

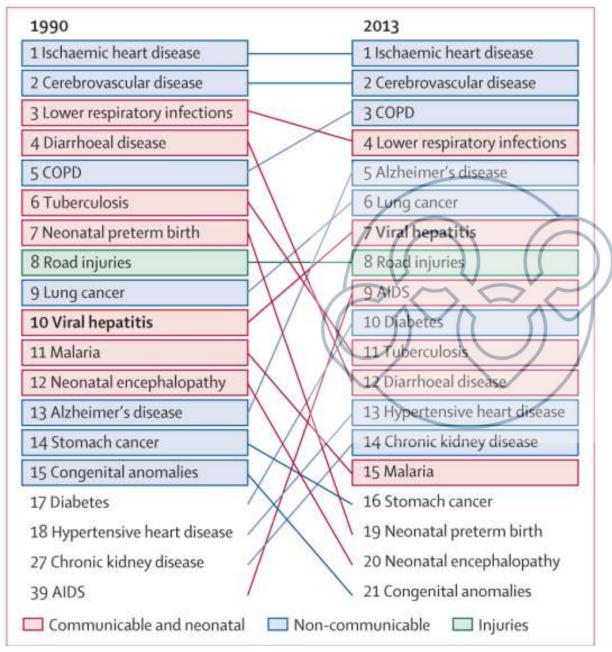
Dipartimento di Medicina Trasfusionale ed Ematologia Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico Il sottoscritto, in qualità di Relatore dichiara che

nell'esercizio della Sua funzione e per l'evento in oggetto, NON È in alcun modo portatore di interessi commerciali propri o di terzi; e che gli eventuali rapporti avuti negli ultimi due anni con soggetti portatori di interessi commerciali non sono tali da permettere a tali soggetti di influenzare le mie funzioni al fine di trarne vantaggio.

Hepatitis Epidemiology: Handle with care!

- The collection of epidemiological data on liver diseases across different regions is hindered by the lack of a specific comprehensive study.
- The fragmented current understanding is derived from various organizations' critical reviews, with the backdrop of potential commercial bias in pharmaceutical-sponsored projections.
- Inconsistent methodologies, case definitions, and report accuracies across countries add to the variability, undermining data reliability and comparability.
- Furthermore, many existing local surveys are outdated, not reflecting the latest trends or interventions, which is crucial for informed decision-making and public health policy development.

Leading causes of mortality and trends, 1990–2013



The global burden of viral hepatitis from 1990 to 2013: findings from the Global Burden of Disease Study 2013

Jeffrey D Stanaway, Abraham D Flaxman, Mohsen Naghavi, Christina Fitzmaurice, Theo Vos, Ibrahim Abubakar, Laith J Abu-Raddad, Reza Assadi, Neeraj Bhala, Benjamin Cowie, Mohammad H Forouzanfour, Justina Groeger, Khayriyyah Mohd Hanafiah, Kathryn H Jacobsen, Spencer L James, Jennifer MacLachlan, Reza Malekzadeh, Natasha K Martin, Ali A Mokdad, Ali H Mokdad, Christopher J L Murray, Dietrich Plass, Saleem Rana, David B Rein, Jan Hendrik Richardus, Juan Sanabria, Mete Saylan, Saeid Shahraz, Samuel So, Vasiliy V Vlassov, Elisabete Weiderpass, Steven T Wiersma, Mustafa Younis, Chuanhua Yu, Maysaa El Sayed Zaki, Graham S Cooke

- Viral hepatitis is a significant contributor to mortality and morbidity globally.
- It ranks among the leading causes of death and disability worldwide.
- The annual death toll from viral hepatitis equals or surpasses that of tuberculosis, AIDS, or malaria.
- Unlike many other communicable diseases, the importance of hepatitis has increased since the initial Global Burden of Disease (GBD) Study in 1990.
- The World Health Organization (WHO) is launching a major new effort to address viral hepatitis.
- These data underscore the critical importance of viral hepatitis in shaping global health policy.

Stanaway J et al Lancet 2016



GLOBAL HEALTH SECTOR STRATEGYON VIRAL HEPATITIS 2016-2021

Figure 2. Estimated global number of deaths due to viral hepatitis, HIV, malaria and TB, 2000–2015





WHO Global Health Sector Strategy on Viral Hepatitis 2016–2021



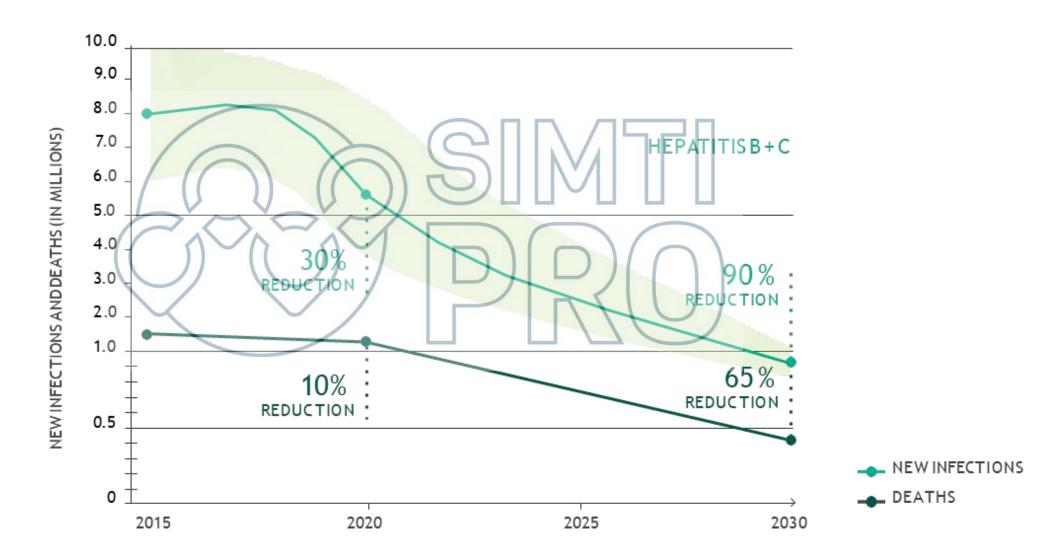


Source: WHO Global Health Sector Strategy on viral hepatitis. Available at: http://apps.who.int/gb/ebwha/pdf_files/WHA69/A69_32-en.pdf?ua=1 (Accessed August 2016)



GLOBAL HEALTH SECTOR STRATEGYON VIRAL HEPATITIS 2016-2021

Figure 6. Targets for reducing new cases of and deaths from chronic viral hepatitis B and C infection



HEPATITIS STRATEGY, 2016: ELIMINATION BY 2030

	Interventions	2030 targets			
1. Service coverage	 Three dose hepatitis B vaccine HBV prevention of mother to child transmission Blood and injection safety Harm reduction Treatment 	90% 90% 100 % screened donations 90% reuse-prevention devices 300 injection sets/PWID/yr 90% diagnosed 80% eligible treated			
2. Impact	A. Incidence reduction	90%			
	B. Mortality reduction	65%			

A che punto siamo?

Global progress report on HIV, viral hepatitis and sexually transmitted infections, 2021

Accountability for the global health sector strategies 2016–2021: actions for impact



Key facts



The World Health Organization (WHO) estimates that during 2019:

- 296 million people worldwide are living with hepatitis B (90% unaware)
- 58 million people worldwide are living with hepatitis C (80% unaware)
- 1.5 million people were newly infected with chronic hepatitis B
- 1.5 million people were newly infected with chronic hepatitis C
- Both hepatitis B and hepatitis C can lead to lifelong infection. WHO estimates that 1.1 million deaths occurred in 2019 due to these infections and their effects including liver cancer, cirrhosis, and other conditions caused by chronic viral hepatitis

Hepatitis B and C new infections and mortality by WHO region, 2019

GLOBAL **REGION OF THE AMERICAS** EUROPEAN REGION WESTERN PACIFIC REGION Hepatitis B Hepatitis B Hepatitis B Hepatitis B New infections: 140 000 New Infection: 1 500 000 New infections: 10 000 New infections: 19 000 [1 100 000-2 600 000] [5 100-26 000] [9 400-38 000] [96 000-210 000] Deaths: 15 000 Deaths: 470 000 Deaths: 43 000 Deaths: 820 000 [450 000-950 000] [8 500-23 000] [34 000-51 000] [200 000-490 000] Hepatitis C Hepatitis C Hepatitis C Hepatitis C New Infection: 1 500 000 New infections: 67 000 New infections: 300 000 New infections: 230 000 [1 300 000-1 800 000] [63 000-73 000] [240 000-320 000] [220 000-260 000] Deaths: 77 000 Deaths: 290 000 Deaths: 31 000 Deaths: 64 000 [39 000-72 000] [77 000-140 000] [230 000-580 000] [19 000-84 000] EASTERN **MEDITERRANEAN** SOUTH-EAST ASIA AFRICAN REGION REGION REGION Hepatitis B Hepatitis B Hepatitis B WHO REGIONS New infections: 990 000 New infections: 100 000 New infections: 260 000 [660 000-1 600 000] [79 000-140 000] [180 000-590 000] African Region Deaths: 80 000 Deaths: 33 000 Deaths: 180 000 Region of the Americas [47 000-110 000] [26 000-60 000] [140 000-300 000] South-East Asia Region Hepatitis C Hepatitis C Hepatitis C European Region New infections: 210 000 New infections: 470 000 New infections: 230 000 Eastern Mediterranean Region [150 000-370 000] [240 000-520 000] [200 000-430 000] Western Pacific Region Deaths: 31 000 Deaths: 38 000 Deaths: 45 000 Not applicable [23 000-72 000] [31 000-74 000] [37 000-130 000]

Global progress report on HIV, viral hepatitis and sexually transmitted infections, 2021. © World Health Organization 2021

World Health

Organization



Coinfections and comorbidities related to HIV and viral hepatitis

Diseases	Summary of the evidence
HIV and viral hepatitis	2.7 million people are coinfected with HIV and hepatitis B virus (2015) (5).
	2.3 million people are coinfected with HIV and hepatitis C virus (2015) (5).
HIV and viral hepatitis	Among people living with HIV, untreated hepatitis coinfection promotes more rapid progression of hepatitis B- and/or C-related liver disease, hepatocellular cancer and untimely death, undermining the gains of effective HIV treatment.
	HIV coinfection doubles the risk of mother-to-child transmission of viral hepatitis (5)
	More than half of all people coinfected with HIV and hepatitis C are people who inject drugs.
	Men living with HIV who have sex with men are at substantially higher risk of hepatitis C infection (17).



Summary: The WHO Progress Report 2021

While significant strides have been made in the expansion of treatments, particularly for hepatitis C, challenges persist. Notably, 1.5 million people annually contract hepatitis B despite the availability of an effective vaccine.

A high mortality rate from hepatitis B and C persists, amounting to 1.1 million deaths in 2019, primarily due to chronic liver disease and liver cancer.

The data emphasizes the need for an accelerated response to improve diagnosis, prevention, and treatment to meet the 2030 targets for elimination.

Hepatitis in the EU



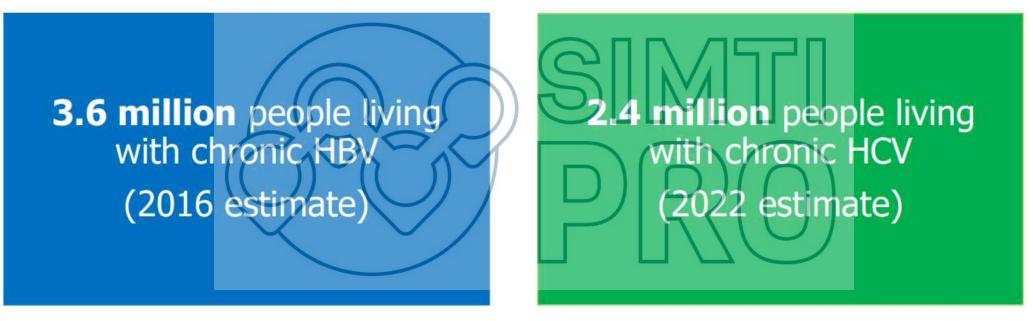
By Chat GPT



The burden of viral hepatitis B and C in the EU/EEA



Estimated numbers with chronic infection



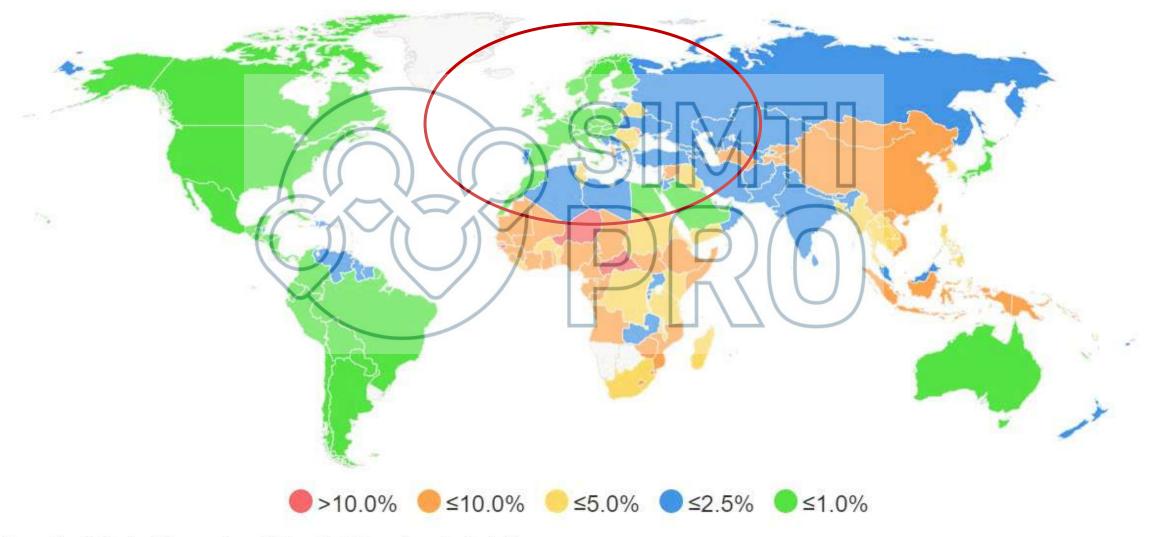
Variation in disease burden across countries and between different population groups

Source: HBV estimate - Hofstraat SHI, Falla AM, Duffell EF, Hahné SJM, Amato-Gauci AJ, Veldhuijzen IK, Tavoschi L. Current prevalence of chronic hepatitis B and C virus infection in the general population, blood donors and pregnant women in the EU/EEA: a systematic review. Epidemiol Infect. 2017 Oct;145(14):2873-2885. HCV estimate - ECDC HCV modelling project – work currently unpublished)





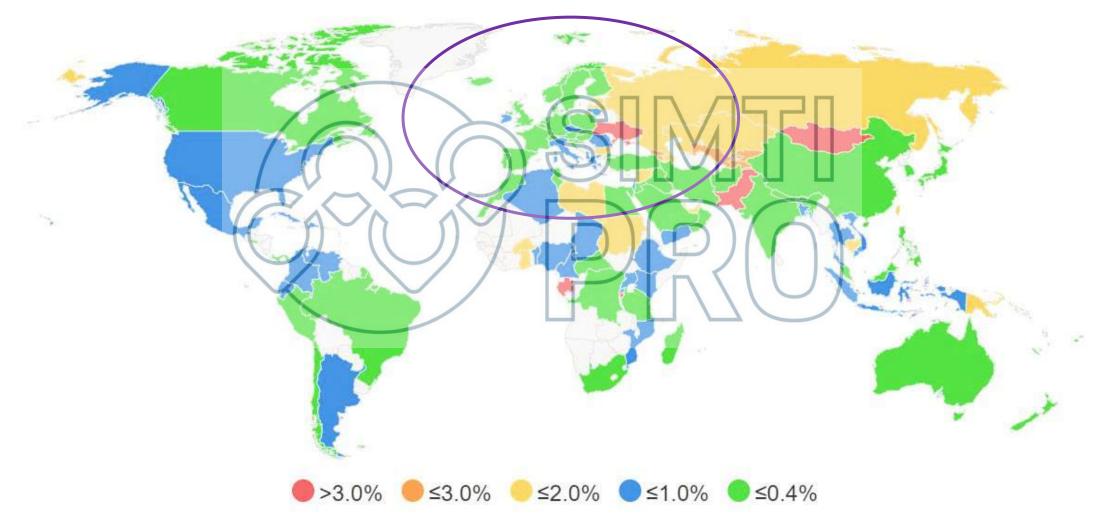
HBsAg Prevalence — 2022



From the Polaris Observatory (https://cdafound.org/polaris/)

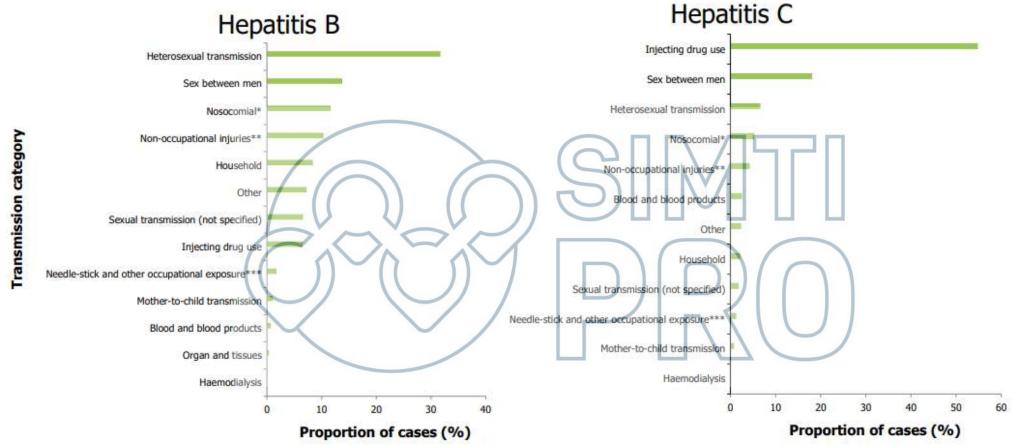


Hepatitis C Viremic Prevalence — 2022



From the Polaris Observatory (https://cdafound.org/polaris/)

Transmission category of acute hepatitis B and C cases, EU/EEA, 2020



Source: European Centre for Disease Prevention and Control (ECDC). Hepatitis B: Annual Epidemiological Report for 2020; European Centre for Disease Prevention and Control (ECDC). Hepatitis C: Annual Epidemiological Report for 2020.

* Nosocomial refers here to patient infections in healthcare settings

**: 'Non-occupational injuries' include needle sticks that occur outside a health care setting, bites, tattoos, piercings

*** Occupational exposure includes needle-stick and other occupational injuries

Prevalence of hepatitis B and C in different population groups



Hepatitis B (HBsAg prevalence)	Hepatitis C (anti-HCV)
Migrant populations 0.9 - 31.7%	People who inject drugs 15.4 – 96.8% (RNA prevalence 15.0 – 64.2%)
People who inject drugs 0 - 16.9%	Peopte in prison 2.3 – 82.6%
People in prison 0.3 - 8.3%	Migrant populations 0 - 16.8%
Men who have sex with men 2.3 - 4.3%	Men who have sex with men 0.6 – 4.8%

Source: Bivegete S TA, et al. Estimates of hepatitis B virus prevalence among general population and key risk groups in EU/EEA/UK countries: a systematic review. Submitted for peer review publication 2022; ECDC HCV MPES modelling work – publication pending; EMCDDA Viral Hepatitis Elimination Barometer hilps://www.emcdda.europa.eu/publications/html/viral -hepatitis-elimination-barometer en; ECDC hepatitis C prevalence data base <u>hilps://www.ecdc.europa.eu/en/infectious-disease-topics/z-disease-list/hepatitisc/tools/hepatitis-c-prevalence-database</u>; Nakitanda et al. Hepatitis C virus infection in EU/EEA and United Kingdom prison: opportunities and challenges for action hilps://www.ncbi.nlm.nih.gov/pmc/articles/PMC7650151/pdf/12889_2020_Article_9515.pdf.

Hepatitis B and C among migrant populations

ECDC report in 2016 to estimate burden of hepatitis B and C among migrant populations in Europe

Based on:

- Number of migrants in EU countries
- Prevalence in country of origin

Estimated 25% of the chronic hepatitis B burden in the EU/EEA was among migrant populations and for hepatitis C this was 14%

Proportion of migrants in the total population at that time was considerably lower (5%)





TECHNICAL REPORT

Epidemiological assessment of hepatitis B and C among migrants in the EU/EEA



Hepatitis B and C in Europe: an update from the Global Burden of Disease Study 2019

GBD 2019 Europe Hepatitis B & C Collaborators*

- HBV-Related Cirrhosis and Liver Cancer: In the period 2010-2019, despite reduced cirrhosis rates, HBV-related liver cancer remains stable, highlighting persistent challenges in control.
- HCV Dynamics: Slight decline in acute HCV (-3.24%) with significant mortality rate drop (-35.73%). Yet, only minor decrease in HCV-related cirrhosis prevalence (-6.37%) and a concerning rise in liver cancer cases (+16.41%), underscoring the urgent need for better HCV management strategies.
- **DALYs:** Both HBV and HCV show DALY reductions, with more pronounced improvements in HBV, indicating effective control measures and emphasizing the necessity for augmented HCV efforts.
- Public Health Implications: Data calls for improved surveillance, vaccination, treatment access, and tailored public health policies to curb these infections' incidence and mortality, particularly regarding the uptick in HCV-related liver cancer.

Hepatitis in Italy



By Chat GPT

Epidemiological and clinical aspects of hepatitis B virus infection in Italy over the last 50 years

Caterina Sagnelli, Antonello Sica, Massimiliano Creta, Armando Calogero, Massimo Ciccozzi, Evangelista Sagnelli

1. Major Factors for Decline of HBV infection over the past 50 years:

- Improved socio-economic and hygiene conditions.
- Effective educational campaigns and uninterrupted HBV vaccination since 1991.
- Reduction in major HBV risk factors, including vertical transmission and household contacts.
- Mandatory HBV screening for blood donations and the elimination of improperly sterilized medical instruments.

2. Current Statistics:

- HBV chronic carrier prevalence: 0.8%.
- Acute HBV (AHB) incidence: 0.21 per 100,000 inhabitants, higher among males and individuals over 41.

3. Transmission Trends:

• Sexual transmission is now the primary mode of HBV spread in Italy, attributed to infrequent condom use.

4. Migrant Population:

• Higher HBV acquisition risk compared to Italian citizens, prompting WHO to recommend HBV vaccination protocols for all unvaccinated migrants.



Lo screening nazionale gratuito per l'HCV Risultati preliminari – Rendicontazione al 31/12/2022

Popolazione generale (69-89

ESTENSIONE =	COPERTURA =	ADESIONE =	PØSITIVI test	ADESIONE AL	POSITIVI test	DETECTION	SOGG. CON INF.
INVITATI/	TESTATI/	TESTATI/	ricerca Ab (%)	TEST DI	di conferma	RATE (%) =	ATTIVA AVVIATI AL
TARGET	TARGET			CONFERMA	L (%)	INF. ATTIVA/	TRATTAMENTO (%)
		ME		(%)		TESTATI*1000	
18,0	4,1	22,9	0,7	86,2	29,1	1,8	32,7

Identificati n. 892 soggetti con infezione attiva da HCV

Totale soggetti screenati: 488.571

~0.18%



25,4

59.3

34.0

57,4

Identificati n. 5.439 soggetti con infezione attiva da HCV

95,2

Totale soggetti screenati: 50.205

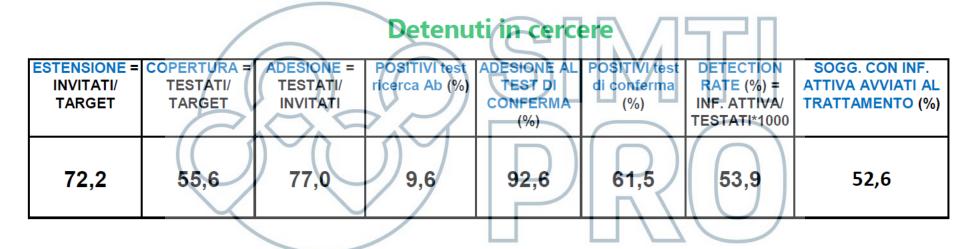
44,8

108,3

54,1



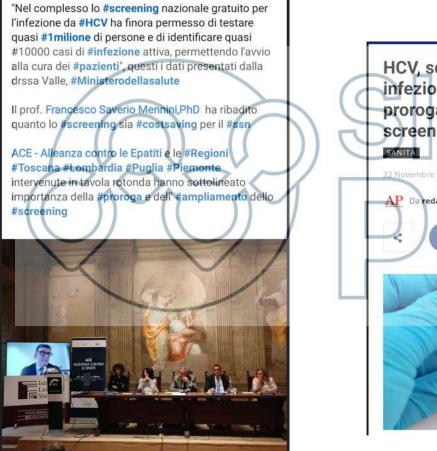
Lo screening nazionale gratuito per l'HCV Risultati preliminari – Rendicontazione al 31/12/2022



Identificati n. 1.324 soggetti con infezione attiva da HCV

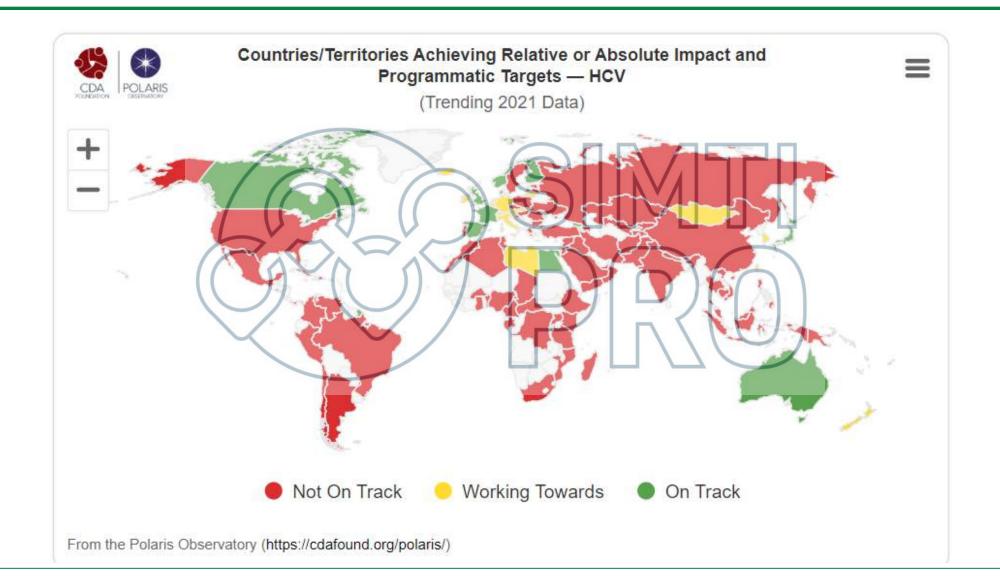
Totale soggetti screenati: 24.571

HCV Screening in Italy: Updated Figures





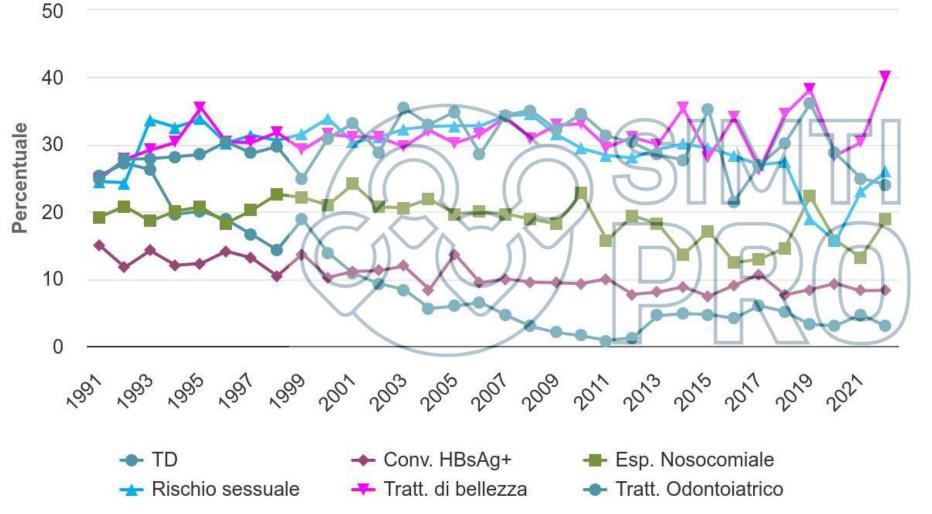
Italy is Not on Track to Achieve HCV Elimination



Italy is Not on Track to Achieve HCV Elimination

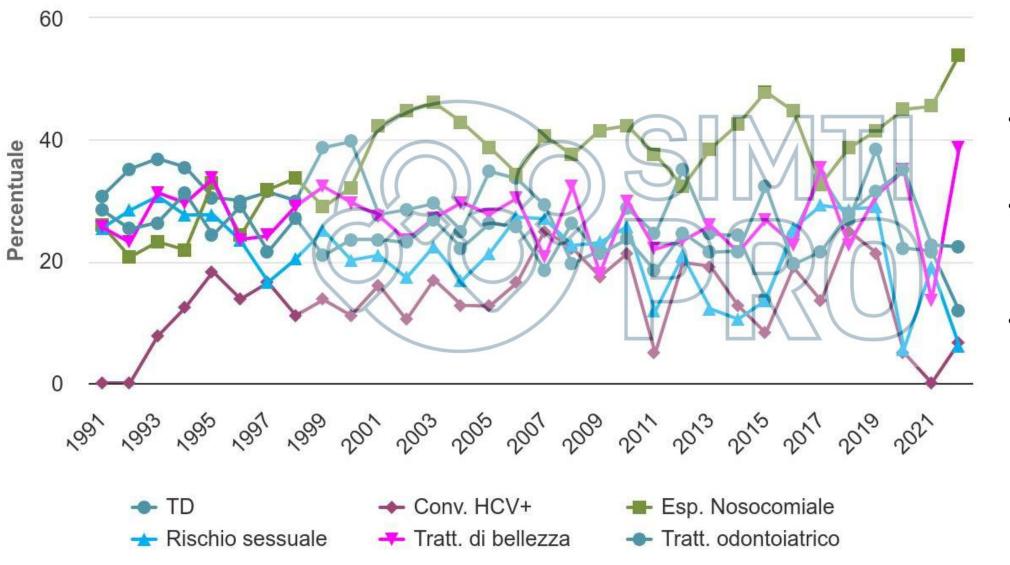


Casi di epatite B acuta per fattore di rischio (2022)



- Manicure, pedicure, piercing e tatuaggi: 40%个
- Comportamenti sessuali promiscui: 26,0%个
- Rischio di trasmissione nosocomiale: 18,9%个

Casi di epatite C acuta per fattore di rischio (2022)



- Esposizione
 nosocomiale:
 54,0%个
- Trattamenti estetici (manicure, piercing, tatuaggi): 38,8% dei casi
- Esposizione sessuale andamento altalenante, con un calo nel periodo pandemico.

The Incidence and Risk Factors of Community-Acquired Hepatitis C in a Cohort of Italian Blood Donors

DANIELE PRATI,¹ CARMEN CAPELLI,¹ CARLA SILVANI,¹ CLAUDIA DE MATTEI,¹ PATRIZIA BOSONI,¹ MARCO PAPPALETTERA,¹ FULVIO MOZZI,¹ MASSIMO COLOMBO,² ALBERTO ZANELLA,³ AND GIROLAMO SIRCHIA¹

The incidence of hepatitis C virus (HCV) infection in a cohort of Italian blood donors at low risk for blood-borne diseases was 1 per 10,000 person-years, with nosocomial exposure being a significant risk factor.

Case	Sex	Age (yr)	No. of Donations*	ALT (U/L)			HCV RNA				$(\land \land \land$	
				Presero- conversion	At Onset	During Follow-up†	Presero- conversion	At	During Follow-up	HCV Type	Liver Histology	Risk Factors
1	M	24	7	9	15	64 (20-118)	pos	pos	pos	Ъ	Chronic persistent hepatitis	Minor surgery
2	М	59	26	13	23	22 (15-44)	neg	pos	neg‡	2a	Not done	Frequent venipuncture
3	М	32	8	10	1,246	273 (38-1,430)	neg	pos	pos	2a	Mild chronic active hepatitis	Major surgery
4	М	55	20	11	71	59 (28-122)	neg	pos	pos	2a	Chronic persistent hepatitis	Minor surgery
5	F	27	9	19	44	47 (32-73)	neg	pos	pos	3a	Chronic persistent hepatitis	HCV-infected partner

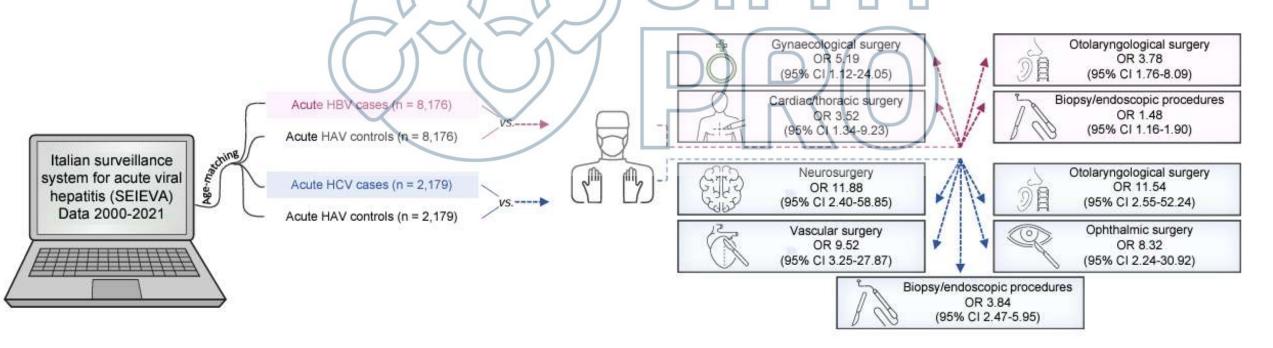
Risk of parenterally transmitted hepatitis following exposure to invasive procedures in Italy: SEIEVA surveillance 2000-2021

Susanna Caminada¹, Annamaria Mele^{1,2}, Luigina Ferrigno³, Valeria Alfonsi⁴, Simonetta Crateri³, Giuseppina lantosca³, Marise Sabato¹, Maria Elena Tosti^{3,*}, the SEIEVA Collaborating Group[†]

Journal of Hepatology 2023. vol. 79 | 61-68

Overview:

Utilizing data from SEIEVA surveillance, this study investigates the association between specific types of invasive procedures and the risk of acute HBV and HCV infections in Italy.



Risk of parenterally transmitted hepatitis following exposure to invasive procedures in Italy: SEIEVA surveillance 2000-2021

Susanna Caminada¹, Annamaria Mele^{1,2}, Luigina Ferrigno³, Valeria Alfonsi⁴, Simonetta Crateri³, Giuseppina lantosca³, Marise Sabato¹, Maria Elena Tosti^{3,*}, the SEIEVA Collaborating Group[†]

Journal of Hepatology 2023. vol. 79 | 61-68

Key Findings

- Significant risk of acquiring hepatitis B and C following exposure to invasive procedures.
- Strongest associations for HBV linked to gynecological, otolaryngological, and cardiac/thoracic surgeries.
- Highest risks for HCV found in neurosurgery, otolaryngological surgery, and vascular surgery.
- Minor surgeries, biopsy, and endoscopy also showed a significant association with both HBV and HCV infections.

Risk of parenterally transmitted hepatitis following exposure to invasive procedures in Italy: SEIEVA surveillance 2000-2021

Susanna Caminada¹, Annamaria Mele^{1,2}, Luigina Ferrigno³, Valeria Alfonsi⁴, Simonetta Crateri³, Giuseppina lantosca³, Marise Sabato¹, Maria Elena Tosti ^{3,*}, the SEIEVA Collaborating Group[†]

Journal of Hepatology 2023. vol. 79 | 61-68

Conclusions and Healthcare Implications

- Despite advancements in healthcare, invasive procedures remain a significant risk factor for transmitting hepatitis viruses.
- Necessity of strict adherence to universal precautions in healthcare settings.
- Importance of minimizing iatrogenic transmission risks during all medical procedures, including minor ones.
- Need for further education and training on infection control practices among healthcare professionals.

Summary

- HBV and HCV remain significant public health challenges, with millions living with these infections globally and a substantial annual death toll.
- While advancements in treatment, especially for HCV, have been made, the persistence of new infections underscores the need for improved vaccination, diagnosis, and treatment strategies.
- Achieving the WHO's target of eliminating viral hepatitis requires an accelerated and coordinated global response, emphasizing the need for comprehensive public health policies, enhanced surveillance, and increased access to prevention and treatment services.
- Data from Italy highlight the importance of tailored strategies. The continuing spread due to preventable causes (nosocomial, unprotected sex) is of concern.

Credits

- WHO (https://www.who.int/health-topics/hepatitis#tab=tab_1)
- ECDC (https://www.ecdc.europa.eu/en/viral-hepatitis)
- Polaris Observatory (https://cdafound.org/polaris/)
- SEIEVA (https://www.epicentro.iss.it/epatite/seieva)
- Prof. Alessio Aghemo, Humanitas University, Milan