

Identification and management of persons with chronic viral hepatitis in Europe

The experience and the vision on screening for chronic hepatitis in Italy

Daniele Prati, MD

VHPB meeting
Budapest, Hungary
18-19 march 2010

Sources

- Medical literature
- Data, recommendations and official documents of the Italian Association for the Study of the Liver
- Joint documents with other scientific societies
- Data from Italian National Institute of Statistics (ISTAT) and from the Italian National Institute of Health (ISS)

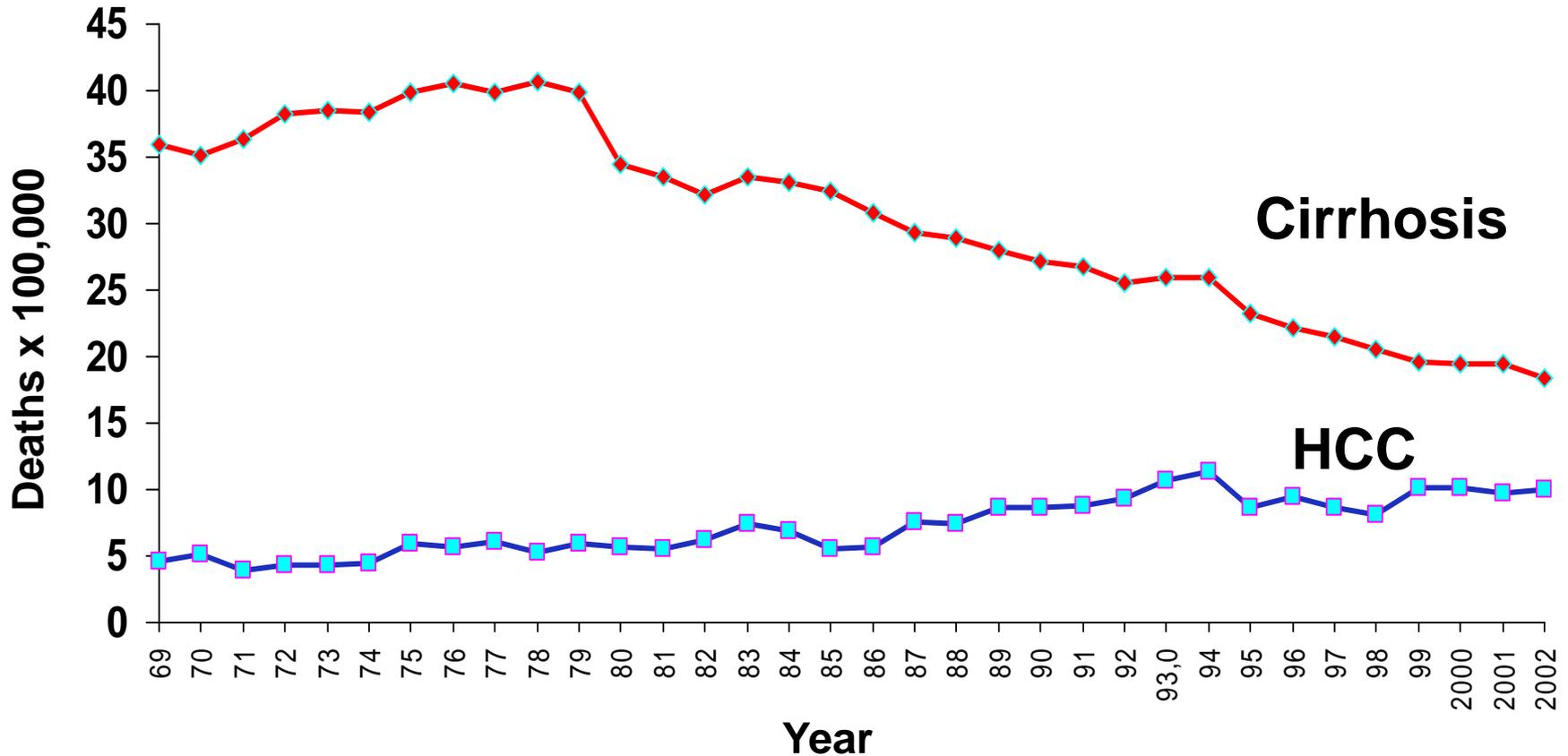
Burden of disease in Italy

- **Chronic liver disease (CLD) is a leading health problem in Italy**
 - 2.5 million are infected by HBV or HCV
 - 21,000 deaths/year due to cirrhosis or tumors
 - Costs for the management of CLD are continuously increasing

Data from the Italian Association for the Study of the Liver (AISF)

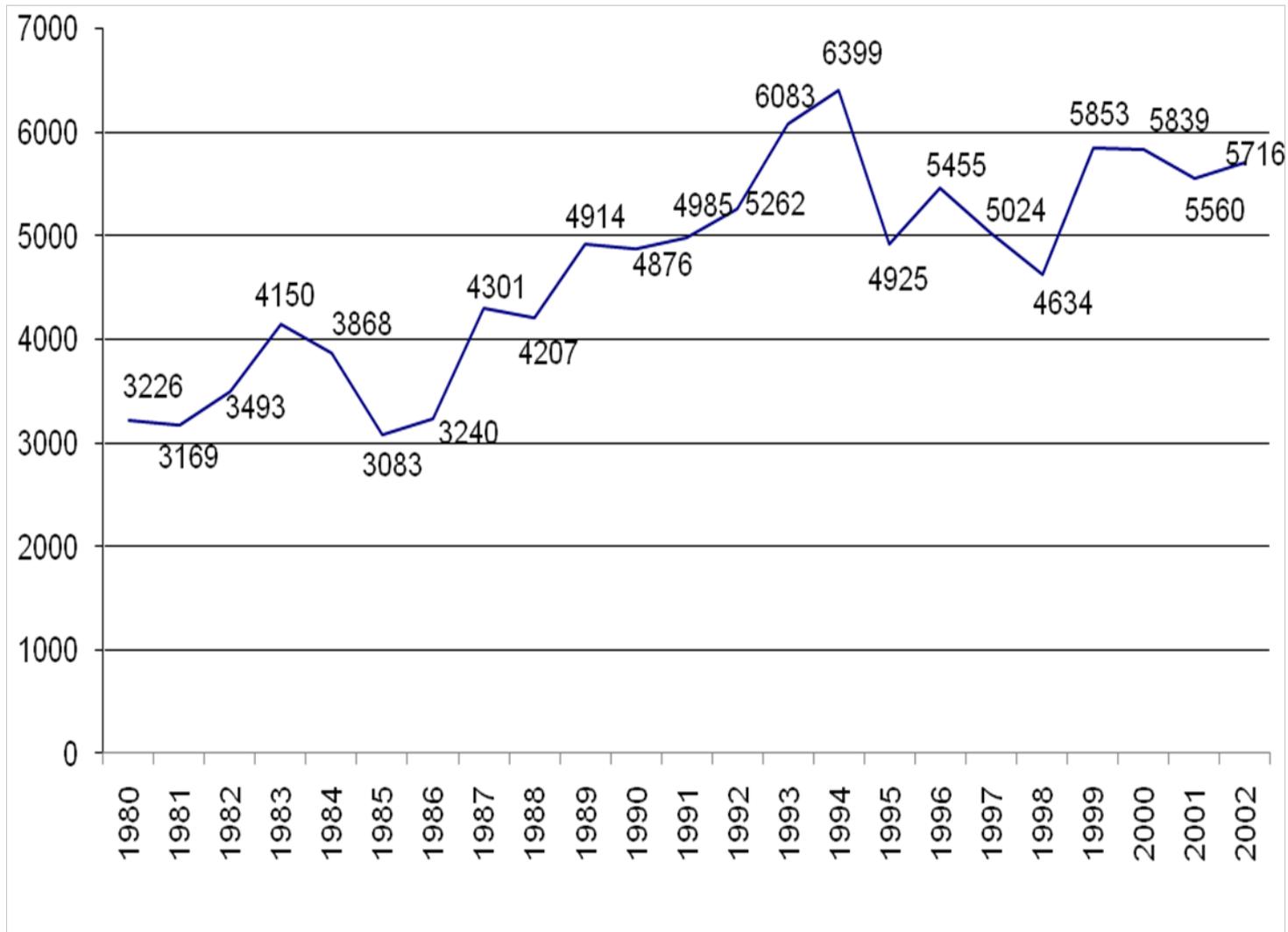
Temporal trend in Italy.

Mortality rates (per 100,000 inhabitants) of liver cirrhosis and HCC, 1969-2002.



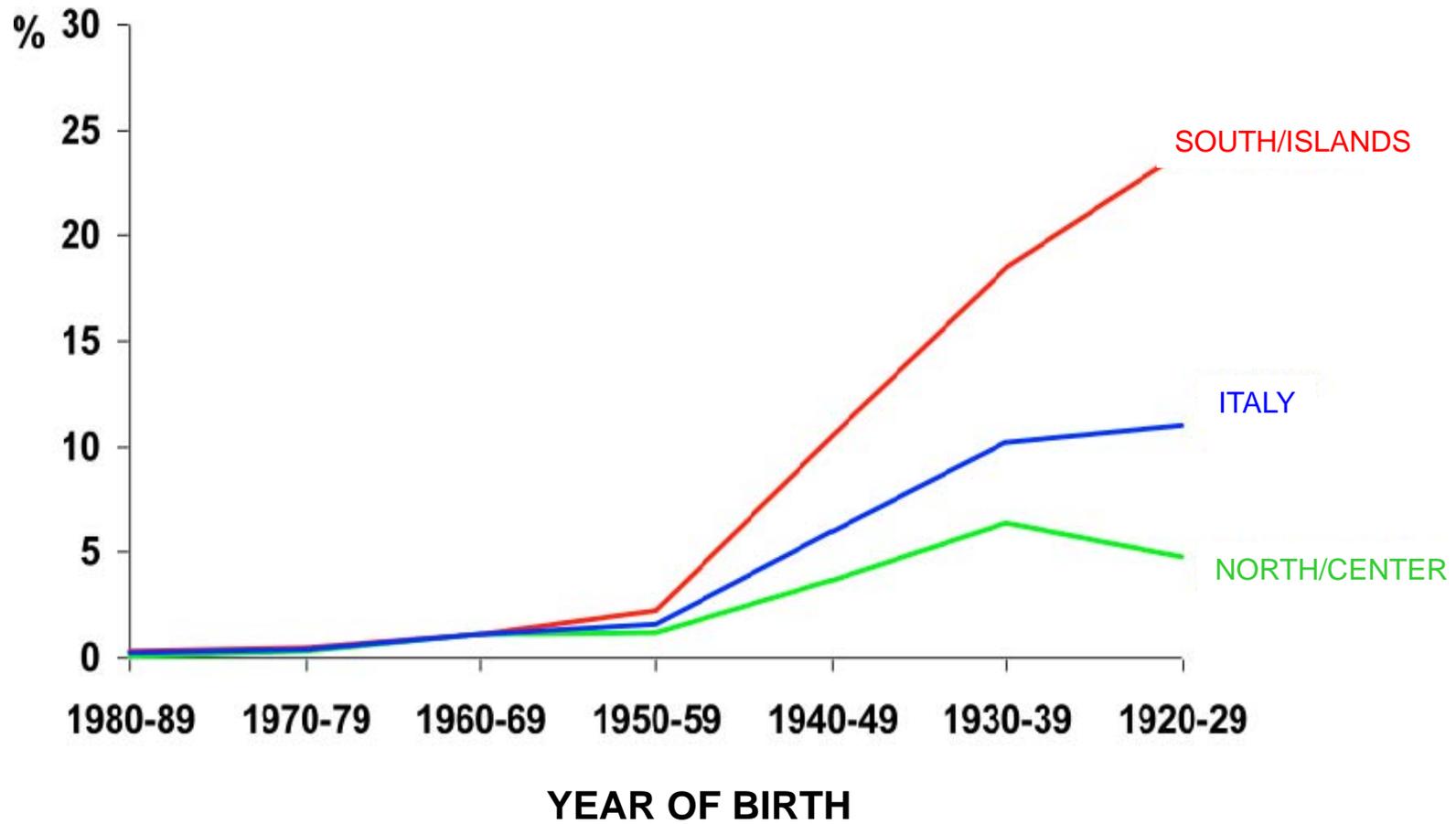
Source of data: ISTAT

Mortality for hepatocellular carcinoma in Italy, 1980-2002



AISF; data from National Institute of Statistics (ISTAT)

Prevalence of HCV RNA among the general population in Italy. (Data pooled from different studies)



Current Epidemiology of HBV infection in Italy

- **Hepatitis B has significantly declined in Italy in the past decades due to non-specific and specific preventive measures**
 - Low incidence of AHB, mostly sexually transmitted
 - Low endemicity (HBsAg prevalence < 2%)
- **Long-term protection in immunocompetent individuals vaccinated as infants and teenagers (currently 30 years old or younger)**
- **Prevision for greater import of non-D genotypes and circulation of antiviral resistant mutants**

Epidemiology in the clinical setting

Temporal trends of pathogenic factors of chronic hepatitis in Italy

Pathogenetic factor	1980 (n=501) ¹	1989 (n=608) ¹	2001 (n=6210) ²
HBV	44.0	34.2	9.2
HCV	43.6*	52.8*	62.6
Alcohol	6.2	8.1	5.5

1. Giusti et al, Hepatogastroenterology 1994
2. Stroffolini et al., Dig Liv Dis. 2005

(*) Presumably HCV

Frequency of etiological factors of hepatocellular carcinoma cases in three different surveys in Italy

Author	DeBac	Stroffolini	Sagnelli
Year of the Study	1992	1997	2001
N. of cases	217	1148	341
• HBsAg+ %	12.5	11.5	12.3
• HCV+ %	70.1	71.1	71.3
• HBsAg+/HCV+ %	2.3	5.3	3.2
• Other causes %	8.2	8.4	10.6
• Cryptogenic %	6.9	3.7	2.6

The screening strategy in Italy

General Strategy

- In Italy, it is currently agreed that testing for Hepatitis B and C among risk groups with elevated prevalence (i.e., *case finding*) is likely to be more cost-effective than a *mass screening* approach.
- **Well managed** screening for signs and symptoms of liver disease and risk factors for infection is therefore seen as the a key instrument of prevention.

HBV and HCV: preventive measures currently adopted in Italy

- HBV vaccination in children and persons at risk
- Mandatory HBsAg screening of pregnant women
- Highly sensitive tests for blood donations (including NAT for HBV and HCV)
- Screening for risk factors of viral hepatitis and subsequent testing (HBsAg, anti-HCV) of those who are positive

HBV: Who should be screened

- Persons with elevated liver enzymes and/or clinical sign of hepatitis
- Patients with liver cirrhosis or fibrosis
- Patients with hepatocellular carcinoma
- People who share or have ever shared needles (injecting drug users)
- People with long-term imprisonment history
- People who are undergoing or have undertaken hemodialysis
- Men who have sex with men or heterosexual persons with multiple sex partners
- People with HIV or HCV infection
- Families and household members or sexual partners of persons infected with HBV Patients and staff in psychiatric institutions or residents of welfare institutions for mentally disabled persons
- Pregnant women and newborns of HBV-infected mothers
- Recipients of organ transplants and blood products
- Blood and organ donors
- Patients before or during immunosuppressive treatment or chemotherapy
- Migrants from countries with high prevalence of Hepatitis B
- Unvaccinated healthcare workers and public safety workers who undertake exposure-prone procedures

HCV: Who should be screened

- Persons with elevated liver enzymes and/or symptoms of hepatitis
- Patients with liver cirrhosis or fibrosis
- People who share or have ever shared needles (injecting drug users)
- People with long-term imprisonment history
- People who are undergoing or have undertaken hemodialysis
- People who have received repeated percutaneous injections
- People who have had invasive medical and paramedical or dental work in countries with high prevalence or poor sterilisation procedures, such as use of multidose vials
- People who received blood transfusions or other blood derived products outside the EU or before 1992 in the EU
- People who received organs and tissues transplants outside the EU or before 1992 in the EU
- Blood and organ donors
- Haemophiliacs who received concentrated coagulation factors before 1987
- People with HIV infection
- People with body piercings if being performed in non hygienic environments
- Children of HCV-infected mothers
- Migrants from countries with high prevalence of Hepatitis C

Follow-up and Treatment Strategies: HBV

Digestive and Liver Disease 40 (2008) 603–617

Progress Report

Treatment of chronic hepatitis B: Recommendations from
an Italian workshop[☆]

G. Carosi^{a,*}, M. Rizzetto^b

ISSUES:

1. Patients with HBeAg positive chronic hepatitis B
2. Patients with HBeAg negative chronic hepatitis B
3. Compensated cirrhosis
4. Decompensated cirrhosis
5. Immune suppressed patients
6. Co-infections
 - a) Co-infection with HCV
 - b) Co-infection with HDV
 - c) Co-infection with HDV and HCV
 - d) Co-infection with HIV

Follow-up and Treatment Strategies: HCV

Digestive and Liver Disease 42 (2010) 81–91

Progress Report

Practice guidelines for the treatment of hepatitis C: Recommendations from an AISF/SIMIT/SIMAST Expert Opinion Meeting[☆]

Writing committee: Daniele Prati, Antonio Gasbarrini, Teresa Santantano, Alfredo Alberti, Maria Grazia Rumi, Savino Bruno, Stefano Faggioli, Paolo Grossi, Raffaele Bruno, Giovanni Battista Gaeta, Giorgio Francesco Antonucci, Claudio Puoti, Calogero Cammà, Antonio Craxì.

ISSUES:

- Acute hepatitis C
- Individualised therapy
- Non-responders and relapsers
- Antiviral treatment in HCV cirrhosis
- HCV reinfection after liver transplantation
- HIV/HCV co-infection
- HCV/HBV ± HDV co-infection
- Elderly patients
- Patients with normal ALT levels

What should be improved

Open issues

- Is case finding **well managed** in Italy?
 - Subjects with increased ALT levels
 - “Vulnerable” subjects
 - Immigrants from endemic areas
 - Prisoners
 - Intravenous drug users

ALT evaluation by General Practitioners in Italy

- Data from 418 Italian General Practitioners using the HS/Thales electronic clinical record (648,091 patients)
- According to electronic clinical records, 70% of patients underwent at least one ALT determination
- Among them, the prevalence of ALT increase is substantial (on average 10%, up to 29% in males of 45-54 years)
- Only 37% of patients with ALT increase underwent anti-HCV testing
- Only 54% of anti-HCV positive patients underwent HCV RNA testing

→ *Recommendations are not properly followed*

HBV and HCV screening in Italian IVDU Primary Care Centers (2008 Report)

HCV

Percent tested for anti-HCV: 46%

Percent of reactivity: 59.2%

HBV

- Percent tested for HBV makers: 42%
- Percent of reactivity: 32.3%

National data on HBV vaccination and HCV treatment are currently unavailable.

HBV and HCV screening in Italian prisoners

- 973 Italian inmates
 - 87.0% males,
 - median age of 36 years,
 - 30.4% intravenous drug users
 - 0.6% men who have sex with men.
- High seroprevalence rates were found
 - HIV: 7.5%
 - HCV: 38.0%
 - anti-HBc: 52.7%
 - HBsAg: 6.7%.

No comprehensive strategy to identify infected persons

Foreign citizens officially resident in Italy, grouped according their area of origin

YEAR	Europe	Africa	Asia	America	Oceania	Stateless	TOTAL
1970	61,3	3,3	7,8	25,7	1,9	-	143.838
1980	53,2	10,0	14,0	21,0	1,4	0,4	298.749
1990	33,5	30,5	18,7	16,4	0,8	0,1	781.138
2000	40,7	28,0	19,2	11,8	0,2	0,0	1.379.749
2006 - %	49,6	22,3	18,0	9,7	0,1	0,3	3.690.052
2006 - v.a.	1.829.982	822.191	662.748	356.144	4.023	14.964	3.690.052

SOURCE: Caritas/Migrantes Report; data from the Italian Ministry of Interior

HBV and HCV screening in immigrants

- 182 illegal migrants from Sub Saharian Regions living in Verona (North-East)
 - 67.6% anti-HBc+
 - 9.3% HBsAg+
 - 4.4% anti-HBs+ (vaccinated)
 - 2.7% anti-HCV+

No comprehensive strategy to identify infected persons

Impact of chronic liver disease on National Health System

- The Italian National Health System covers the entire population, irrespective of income or contributions, employment or pre-existing health conditions
- Liver-related costs are increasing due to increase of:
 - The relative increase of individuals with long lasting HBV and HCV infections
 - The introduction of novel high costs therapies (HCC, antivirals)
 - The increase of metabolic and behavioral causes of liver disease (overweight, alcohol use, physical inactivity)
- These issues might have important consequences in the long term

Costs of liver-related hospital stay in Italy

	Mean days of hospital stay	N. of cases	Mean number of hospital days (Italy)	Total costs
Cirrhosis and alcoholic hepatitis	11.5	55,460	637,790	€ 306,776.990
HCC	10.74	12,000	128,880	€ 53,871.840
Other liver diseases	2.5	57,239	143,097	€ 59,814.755
Liver Transplant		1,079		€ 1,611,850.000
TOTAL COSTS				€ 2,032,313.400

Research Grants for Liver Disease and HIV- Italian data

	Liver	HIV	Ratio
HBV vs. HIV infections	570.000	130.000	(4:1)
HCV vs HIV infections	1.700.000	130.000	(13:1)
Alcohol related liver disease vs HIV	3.700.000	130.000	(28:1)
NAFLD vs HIV	14.250.000	130.000	(110:1)
Deaths for cirrhosis or HCC vs HIV	22.000	200	(110:1)
Deaths for HCC vs HIV	10.000	200	(50:1)
European Research Grants	??	20 ML €	

Number of articles on liver disease published in peer reviewed journals in 2007, grouped according to the country of affiliation (PubMed Search)

- Italy 752
- Germany 743
- UK 619
- France 512
- Spain 431
- USA 3108

Future Plans

- Reinforce dissemination of case-finding guidelines, including screening programs among high risk groups;
- Encourage the implementation of best practice in targeted screening strategies
- Support awareness raising campaigns on viral hepatitis and increase uptake of screening;
- Help reduce health inequalities, addressing those most vulnerable and least likely to actively manage their health (prisoners, IVDUs, immigrants);
- Promote research on prevention and cure of Hepatitis B and C;
- Promote healthy lifestyles and behaviors



- **fire**: The Italian Foundation for Research in Hepatology
- Founded in 2009 by the Italian Association for the Study of the Liver (AISF)
- Specific aims (not addressed by AISF):
 - Improve fund raising to help scientific research, also encouraging cooperation with non-pharmaceutical companies
 - Support awareness raising campaigns on liver disease and increase uptake of screening
 - Promote healthy lifestyles and behaviors

Conclusions

(What we absolutely need)

- A coordinated effort to increase awareness on liver disease
- To translate good recommendations and guidelines into good clinical practice
- A transparent discussion and disclosure of interests among the parties involved in improving screening policies
 - Patients (including the most vulnerable categories)
 - Physicians
 - National Health System
 - Pharmaceutical companies