# 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

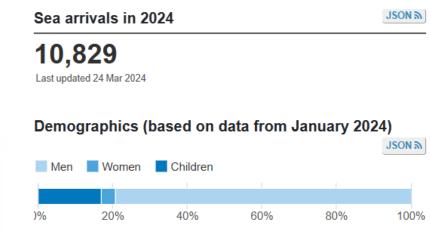
...Burden of migrants in Italy...



### ...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

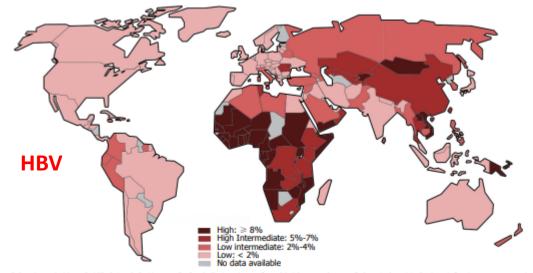
HBV, HCV and HIV infections

### ...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...

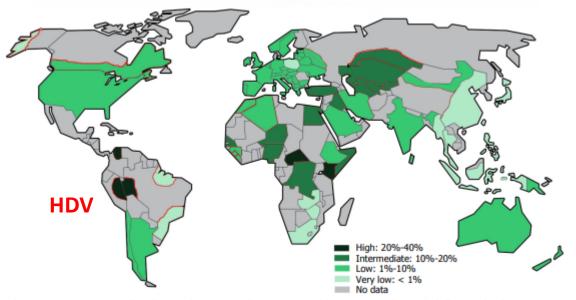


Source: Schweitzer A, Horn J, Mikolajczyk R, Krause G, Ott J. Estimations of worldwide prevalence of chronic heptitis B virus infection: a systematic review of data published between 1965 and 2013. The Lancet. 2015 Jul 28; 386(10003): 1546-1555.

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

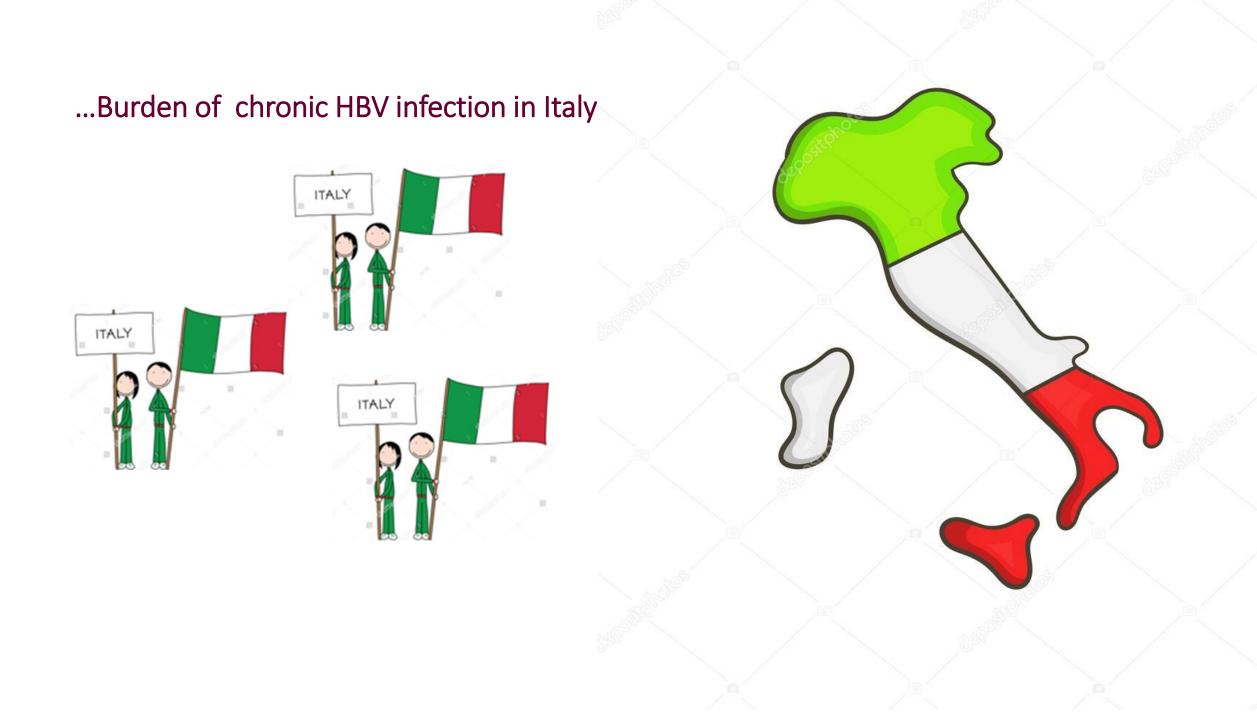


0.0-< 0.6%

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<sup>a,b,1</sup>, Francesca Saffioti<sup>a,1</sup>, Benito Chiofalo<sup>c,d</sup>, Roberta Granese<sup>c,d</sup>, Roberto Filomia<sup>b</sup>, Roberta Grasso<sup>c,d</sup>, Onofrio Triolo<sup>c,d</sup>, Giovanni Raimondo<sup>a,b,\*</sup>

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) <sup>a</sup> |
|           | n-IT                   | 711 (9)   | 142 (20)       | 17/559 (3          | 214 (30)       | 0/497 (0)" <               |

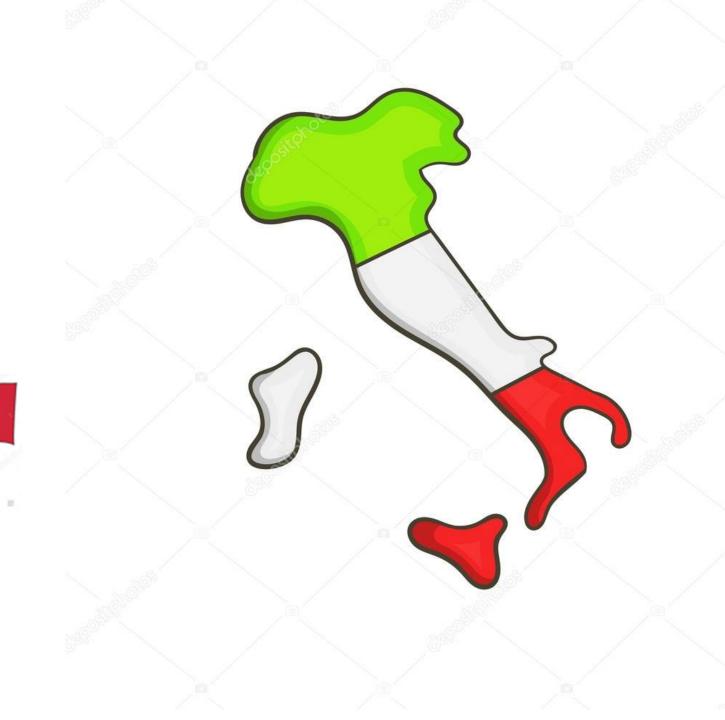
Abbreviations: HBsAg, Hepatitis B surface antigen; Anti-HCV, anti-Hepatitis C virus antibodies; IT, Italians; n-IT, non-Italians; Pos., positive. Values are expressed as numbers (%).

\* P<0.001.

<sup>a</sup> P=n.s.







FULL PAPER

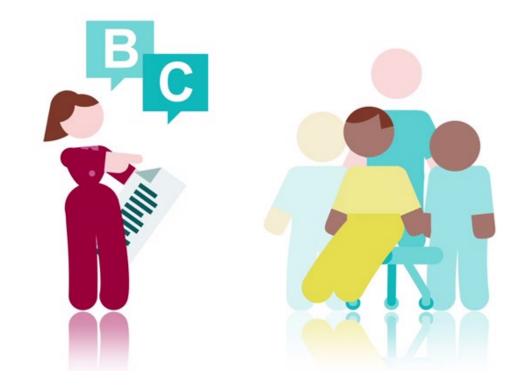
Prevalence of hepatitis C virus estimates of undiagnosed individuals in different Italian regions: a mathematical modelling approach by route of transmission and fibrosis progression with results up to January 2021

Loreta A. Kondili<sup>1</sup>, Massimo Andreoni<sup>2</sup>, Alessio Aghemo<sup>3,4</sup>, Claudio Maria Mastroianni<sup>5</sup>, Rocco Merolla<sup>6</sup>, Valentina Gallinaro<sup>6</sup>, Antonio Craxi<sup>7</sup> <sup>1</sup>Center for Global Health, Istituto Stuperiore di Sanità, Rome, Italy: <sup>2</sup>Diviersity of Tor Vergata, Rome, Italy: <sup>3</sup>Division of Internal Medicine and Hepatology. Department of Gastroenterology, IRCCS Humanitas Research Hospital, Rozzano, Italy; <sup>4</sup>Department of Infectious Diseases, Azienda Policlinico Umberio I, Rome, Italy; <sup>4</sup>Medical Department of Materia Diseases, Azienda Policlinico Umberio I, Rome, Italy; <sup>4</sup>Medical Department AbbVe Italy, Rome Italy; <sup>5</sup>Gastroenterology 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**

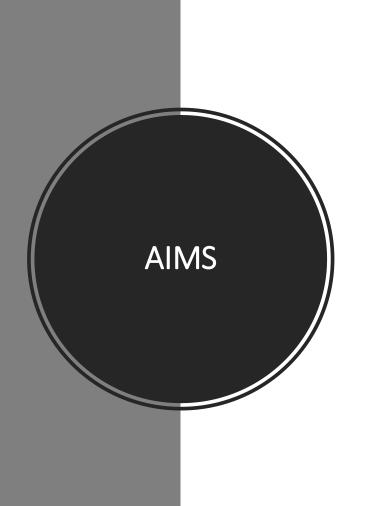
- Fragmented data
- Research group initiatives
- There is a lack of structured surveillance data

| 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-<br>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<br>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.





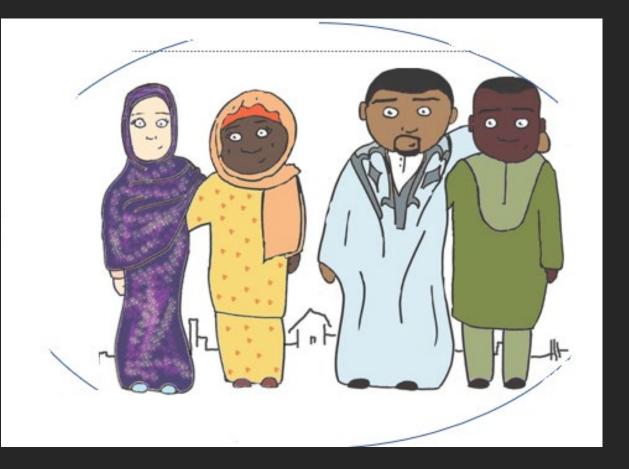


To validate an innovative elimination model for diagnosis and treatment of viral hepatitis in migrants in Italy

## 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

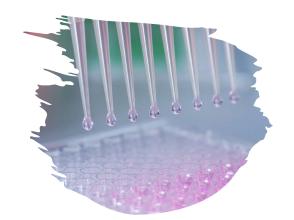
## **MIGRANTS**

### **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



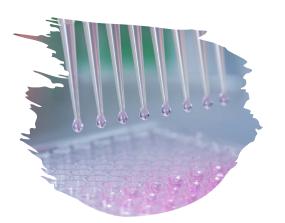
The first-level clinical centers are general practice clinics that are attended mainly by migrantsfor low back pain, headache, hypertension and allergy symptoms; thus, they have proven experience in managing vulnerable groups and are greatly appreciated by the migrants.

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

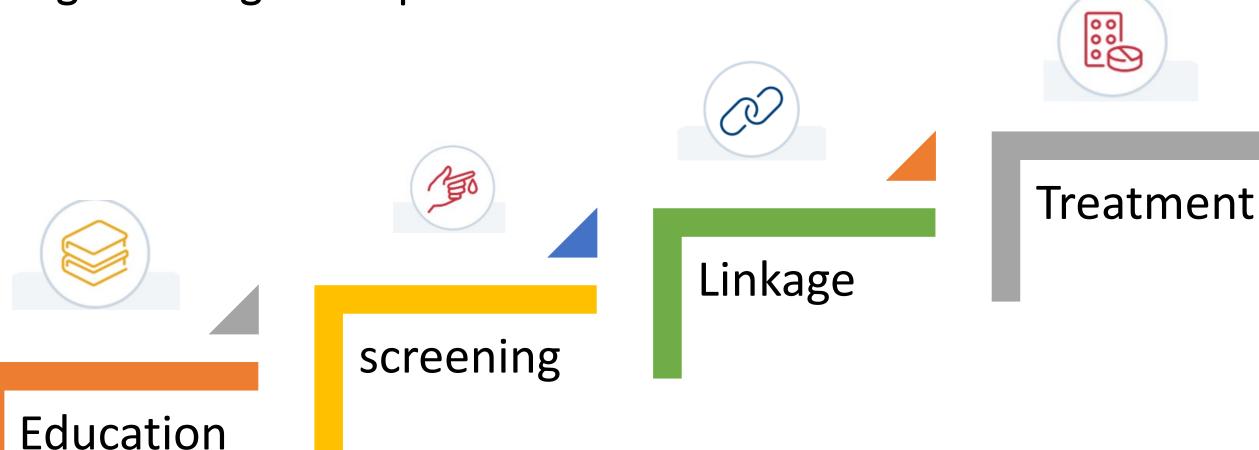


Each migrant who agreed to join the study signed a consent written in the immigrant's own language and in the English language and filled out an anonymous questionnaire on the epidemiologic data administered by the researchers with the assistance of a cultural mediator

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



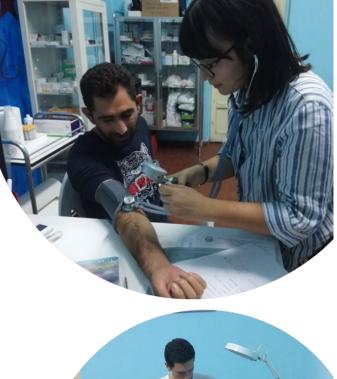
Free HBsAg, anti-HCV, and anti-HIV screening

- 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<sup>a,b,\*</sup>, Caterina Monari<sup>a,b</sup>, Loredana Alessio<sup>b,c</sup>, Lorenzo Onorato<sup>a,d</sup>, Luciano Gualdieria, Caterina Sagnellia, Carmine Minichinia, Evangelista Sagnellia, Giovanni Di Caprio<sup>b,c</sup>, Lorenzo Surace<sup>8</sup>, Gaetano Scotto<sup>h</sup>, Margherita Macera<sup>a,c</sup>, Gianfranco Griffo<sup>8</sup>, Italo Francesco Angelillo<sup>1</sup>, Mariantonietta Pisaturo<sup>a,d</sup>



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 (%):<br>- HBsAg+<br>- HBsAg-/anti HBc+<br>- Anti-HCV+<br>- Anti-HIV+<br>- HBsAg-/anti-HBc-/anti-HCV-/anti-HIV -  | 381 (9.9)<br>1,448 (37.7)<br>136 (3.5)<br>62 (1.6)<br>1,933 (50.6)                          |
| With multiple infection, n (%):<br>- HBsAg+/anti-HCV+<br>- HBsAg+/anti-HIV+<br>- Anti-HCV+/anti-HIV +<br>- HBsAg+/anti-HCV+/anti-HIV+  | 28 (0.7)<br>9 (0.2)<br>9 (0.2)<br>8 (0.2)<br>2 (0.05)                                       |
| <ul> <li>Geographical area of origin, n (%)**:</li> <li>northern Africa</li> <li>western Africa</li> <li>eastern Africa</li> <li>central-southern Africa</li> <li>India-Pakistan Subcontinent</li> <li>eastern Asia</li> <li>eastern Europe</li> </ul> | 127 (3.3)<br>2,299 (59.9)<br>146 (3.8)<br>54 (1.4)<br>578 (15.1)<br>185 (4.8)<br>383 (10.0) |

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

|                     | Northern Africa,<br>n° (%) | Eastern<br>Africa,<br>n° (%) | Western<br>Africa,<br>n° (%) | Central-southern Africa,<br>n° (%) | Eastern Europe,<br>n° (%) | India- Pakistan area,<br>n° (%) | P value                |
|---------------------|----------------------------|------------------------------|------------------------------|------------------------------------|---------------------------|---------------------------------|------------------------|
| N° of subjects      | 127                        | 146                          | 2,299                        | 54                                 | 383                       | 578                             |                        |
| Mean age, years +SD | $34.3 \pm 11.1^{\circ}$    | $27.2 \pm 10.3$              | 26.0 ± 8.1                   | $28.7 \pm 10.9$                    | $38.2 \pm 12.7$ §         | 28.1 ± 8.9                      | < 0.0001§<br>< 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

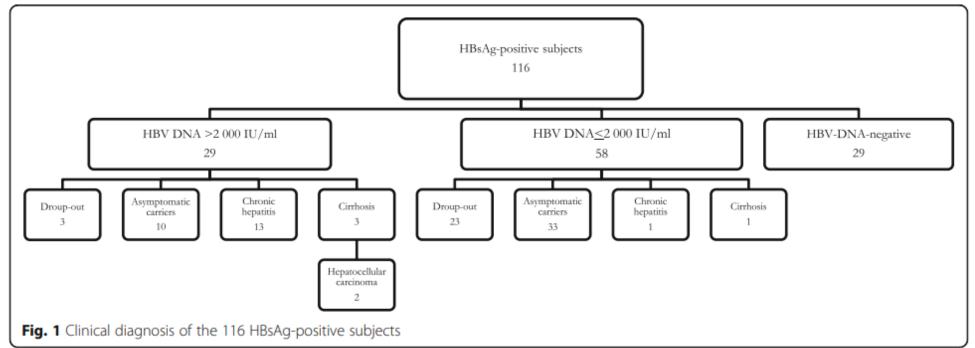
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(E) CrossMark

#### RESEARCH ARTICLE

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

Nicola Coppola<sup>1\*</sup>, Loredana Alessio<sup>1,2</sup>, Luciano Gualdieri<sup>3</sup>, Mariantonietta Pisaturo<sup>4,5</sup>, Caterina Sagnelli<sup>6,7</sup>, Carmine Minichini<sup>1</sup>, Giovanni Di Caprio<sup>1,2</sup>, Mario Starace<sup>1</sup>, Lorenzo Onorato<sup>1,2</sup>, Giuseppe Signoriello<sup>8</sup>, Margherita Macera<sup>1</sup>, Italo Francesco Angelillo<sup>9</sup>, Giuseppe Pasquale<sup>1</sup> and Evangelista Sagnelli<sup>5</sup> 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.  |  |

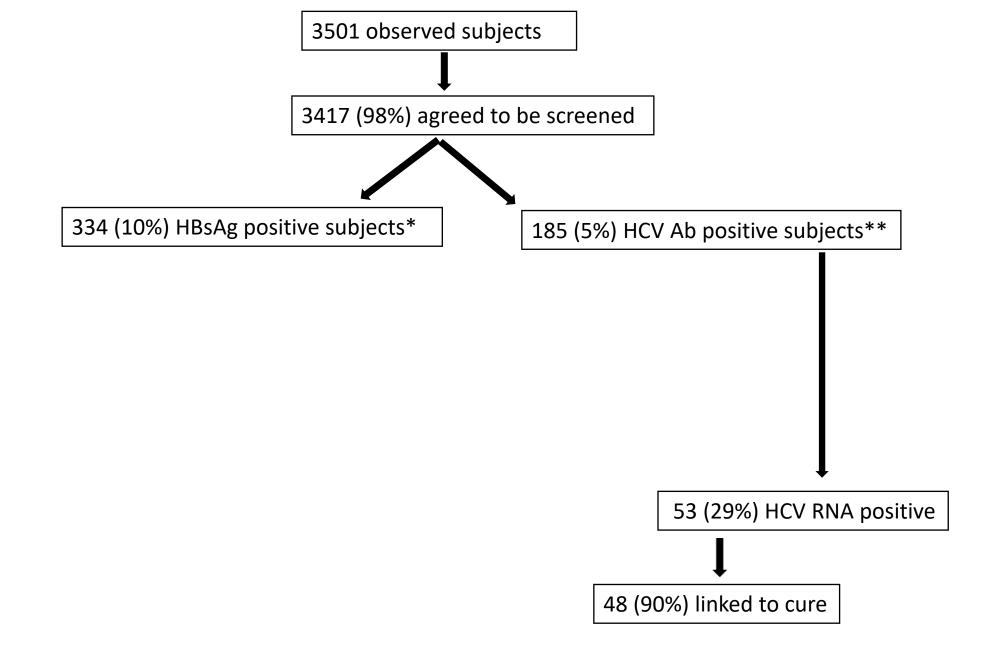
characteristics of the 3417 participants screened.

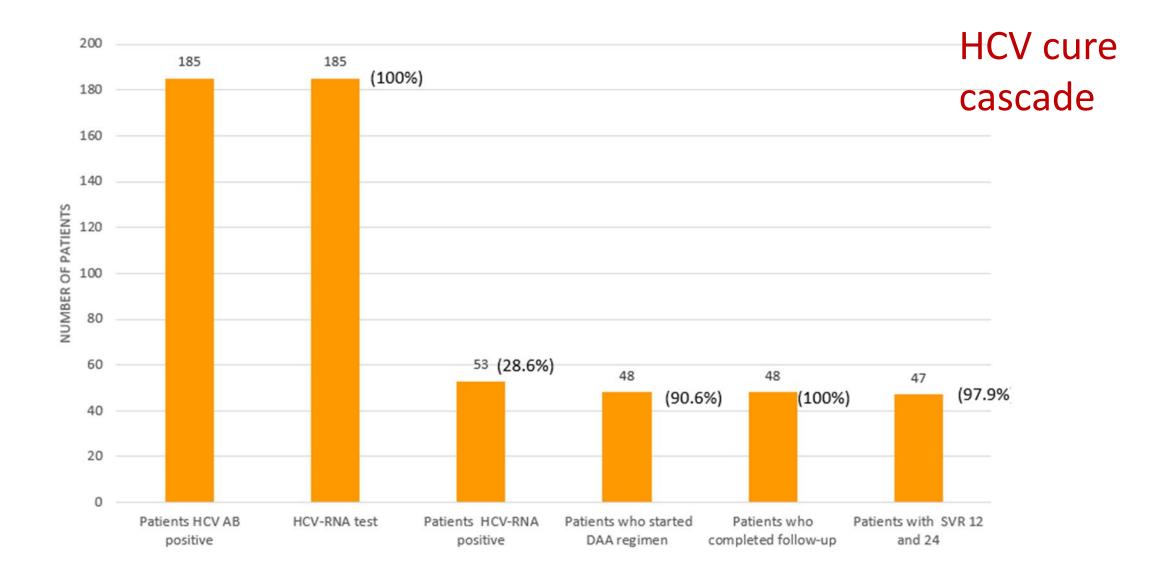
## Program design

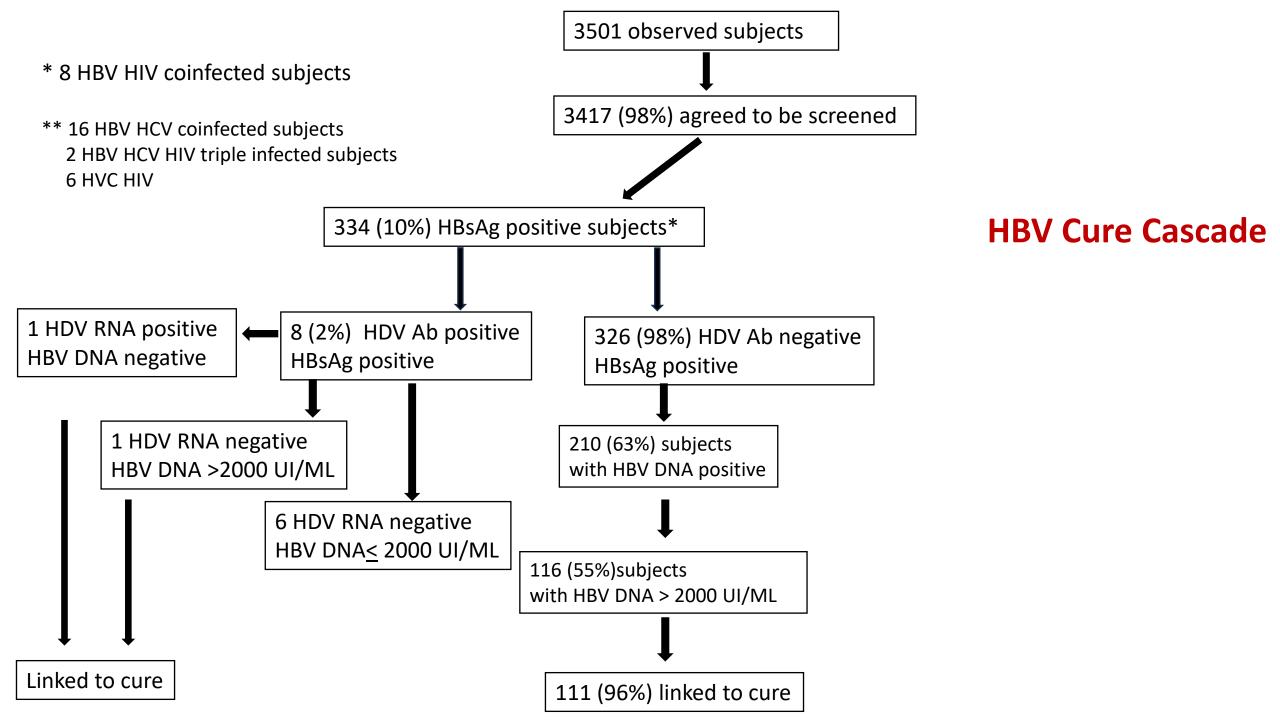


#### Treatment

- 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.







# 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

