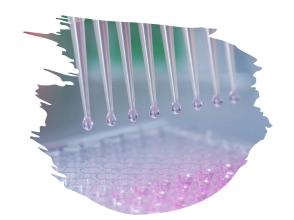
MIGRANTS

Geographical areas of the study



Study design

All >18-year-old migrants consecutively evaluated for clinical consultation at one of the first-level centers were enrolled and organized in 4 phases: educational, screening, linkage to care, and treatment phase



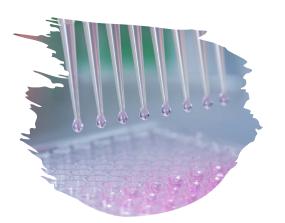
The first-level clinical centers are general practice clinics that are attended mainly by migrantsfor low back pain, headache, hypertension and allergy symptoms; thus, they have proven experience in managing vulnerable groups and are greatly appreciated by the migrants.

These first-level centers are linked with the Italian humanitarian organizations "which welcome migrants who need help offering refuge even if temporary, hot meals, and medical and legal assistance. The migrants willingly frequent these associations because they know they can find help to obtain temporary documents, in order to find work and to join their families in other European countries

Study design

All >18-year-old migrants consecutively evaluated for clinical consultation at one of the first-level centers were enrolled and organized in 4 phases: educational, screening, linkage to care, and treatment phase

An anonymous serologic screening for HBV, HCV, and HIV was offered

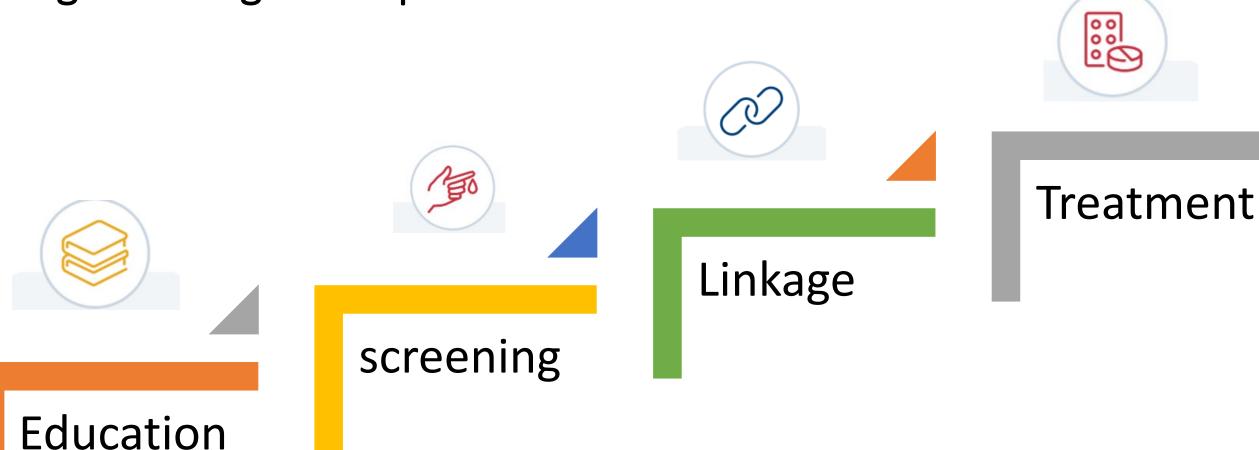


Each migrant who agreed to join the study signed a consent written in the immigrant's own language and in the English language and filled out an anonymous questionnaire on the epidemiologic data administered by the researchers with the assistance of a cultural mediator

The mediator guaranteed that the migrant had understood the type of study and specified that participation in the study did not in any way guarantee permanence in Italy.

All participants included in the study were screened for hepatitis B surface antigen (HBsAg), anti-HCV, and anti-HIV. The sera of HBsAg-positive participants were tested for serum HBV DNA(tested twice)and anti-delta. The sera of anti-HCV-positive participants were tested for HCV-RNA (tested twice). The participants who were positive for viral hepatitis infection and/or for HIV were referred for linkage to care at one of the tertiary units of infectious diseases

Program design: four phases



Program design first phase: education



Education

 Information and illustrated brochure on transmission and prevention of viral infections, related diseases and treatment











COS'S THIN?

no

Program design second phase: screening



Education

 Information and illustrated brochures on transmission and prevention of viral infections, related diseases and treatment



- Free HBsAg, anti-HCV, and anti-HIV screening
- offered to all undocumented migrants and low-income refugees
- Review by a physician and cultural mediator at 1st-level clinical center



Program design third phase: linkage



Education

 Information and illustrated brochures on transmission and prevention of viral infections, related diseases and treatment



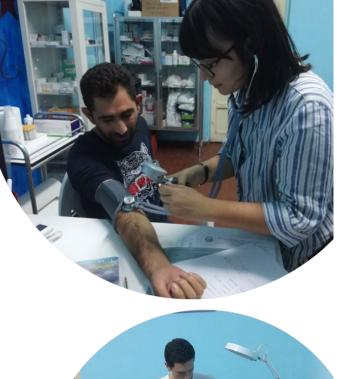
Free HBsAg, anti-HCV, and anti-HIV screening

- offered to all undocumented migrants and low-income refugees
- Review by a physician and cultural mediator at 1st-level clinical center



Linkage

 for viral hepatitis infection and/or for HIV were referred for linkage to care at one of the tertiary units of infectious diseases.







Study design

Key partners/stakeholders



Community mediators

Volunteer associations dealing with disadvantaged people

 The present study program was facilitated by the work of cultural mediators, professionals who facilitate the communication between people speaking different languages and from different cultural backgrounds.

our data



Contents lists available at ScienceDirect Travel Medicine and Infectious Disease

journal homepage: www.elsevier.com/locate/tmaid

Blood-borne chronic viral infections in a large cohort of immigrants in southern Italy: A seven-centre, prospective, screening study

Nicola Coppola^{a,b,*}, Caterina Monari^{a,b}, Loredana Alessio^{b,c}, Lorenzo Onorato^{a,d}, Luciano Gualdieria, Caterina Sagnellia, Carmine Minichinia, Evangelista Sagnellia, Giovanni Di Caprio^{b,c}, Lorenzo Surace⁸, Gaetano Scotto^h, Margherita Macera^{a,c}, Gianfranco Griffo⁸, Italo Francesco Angelillo¹, Mariantonietta Pisaturo^{a,d}



1224

- A prospective screening program was performed in seven clinical centers operating in Campania, Apulia and Calabria regions in southern Italy
- 3,839 agreed to be screened for serum HBsAg, anti-HBc, antiHCV and anti-HIV and were enrolled in the present study (January 2012 and June 2018)

Supplementary table 1: Demographics and serum viral markers of the study participants

	Total
Number of subjects	3,839
Mean Age, years (±SD)	28 (±10)
<u>Males</u> , n (%)*	3,224 (84.0)
Females, n (%)*	610 (15.9)
Serological status, n (%): - HBsAg+ - HBsAg-/anti HBc+ - Anti-HCV+ - Anti-HIV+ - HBsAg-/anti-HBc-/anti-HCV-/anti-HIV -	381 (9.9) 1,448 (37.7) 136 (3.5) 62 (1.6) 1,933 (50.6)
With multiple infection, n (%): - HBsAg+/anti-HCV+ - HBsAg+/anti-HIV+ - Anti-HCV+/anti-HIV + - HBsAg+/anti-HCV+/anti-HIV+	28 (0.7) 9 (0.2) 9 (0.2) 8 (0.2) 2 (0.05)
 Geographical area of origin, n (%)**: northern Africa western Africa eastern Africa central-southern Africa India-Pakistan Subcontinent eastern Asia eastern Europe 	127 (3.3) 2,299 (59.9) 146 (3.8) 54 (1.4) 578 (15.1) 185 (4.8) 383 (10.0)

Demographic and serum viral markers of the study participants, by the geographical area of origin.

	Northern Africa, n° (%)	Eastern Africa, n° (%)	Western Africa, n° (%)	Central-southern Africa, n° (%)	Eastern Europe, n° (%)	India- Pakistan area, n° (%)	P value
N° of subjects	127	146	2,299	54	383	578	
Mean age, years +SD	$34.3 \pm 11.1^{\circ}$	27.2 ± 10.3	26.0 ± 8.1	28.7 ± 10.9	38.2 ± 12.7 §	28.1 ± 8.9	< 0.0001§ < 0.0001°
Males	117 (92.1)	117 (80.1)	2051 (89.2)	39 (72.2)	141 (36.8)§	565 (97.8)	< 0.0001§
Serological status							
HBsAg+	4 (3.1)	9 (6.2)	297 (12.9)*	4 (7.4)	32 (8.4)	26 (4.5)	< 0.0001*
HBsAg-/antiHBc+	19 (15.0)	45(30.8)	1,067(46.4)*	21(38.9)	120(31.3)	129(22.3)	< 0.0001*
Anti-HCV+	2 (1.6)	3 (2.1)	79 (3.4)	3 (5.6)	17 (4.4)	28 (4.8)ç	0.07ç
Anti-HIV+	0 (0.0)	3 (2.1)	48 (2.1)*	1 (1.9)	5 (1.3)	3 (0.5)	0.004*

Infectious Diseases of Poverty

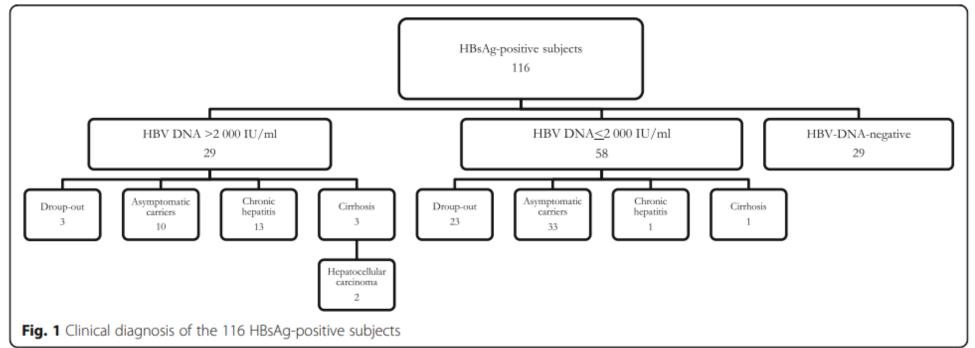
Open Access

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RESEARCH ARTICLE

Hepatitis B virus infection in undocumented immigrants and refugees in Southern Italy: demographic, virological, and clinical features

Nicola Coppola^{1*}, Loredana Alessio^{1,2}, Luciano Gualdieri³, Mariantonietta Pisaturo^{4,5}, Caterina Sagnelli^{6,7}, Carmine Minichini¹, Giovanni Di Caprio^{1,2}, Mario Starace¹, Lorenzo Onorato^{1,2}, Giuseppe Signoriello⁸, Margherita Macera¹, Italo Francesco Angelillo⁹, Giuseppe Pasquale¹ and Evangelista Sagnelli⁵ Of the 1 212 immigrants, 116 (9.6%) were HBsAg positive40 (3.6%) were anti-HCV positive, 14 (1.3%) were anti-HIV positive, 2 HDV ab Positive (1,7%)



1212 enrolled subjects, mostly young (median age 32 years, range 12–74 years), prevalently males (75.2%), and had been living in Italy for a mean period of 50.3 months (SD ± 53.0). Of the 1,212 immigrants, 668 (55.1%) came from SSA

Of the 47 genotyped patients,

11(23.4%) had HBV genotype A, 7 (14.9%) had genotype D, 28 (59.6%) had genotype E, and only one (2.1%) had genotype C.

Program design fourth phase: treatment



Education

 Information and illustrated brochures on transmission and prevention of HCV, related diseases and treatment



Free HCV screening

- offered to all undocumented migrants and low-income refugees
- Review by a physician and cultural mediator at 1st-level clinical center



Linkage

 of anti-HCV-positive patients to 3rd-level ID units (HCV RNA and genotyping)



Treatment

- All the HCV-RNA–positive participants were offered antiviral treatment with sofosbuvir/velpatasvir.
- The HBV-DNA–positive participants with a viral load higher than 2,000 IU/mL were offered antiviral treatment with nucleos(t)ide analogue (NA) according to international guidelines;
- all HIV- positive participants were offered antiviral treatment.

RESULTS

3,501 migrants observed in the study period

3417 (98%) agreed to be screened



Number of patients	3,417	
Age, median (IQR)	27 (18-74	
Males, n ° (%)	2,805 (61	
Months of stay in Italy, median (SD)	28.3 (±45.	
Geographical area of origin n ° (%)		
Eastern Europe	310 (9,07	
India-Pakistan	642 (18.7	
North Africa	141 (4.12	
Sub-Saharan Africa	2,066 (60,	
South America	34 (0.99)	
Not known	224 (6,5)	
Serological marker nº (%)		
HBsAg-positve, anti-HCV-negative, anti-delta-negative, anti HIV-negative	300 (8.7	
HBsAg negative/ anti-HCV positive/anti-HIV-negative	161 (4.7	
HBsAg-positive, anti-HCV-positive, anti-delta-negative, anti HIV negative	16 (0.5)	
HBsAg-positive, anti-delta-positive, anti-HCV-negative, anti HIV negative	8 (0.2)	
HBsAg-negative, anti-HBc-positive, anti HIV negative, anti HCV negative	1,332 (3)	
HBsAg positive/anti-HIV positive/anti-HCV negative	8 (0.2)	
HBsAg positive/anti-HIV positive/anti-HCV positive	2 (0.05)	
HBsAg negative /anti-HCV positive/anti-HIV positive	6 (0.1)	
HBsAg negative/ anti- HIV positive/anti-HCV negative	60 (1.7)	
HBsAg /anti-HCV /anti-HIV/anti-HBc negative	1,524 (4.	

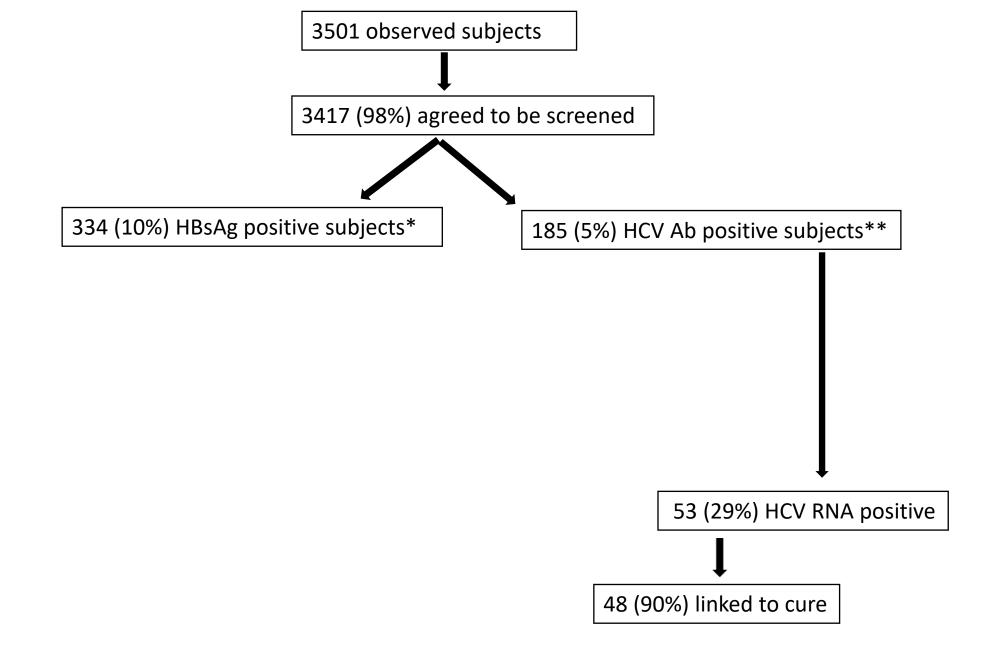
characteristics of the 3417 participants screened.

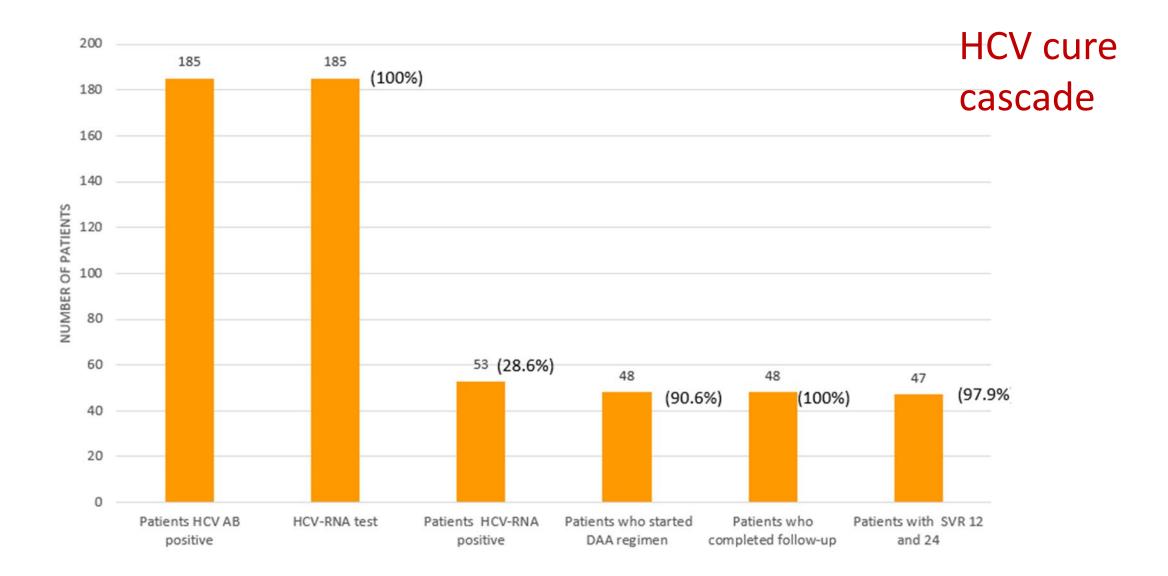
Program design

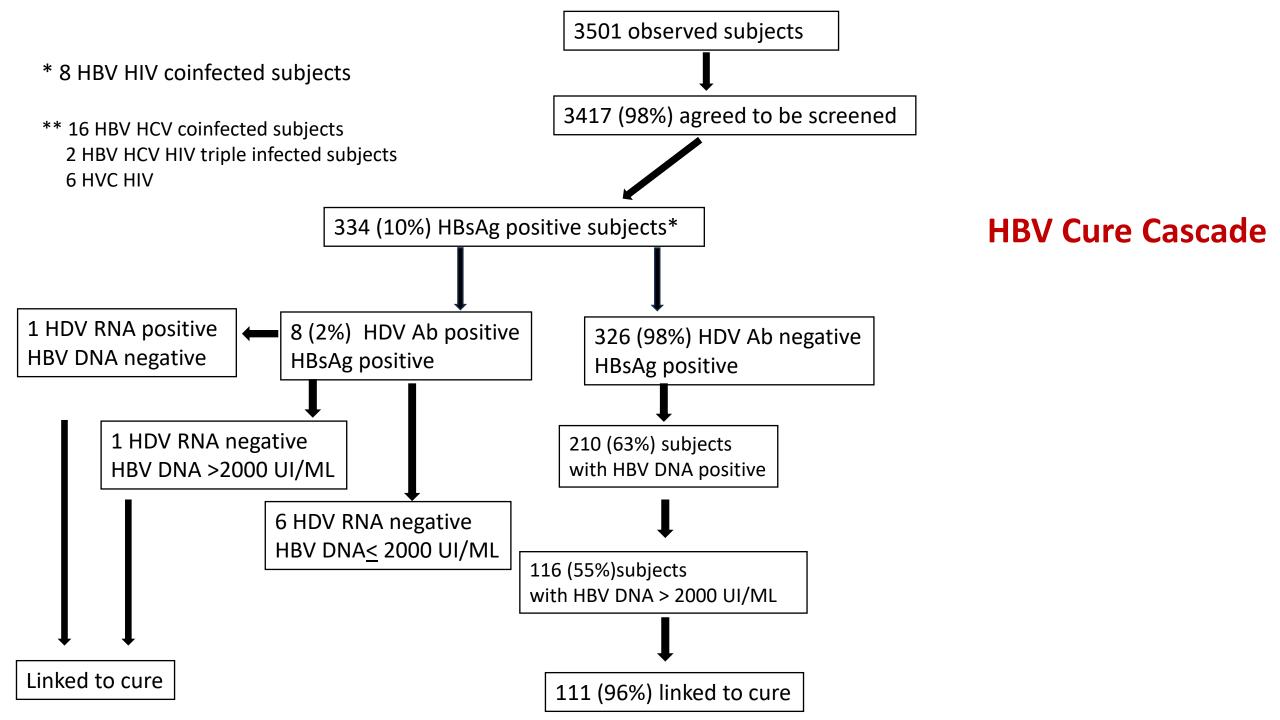


Treatment

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- The HBV-DNA–positive participants with a viral load higher than 2,000 IU/mL were offered antiviral treatment with nucleos(t)ide analogue (NA) according to international guidelines;
- all HIV- positive participants were offered antiviral treatment.







Conclusions

- With the present model, we enrolled about 3500 migrants.
- Migrants lack access to optimal health care services because of different barriers, such as patient-physician communication, language problems, legal and bureaucratic barriers, and inadequacies arising from socioeconomic problems including a lack of family support.



Conclusions

After an educational phase on the route of transmission and treatment availability, nearly 98% of participants agreed to be screened and evaluated for hepatitis virus infections

The protagonist of this success was the cultural mediator



Conclusions

- The rate of linkage to care and of start of antiviral treatment was more than 90% for both viruses.
- Therefore, our model seems useful in viral hepatitis screening, linkage to care, and treatment in a difficult-to-treat population, such as the migrant population.



Key message

Eliminating viral infections among migrants will have a positive long-term impact, societally from a public health perspective and economically on healthcare resource utilization



Thanks for the attention

