Barbara Coco

PITER: Coorte B/Delta

U.O. Epatologia

Azienda Ospedaliero Universitaria Pisana

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No Disclosures

Coordinamento dello studio:
Lo studio è coordinato dall'Istituto Superiore di Sanità (ISS), dall'Associazione Italiana Studio Fegato (AISF) e della Società Italiana di Malattie Infettive e Tropicali (SIMIT) attraverso un Comitato esecutivo

Comitato esecutivo: E. Villa, S. Vella, T. Santantonio, G. Raimondo, M. Puoti, A. Marzano, P. Lampertico, L. Kondili, GB Gaeta, C. Ferrari, V. Di Marco, B. Coco and MR Brunetto
AISF: Vincenza Calvaruso SIMIT: Massimo Andreoni

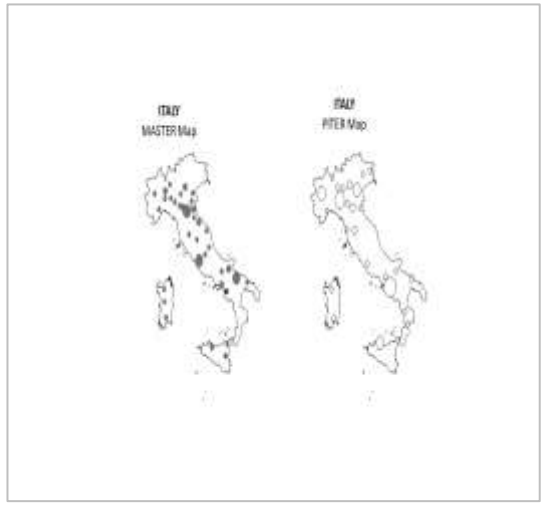
PITER HBV/HDV si propone come uno *studio prospettico multicentrico nazionale* mirato a valutare complessivamente l'epidemiologia clinica dell'infezione e malattia HBV/HDV correlata in Italia

Disegno dello studio: arruolamento *consecutivo di soggetti con infezione cronica da HBV /HDV con o senza malattia, indipendentemente dallo stato di terapia antivirale*.
Ciascun centro partecipante potrà arruolare i pazienti osservati nell'arco temporale di un anno. I pazienti arruolati saranno seguiti con frequenza annuale per un *periodo di 5 anni*.

Criteri di inclusione:
- Infezione cronica da HBV documentata da HBsAg pos da almeno 6 mesi con o senza coinfezione da HDV, HCV ed HIV

Criteri di esclusione:
- Soggetti con infezione da HBV pregressa ma HBsAg negativo al momento dell'arruolamento
- Pazienti con epatite da HBV acuta

65 centri attivati da Nov 2019
5.494 soggetti HBsAg pos arruolati
28 Gastro/Epatol; 29 M Infettive; 8 M Interna



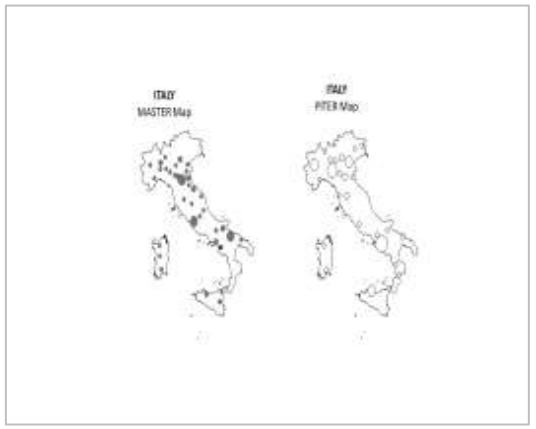
	MASTER B *2012- 2015* n = 2920 % (n)	PITER HBV/HDV *2019 - 2022* n = 4583 % (n)	p
Age (median;years)	49.8	**58.8**	0.0001
Gender (male)	68,6 (2003)	**62.2 (2850)**	0.0001
Origin Italian naive East Europe Africa Asia South Central America Central Western Europe	73.2 (2136) 13.2 (386) 5.9 (173) 6.6 (194) 0.5 (15) 0.4 (12)	**78.2 (3419)** **12.5 (547)** **3.7 (162)** **5.0 (221)** **0.3 (13)** **0.2 (10)**	0.0001
Alchol use	31.1 (783)	**34.2 (1408)**	0.009
HBeAg pos	**12.3 (323)**	7.17 (322)	0.0001
Cirrhosis	24.7 (722)	24.1 (1107)	0.55
Anti HDV	8.3 (161)	9.2 (314)	0.23
On going therapy	34.2 (1000)	**66.6 (3043)**	0.0001

- 5.6% in the PITER cohort with HBV DNA > 20,000 IU/mL were *not* under treatment and 35.9% in the MASTER cohort

G. Brancaccio, B.Coco and PITER investigators, Int J Infec Dis, 2023

Main characteristics in Italian and *non-Italian natives* HBsAg subjects overall PITER HBV study cohort

		Italian % (n)	*non- Italian natives* % (n)	p
Age	years	**62** (16-95)	***42*** *(19 – 84)*	<0.001
Gender	F M	**34.7** (1125) 65.3 (2112)	***47.2*** *(417)* *52.8 (467)*	<0.001
Genotype	D non-D	**83.2** (352) 16.8 (71)	*63.3 (126)* *36.7 (73)*	<0.001
HBeAg	Pos Neg	4.4 (128) 95.6 (2798)	***11.9*** *(100)* *88.1 (743)*	<0.001
Phase of infection	HBe Ag pos infection HBeAg pos CH HBe Ag neg infection HBeAg neg CH	**0.1** (3) **4.0** (114) **19.2** (540) **76.7** (2161)	***1.0*** *(8)* *11.9 (98)* ***32.3*** *(267)* ***54.8*** *(453)*	<0.001
Coinfections	HDV	7.9 (205)	***12.2*** *(94)*	<0.001
Alcohol	On going In the past	24.0 (716) 10.5 (315)	*24.2 (204)* *12.1 (102)*	0.395
Cofactors of liver damage	Steatosis NASH	26.8 (167) 1.7 (56)	*28.0 (30)* *1.5 (13)*	0.537 0.595
Comordities	Diabetes Dyslipidemia CV disease	**11.0** (357) **9.9** (321) **29.8** (965)	*3.9 (35)* *4.7 (42)* *7.9 (70)*	<0.001 <0.001 <0.001
Cirrhosis		**26.1** (896)	***14.8*** *(141)*	<0.001
HCC		**5.06** (171)	***1.2*** *(12)*	<0.001
Treatment status	Treatment on going	**70.3** (2397)	***52.5*** *(501)*	<0.001



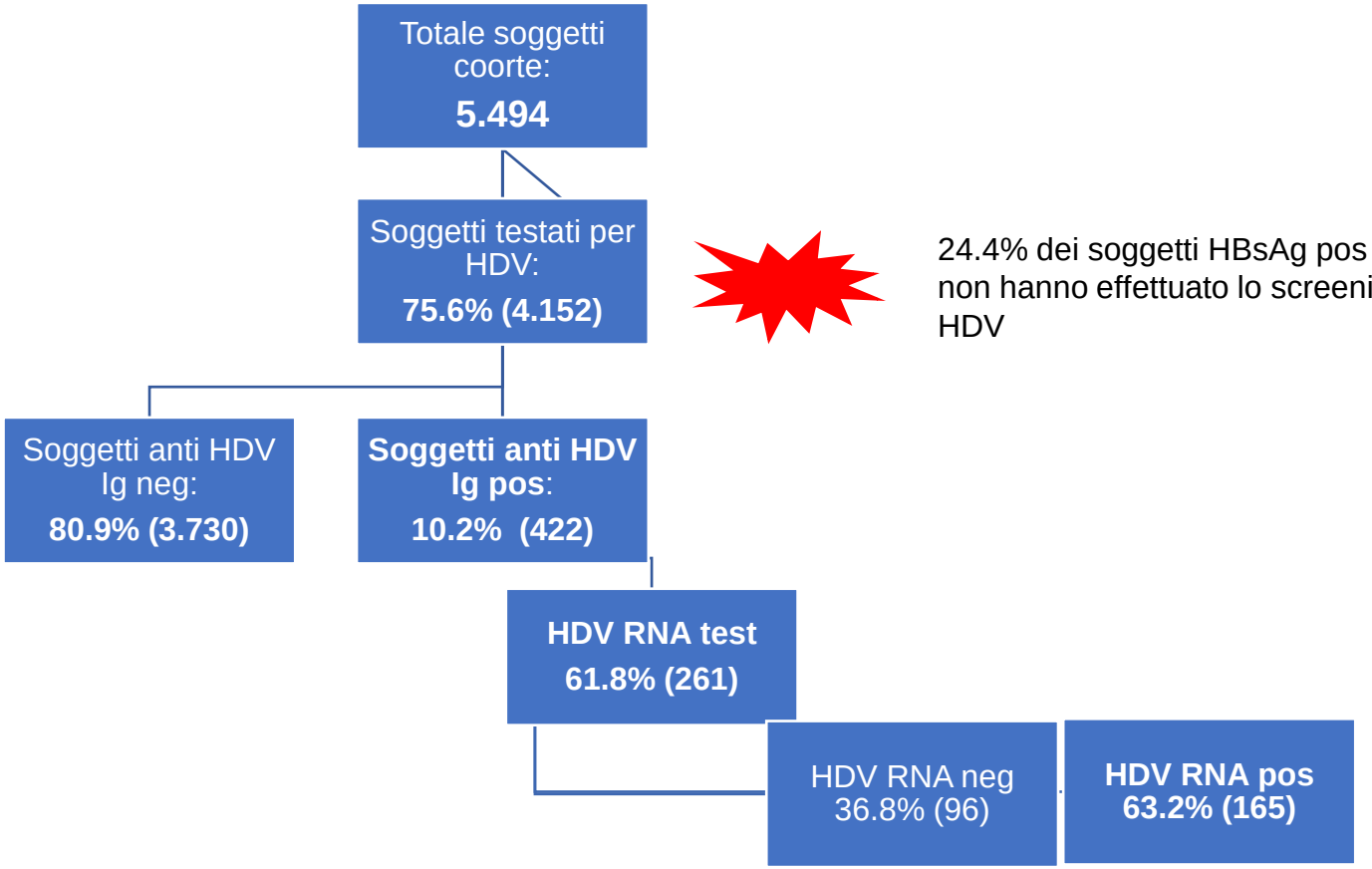
	MASTER *Cirrhosis* n=722 (24.7%)	PITER *Cirrhosis* n=1107 (24.1%)	*p*-value
Age (Years)	57.2	**63.6**	<0.0001
Gender (Males)	79.9 (577)	73.9 (816)	0.0032
BMI >/= 30	25.5 15.3 (127)	25.5 15.1 (92)	0.90
HBV DNA (pos)	**56.5 (392)**	24.6 (257)	<0.0001
Origin Italian natives East Europe Asia Africa America Central Western Europe	 80.6 (578) 7.7 (56) 5.9 (43) 5.8 (42) 0.42 (3) 0 (0)	 **86.4 (896)** 8.5 (89) 2.9 (31) 1.8 (19) 0.1 (1) 0.1 (1)	 <0.0001
Alcohol use (Yes)	29.7 (187)	37.1 (366)	0.0023
HBeAg (Positive)	**12.6 (81)**	4.9 (54)	<0.0001
Anti-HDV (Positive)	17.5 (88)	**24.8 (213)**	0.0017
HCC (Present)	14.0 (99)	16.6 (183)	0.1408
Ongoing therapy (Yes)	50.5 (365)	**91.5 (1012)**	<0.0001

HDV coinfection was the strong factor associated to cirrhosis (OR 10.08; C.I. 7.63-13.43) together with *age, gender, BMI and non Italian origin*

G. Brancaccio, B.Coco and PITER investigators, Int J Infec Dis, 2023

Soggetti con coinfezione HBV/HDV arruolati della coorte PITER

5.494 soggetti HBsAg positivi arruolati da Dic 2019 a Feb 2023

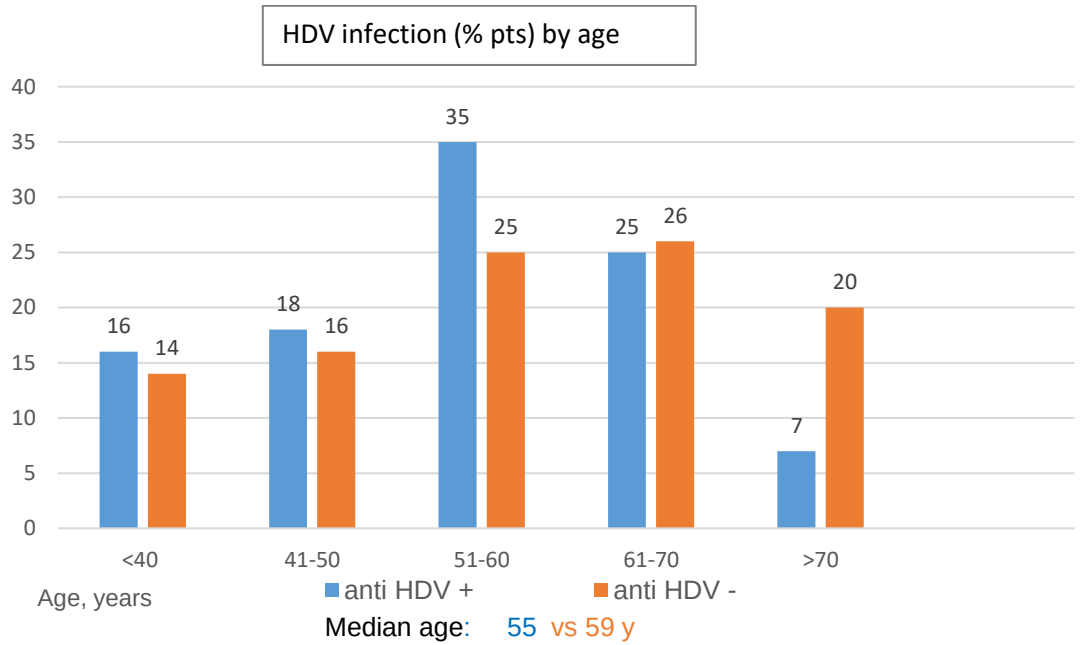


Kondili L and PITER collaborators, submitted

Main baseline characteristics of the PITER HDV cohort

422 anti HDV positive carriers enrolled from Dec 2019 to Feb 2023:
165 out of 261 subjetcs who were tested had HDV RNA positive

	anti-HDV positive N° = 422	anti-HDV negative N° = 3730	p-value
Age median (Q1, Q3)	**55 (**46, 62)	59 (48, 68)	<0.001
Males	253 (60.0)	2335 (62.6)	0.287
Non-Italian natives	**142 (33.6)**	850 (22.8)	<0.001
Injection drug use	**35 (10.0)**	55 (1.7)	<0.001
ALT > 35 IU/L	**243 (59.4)**	566 (15.3)	<0.001
GGT >50 IU/L	**121 (36.3)**	344 (11.1)	<0.001
HBeAg positive	25 (6.1)	253 (6.8)	0.582
Cirrhosis	**299 (70.8)**	892 (23.9)	<0.001
HCC	**42 (10.2)**	106 (2.9)	<0.001
HBV DNA positive	115 (29.1)	1330 (36.5)	0.004
HDV RNA positive (261 tested)	**165 (63.2)**	---	---
Previous IFN	142 (33.6)	580 (15.5)	<0.001
Potential disease co-factors			
Ongoing alcohol use	775 (22.6)	412 (12.0)	0.130
Past use	65 (18.7)	51 (14.7)	
Diabetes	29 (6.9)	375 (10.0)	0.037
BMI 25-30	32 (7.6)	384 (10.3)	0.004
BMI ≥30	109 (25.8)	1.173 (31.4)	
anti-HCV positive	**39 (10.4)**	126 (3.6)	<0.001
anti-HIV positive	**17 (4.8)**	35 (1.1)	<0.001
Ongoing therapy (>95% NUCs)	**323 (76.5)**	2529 (67.8)	<0.001



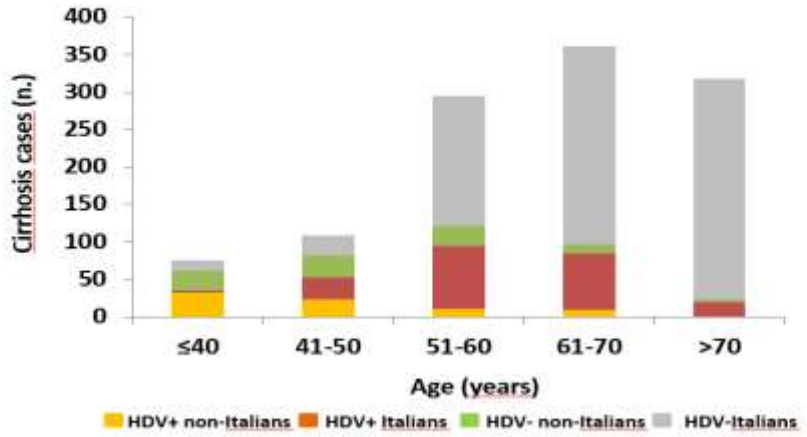
Kondili L and PITER collaborators, submitted

Main baseline characteristics of the PITER HDV cohort

422 anti HDV positive patients enrolled from Dec 2019 to Feb 2023

***299 (70.8%)** anti HDV + pts had cirrhosis: 251 (84 %) Child A; 41 (13.7%) Child B; 7 (2.3%) Child C*

Cirrhosis by age, anti-HDV antibodies pos and patients' origin



Cirrhosis by HDV RNA

	HDV RNA + N = 165	HDV RNA -- N = 96	p-value
Cirrhosis	125 (75.8)	**61 (63.5) ***	0.035
Child			
A	106 (84.8)	**59 (96.7)**	0.028
B	18 (14.4)	**2 (3.3)**	
C	1 (0.8)	**0 (0.0)**	
Complications of cirrhosis	45 (36.0)	**14 (22.9)**	0.073
HCC	25 (15.3)	**3 (3.2)**	0.003
HBV DNA positive	45 (29.0)	**27 (28.7)**	0.958
PLT < 150,000	64 (41.3)	**51 (53.7)**	0.056
MELD >19	2 (1.9)	**1 (2.0)**	>0.999

* **47 (77%) Italian** median age *55 y* (Q1 50, Q3 62)

- **47.4% of patients with HDV infection had one or more comorbidities**: younger (< 55 y) had higher frequency of psychiatric disorders whereas older pts of overweight/obesity, autoimmune disorders and digestive disease
- **46.7% (77) of HDV RNA + pts were elegible to peg-IFN**; 40.6% (67) and 12.7% (21) had absolute or relative controindication

Kondili L and PITER collaborators, submitted

Global prevalence, cascade of care, and prophylaxis coverage of hepatitis B in 2022: a modelling study by Polaris Observatory

HBV scenario in ITALY in 2021 by modelling

HBV prevalence: 0.5% (0.4-0.6%)
HBV population: 308.000 (246-369.000)
Treatment elegible: 92.400 pts

Diagnosed: 30%
Treated of total elegible: 45%

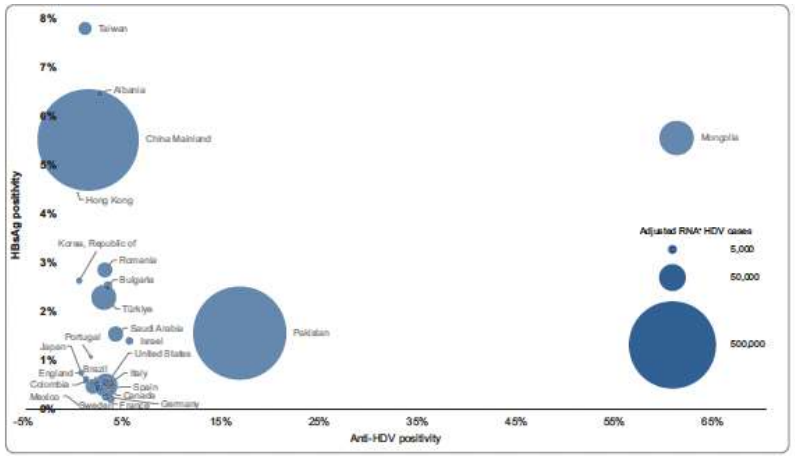
HBV prevalence among 5 years old: <0.1%

Profilaxis:

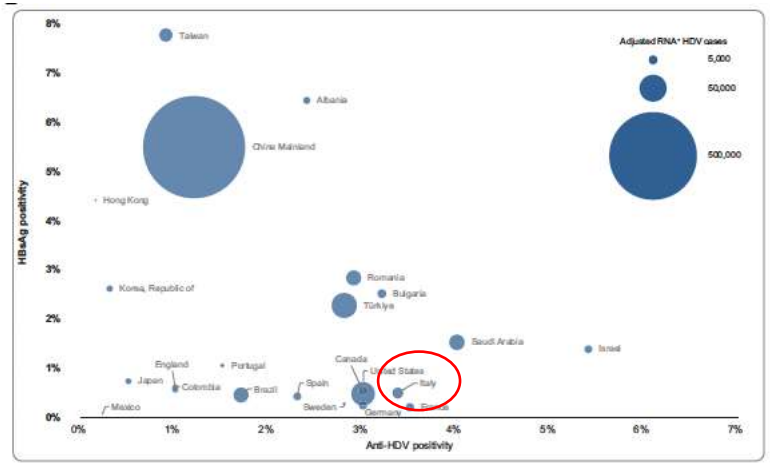
- 3D vaccine 94%
- BD vaccine < 1%
- HBIG + 2D vaccine 100%
- Antiviral therapy of mothers: 10%

Polaris Observatory Collaborators, Lancet Gastroenterol Hepatol 2023

HDV infection prevalence of in 25 countries and territories by Polaris Observatory



Mongolia has 60.1% HDV prevalence but **China** has the highest absolute number of HDV RNA+ cases



HBs Ag, anti HDV and HDV RNA + excluding Pakistan and Mongolia

… after adjusting for geographical distribution, disease stage and special populations, the anti-HDV prevalence among the HBsAg+ population changed from the literature estimate in 19 countries

Country/Territory	2023 HBsAg+	Literature % anti-HDV+	Adjusted % anti-HDV+	RNA+ cases	Adjusted HDV RNA+ prevalence	Adjusted HDV RNA+ cases	Anti-HDV tests to diagnose one case
Albania	183,000	9.0%	2.4%	4,400	62.5%	2,800	41.7
Brazil	1,025,000	3.2%	1.7%	17,400	75.3%	13,100	58.8
Bulgaria	169,000	8.6%	3.2%	5,400	80.0%	4,300	31.3
Canada	214,000	1.8%	3.0%	6,400	64.8%	4,100	33.3
China Mainland	78,548,000	1.2%	1.2%	942,600	66.6%	627,800	83.3
Colombia	302,000	5.2%	1.0%	3,000	69.9%	2,100	100.0
England	418,400	2.9%	1.0%	4,200	50.0%	2,100	100.0
France	142,000	1.8%	3.5%	5,000	75.0%	3,800	26.6
Germany	215,000	5.5%	3.0%	6,500	60.0%	3,900	33.3
Hong Kong	332,000	0.2%	0.2%	500	60.0%	300	666.7
Israel	139,000	6.5%	5.4%	7,000	47.0%	3,300	15.5
Italy	336,400	8.3%	3.4%	11,300	60.5%	6,800	29.7
Japan	926,000	8.5%	0.5%	4,600	40.8%	1,900	200.0
Korea, Republic of	1,360,000	0.3%	0.3%	4,100	54.0%	2,200	333.3
Mexico	116,000	2.4%	0.2%	300	69.9%	200	444.4
Mongolia	191,000	61.0%	61.0%	116,500	61.5%	71,600	1.6
Pakistan	3,762,000	16.6%	16.6%	624,500	85.0%	530,800	6.0
Portugal	110,000	12.6%	1.5%	1,700	72.9%	1,200	66.7
Romania	568,000	23.1%	2.9%	16,500	80.0%	13,200	34.5
Saudi Arabia	570,000	5.3%	4.0%	22,800	60.0%	13,700	25.0
Spain	208,000	5.2%	2.3%	4,800	72.9%	3,500	43.5
Sweden	31,000	3.8%	2.8%	900	75.0%	650	35.7
Taiwan	1,864,000	3.3%	0.9%	16,800	60.0%	10,100	111.1
Türkiye	1,962,000	2.8%	2.8%	54,900	68.0%	37,300	35.7
United States	1,650,000	6.0%	3.0%	49,500	66.0%	32,700	33.3

Polaris Observatory Collaborators, J Hepatol 2024

- The **combined effect** of **vaccination policies** and increasing **flows of immigrants** from HBV highly endemic areas were responsible for the highly dynamic changes of HBV epidemiology in Italy
- Non Italian native HBsAg carriers significantly increased across the last decades
- **Antiviral therapy mitigated** the long lasting infections in **aging Italians with CHB,** as suggested by the stable/slight reduction of cirrhotic patients in the last decade in spite of the older age of the patients

- **There is still large uncertainty in HDV prevalence estimates** as many published HDV prevalence studies are conducted among groups who have a higher probability of being infected with HDV, such as patients in tertiary care centers, specific riskgroups, or high-prevalence regions. When available data are weighted by population size at the national level, the HDV prevalence often decreases.
- Currently Italian epidemiological data suggest that there are **2 distinct subsets of CHD patients**: *older Italian patients* with long lasting history of HDV infection with an indolent, but still **slowly progressive course**, and *younger immigrants* with **active and rapidly progressive disease**

PITER

Piattaforma Italiana per lo studio della Terapia delle Epatiti viRali.

Grazie!

Comitato Esecutivo e i centri partecipanti disponibili in:
www.progettopiter.it