

HIV e HCV

alla ricerca di nuovi modelli organizzativi “sostenibili”
Qual è il ruolo della Real World Evidence?

Villa Doria D'Angri, Napoli
15-dicembre-2017

Valutazione dell'impatto epidemiologico ed economico della coinfezione HIV-HCV



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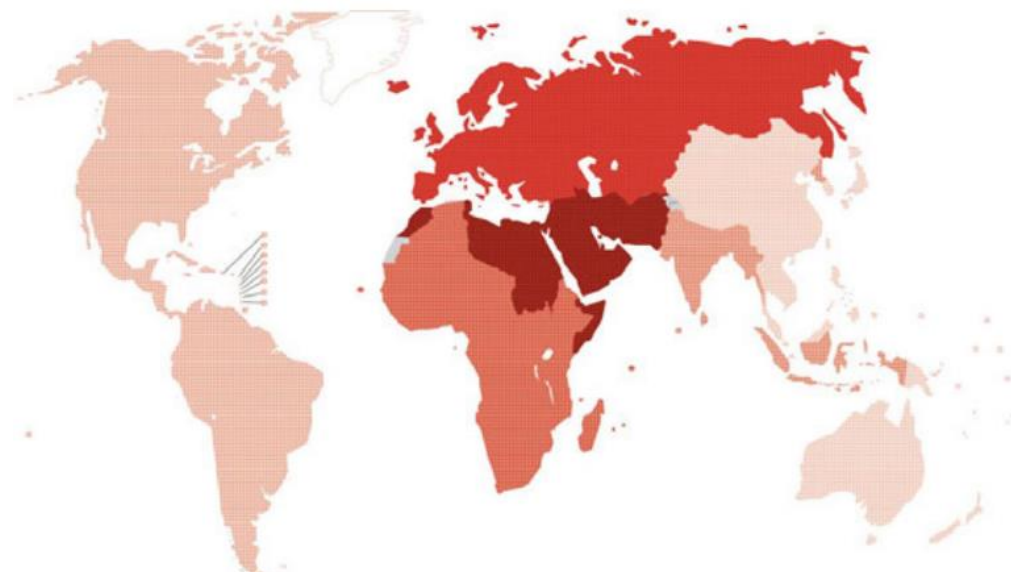
Servizio di Farmacologia Clinica

AOU «San Giovanni di Dio e Ruggi d'Aragona»







**GLOBAL HEPATITIS REPORT,
2017**

71
MILLION PERSONS
WORLDWIDE ARE
LIVING WITH HCV.

Table 3 (with map). Incidence of HCV infection in the general population, by WHO region, 2015:
1.75 million new infections in 2015



Incidence of HCV infection

WHO region	Map key	Incidence rate (per 100 000)		Total number (000)	
		Best estimate	Uncertainty interval	Best estimate	Uncertainty interval
African Region		31.0	22.5–54.4	309	222–544
Region of the Americas		6.4	5.9–7.0	63	59–69
Eastern Mediterranean Region		62.5	55.6–65.2	409	363–426
European Region		61.8	50.3–66.0	565	460–603
South-East Asia Region		14.8	12.5–26.9	287	243–524
Western Pacific Region		6.0	5.6–6.6	111	104–124
Global		23.7	21.3–28.7	1 751	1 572–2 120

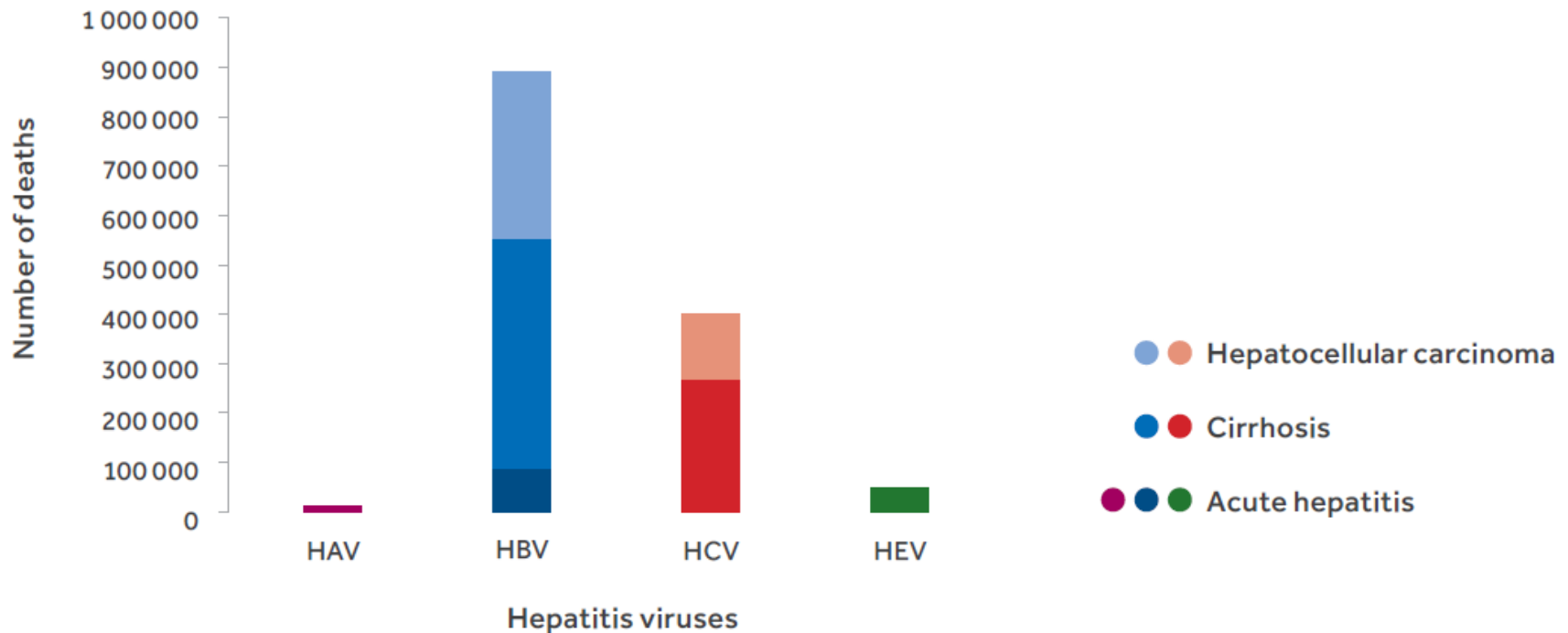
GLOBAL HEPATITIS REPORT,
2017

Prevalence of HCV infection (HCV RNA positive)
in the general population, by WHO region

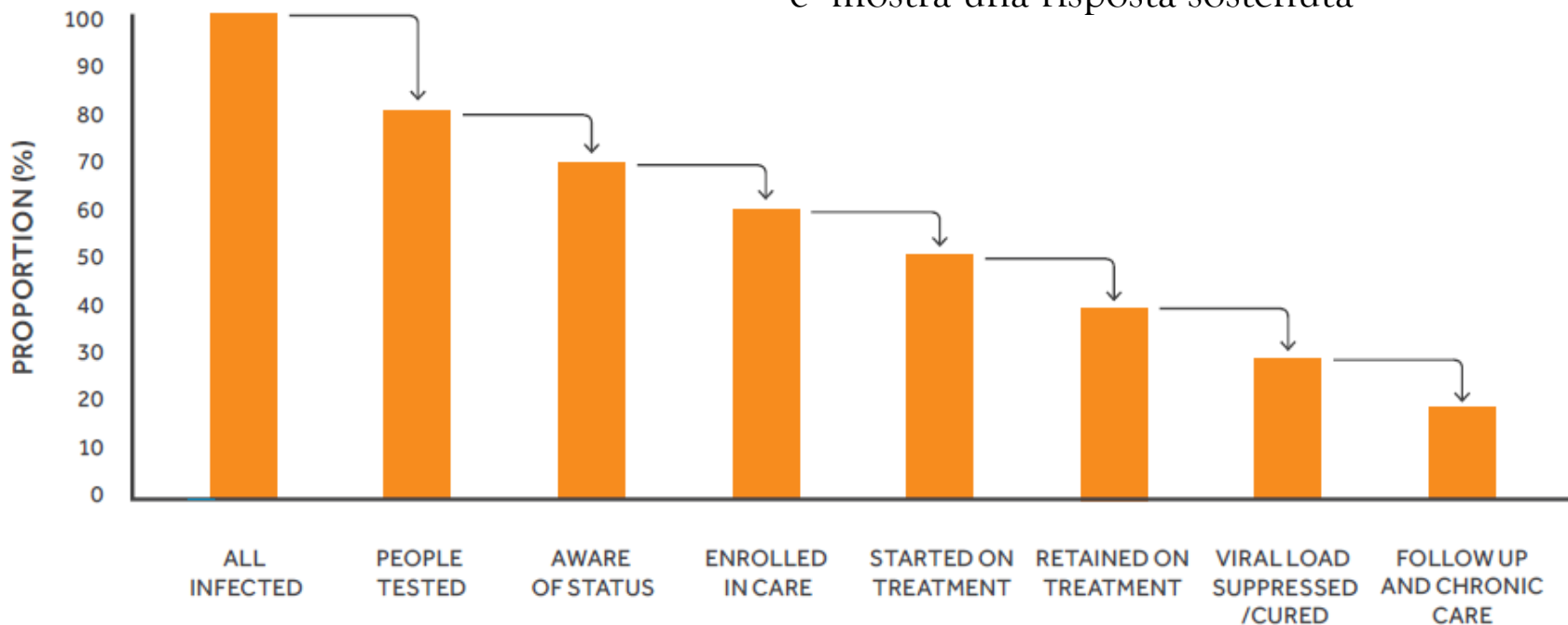


GLOBAL HEPATITIS REPORT,
2017

Deaths from viral hepatitis, by virus and type of sequelae, 2015:
most viral hepatitis deaths are due to **the late complications**
of HBV and HCV infection



«Treatment effectiveness»
proporzione dei pazienti che, completato il trattamento,
e mostra una risposta sostenuta

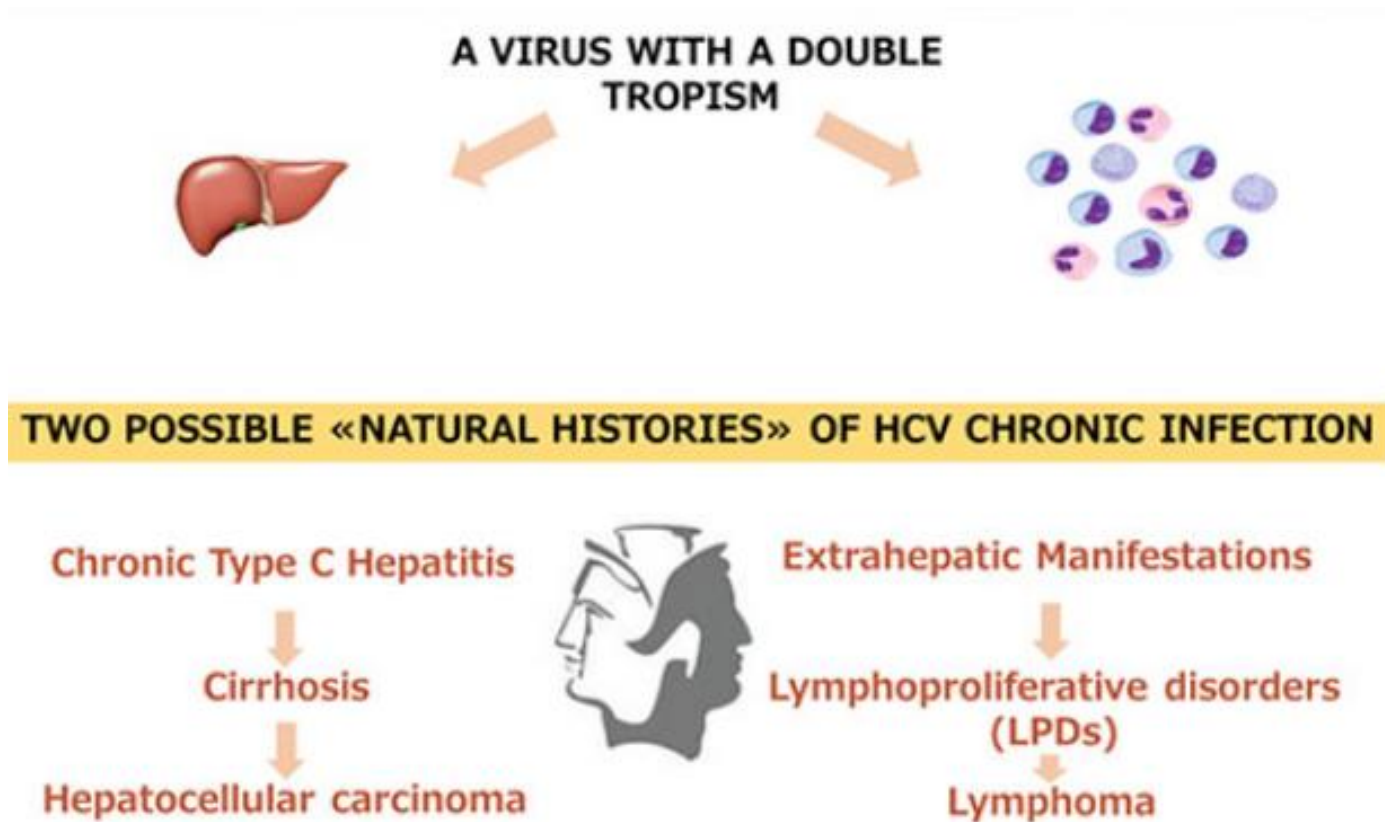


CONTINUUM OF SERVICES – CASCADE OF CARE



Manifestazioni cliniche correlate al virus HCV

Numerose manifestazioni cliniche sia epatiche sia extraepatiche sono correlate alla epatite C



L'HCV cronica ha numerose malattie sistemiche coesistenti. Alcune manifestazioni extra-epatiche sono immuno-mediate, Mentre altre sembrano essere mediate da infiammazione cronica

Manifestazioni extra-epatiche nel paziente HCV+

Immune-related extrahepatic manifestations

Mixed cryoglobulinemia

Cryoglobulinemic vasculitis

B-cell NHL

Sicca syndrome

Arthralgia/myalgia

Autoantibody production (i.e. cryoglobulins, rheumatoid factor, and antinuclear, anticardiolipin, antithyroid and anti-smooth muscle antibodies)

Polyarteritis nodosa

Monoclonal gammopathies

Immune thrombocytopenia

Inflammatory-related extrahepatic manifestations

Type 2 diabetes mellitus type 2

Insulin resistance

Glomerulonephritis

Renal insufficiency

Fatigue

Cognitive impairment

Depression

Impaired quality of life

Polyarthritis/fibromyalgia


Cardiovascular disorders (i.e. stroke, ischemic heart disease)

NHL, non-Hodgkin's lymphoma.

Manifestazioni HCV extra-epatiche: caratteristiche dei pz con crioglobulinemia

Feature	HCV Patients With Life-Threatening Cryoglobulinemia (n=279) No. (%)
Sex (female)	146 (52)
Mean age at diagnosis of cryoglobulinemia (range), yr	54 (25–87)
Mean age at life-threatening involvement (range), yr	55 (25–87)
First clinical manifestation of cryoglobulinemia	232 (83)
Associated conditions	
Chronic viral infection	
HIV coinfection	25 (8.9)
HBV coinfection	7 (2.5)
Autoimmune diseases	15 (5.3)
Sjögren syndrome	6 (40)
SLE	4 (26.6)
Polyarteritis nodosa	2 (13.3)
Mixed connective tissue disease	1 (6.6)
Rheumatoid arthritis	1 (6.6)
Vasculitis ANCA (+)	1 (6.6)
Neoplasia	8 (2.8)

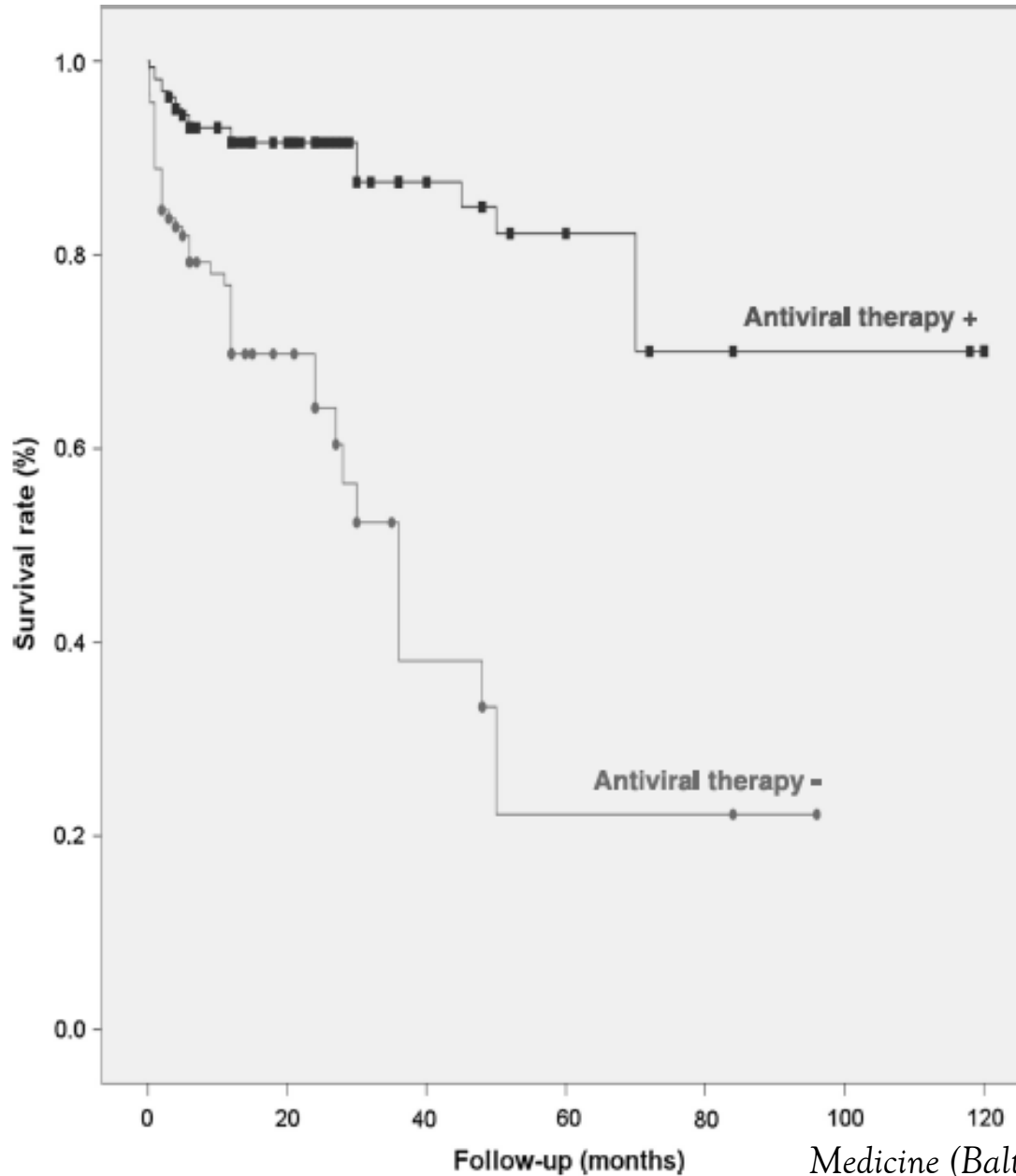
Manifestazioni HCV extra-epatiche: Outcomes nei pz con crioglobulinemia

Feature	HCV Patients With Life-Threatening Cryoglobulinemia (n=279) No. (%)
Outcomes	
Chronic renal failure	38 (13.6)
Relapse	33 (11.8)
Neoplasia	10 (3.5)
Death	63 (22.5) 
Causes of death	
Infectious process	26 (41.2)
Cryoglobulinemia vasculitis	24 (38)
Neoplasia	6 (9.5)
Liver-related process	4 (6.3)
Cardiovascular events	2 (3.1)
Other causes	1 (1.5)

Manifestazioni HCV extra-epatiche: Outcomes nei pz con crioglobulinemia

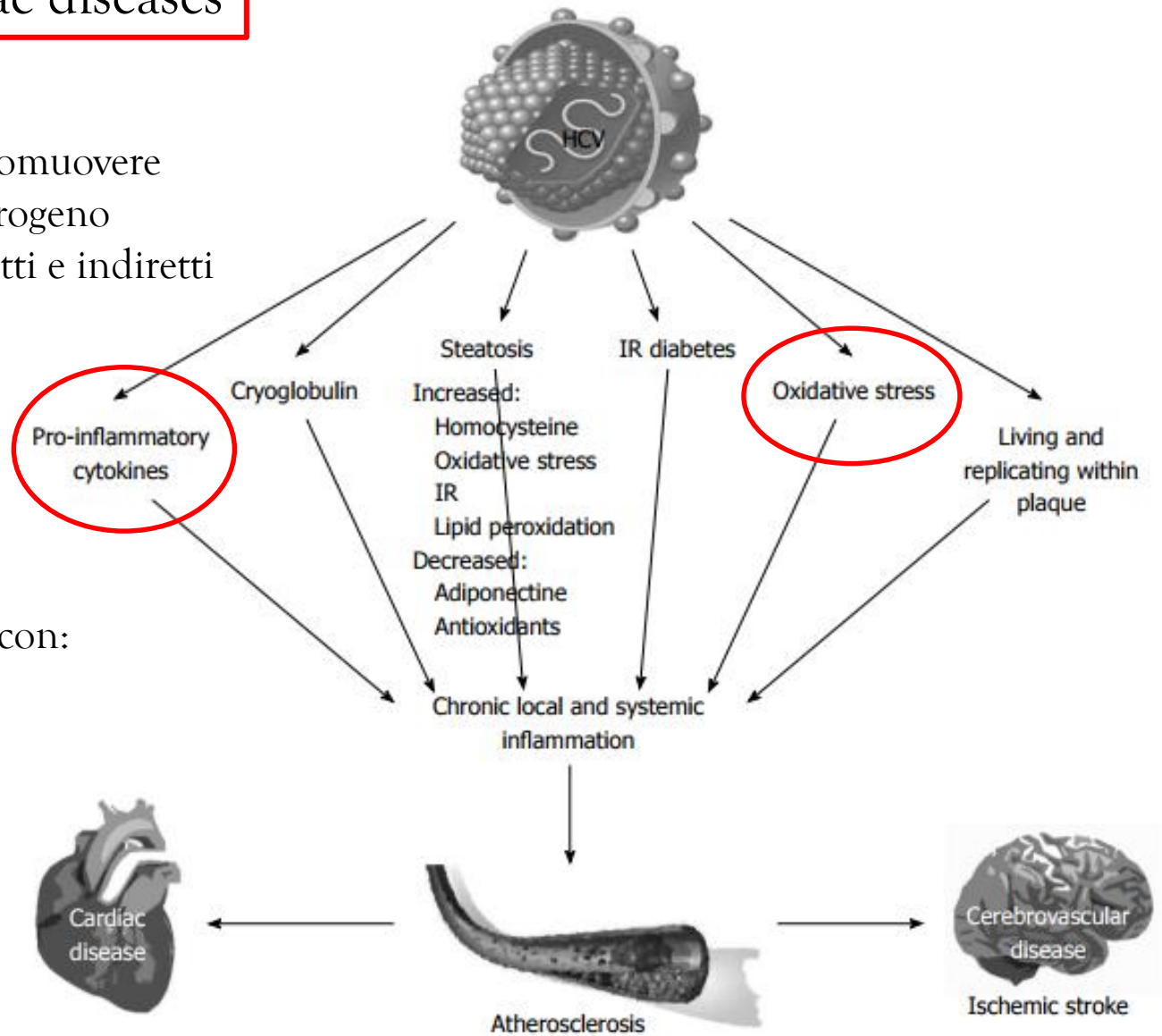
Feature	HCV Patients With Renal Failure (n=205) No. (%)
Mean follow-up of life-threatening cryoglobulinemia, mo	13.2 (3–120)
Outcomes	
Chronic renal failure	39 (19)
Relapse	12 (5.8)
Hemodialysis	10 (4.8)
Neoplasia	7 (3.4)
Death	43 (20.9)
Causes of death	
Infectious processes	18 (41.8)
Cryoglobulinemia vasculitis	10 (23.2)
Multiorgan failure	6 (13.9)
Liver-related processes	3 (6.9)
Neoplasia	3 (6.9)
Cardiovascular events	2 (4.6)
Iatrogenic	1 (2.3)

Impatto della terapia antivirale



HCV and cardiac diseases

HCV potrebbe promuovere
il processo aterogeno
con meccanismi diretti e indiretti



Associazioni trovate con:
scompenso
diabete
insulino resistenza
ipertensione

Effetto della terapia anti-HCV Sulle manifestazioni extraepatiche: focus su malattie cerebrovascolari

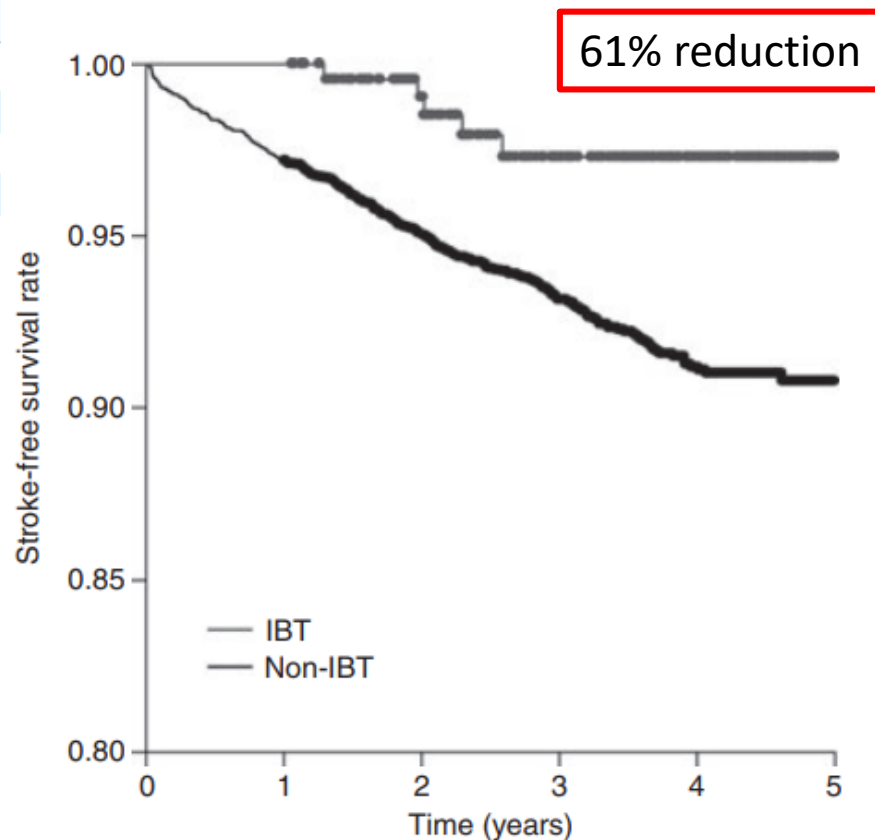
Table 3 | Hepatitis C virus infection and stroke risk

Cohorts	HR	95% CI	P value*
HCV	1.21	1.05–1.40	0.011
Non-HCV	1		
HCV‡	1.23	1.06–1.43	0.006
Non-HCV	1		

HCV ↑ Stroke (23%)

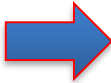
“The IBT-treated group had an increased *stroke-free survival rate* as examined by the Log-rank test during a 1–5-year observation period”.

IBT=Interferon Based Therapy



Interferon-based therapy reduces risk of stroke in chronic hepatitis C patients: a population-based cohort study in Taiwan. Aliment Pharmacol Ther. 2013

HCV-HIV coinfection

Population	Comment
Persons who inject drugs (PWID) (19)	PWID have the highest risk of infection. Globally, the prevalence of anti-HCV antibody is 67% among PWID.
Recipients of infected blood products or invasive procedures in health-care facilities with inadequate infection control practices (20–30)	Risk of HCV infection varies depending upon the frequency of medical procedures (i.e. number of injections/person/year) and level of infection control practices. A high frequency of injections and a low level of infection control can result in a high prevalence of HCV in the general population (e.g. prevalence of chronic HCV infection confirmed by nucleic acid testing was 4.0% in Egypt in 2015) (31).
Children born to mothers infected with HCV (30, 32–35)	HCV transmission risk is estimated as 4–8% among mothers without HIV infection. Transmission risk is estimated as 10.8–25% among mothers with HIV infection.
People with sexual partners who are HCV infected (36–40)	There is low or no risk of sexual transmission of HCV among HIV-uninfected heterosexual couples and HIV-uninfected men who have sex with men (MSM). The risk of sexual transmission is strongly linked to pre-existing HIV infection.
 People with HIV infection (40–48)	Persons with HIV infection, in particular MSM, are at increased risk of HCV infection through unprotected sex.
People who use intranasal drugs (49)	Non-injecting drug use (e.g. through sharing of inhalation equipment for cocaine) is associated with a higher risk of HCV infection.
People who have had tattoos or piercings (50)	Tattoo recipients have higher prevalence of HCV compared with persons without tattoos (odds ratio = 2.24, 95%CI 2.01, 2.50)

HCV-HIV coinfection

(global systematic review and meta-analysis)

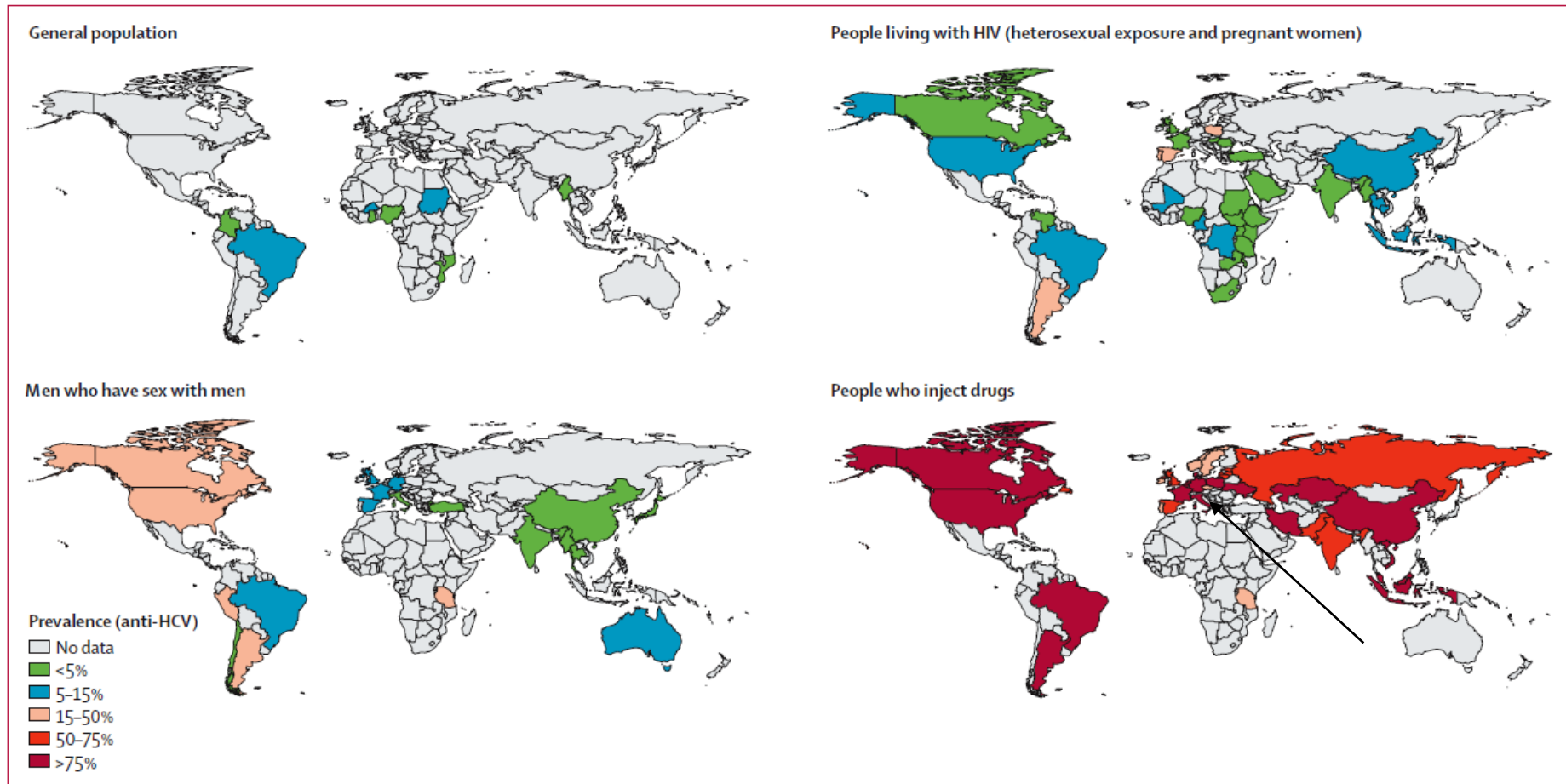


Figure 2: Best estimates of prevalence of hepatitis C virus (HCV) co-infection in four population samples

Consistently higher HCV prevalence in HIV-infected individuals than HIV-negative individuals across all risk groups and regions, but especially in PWID.

HCV-HIV coinfection

(global systematic review and meta-analysis)

La positività HCV aumenta di 5,8 volte negli HIV+ vs HIV- con grande eterogeneità

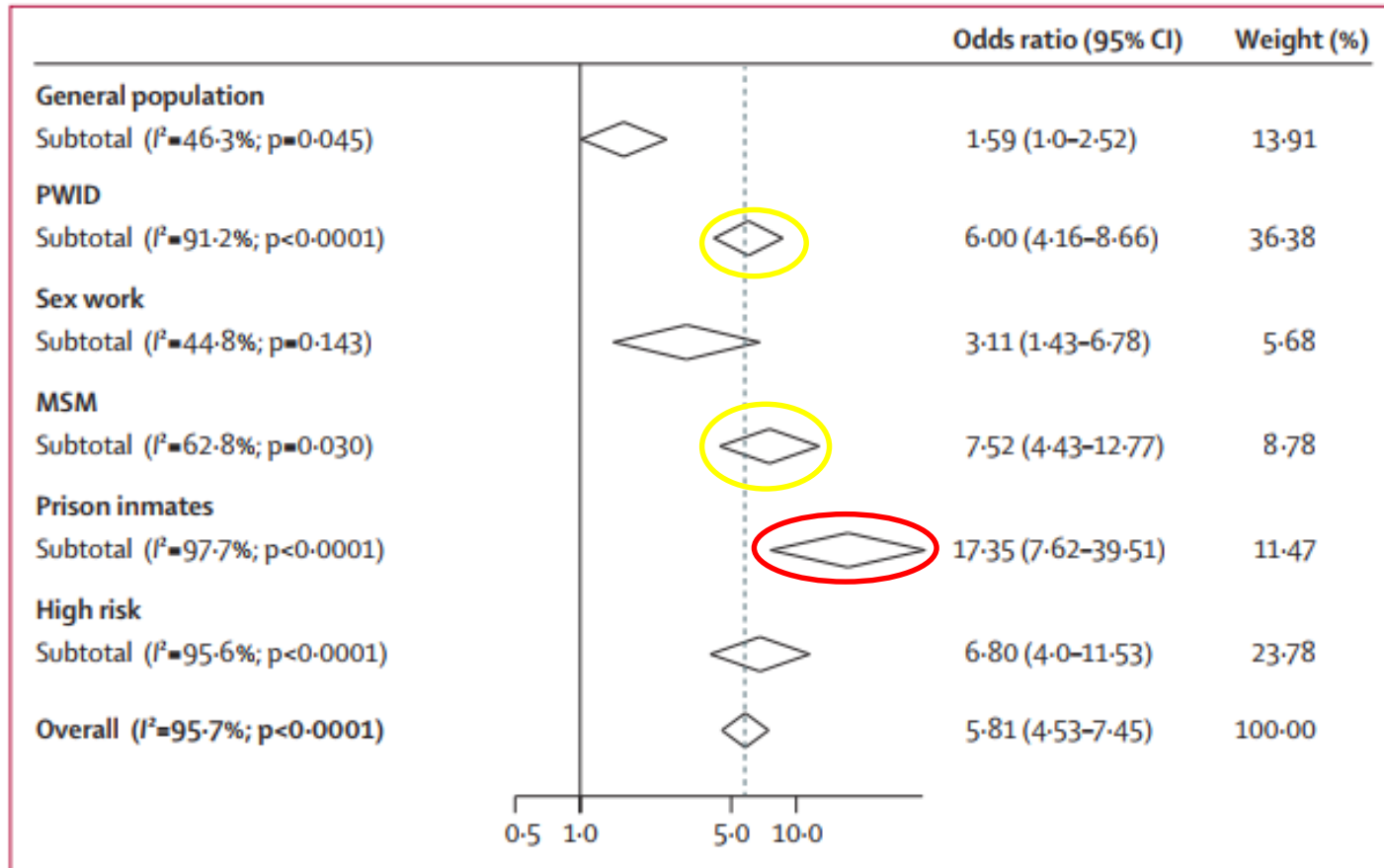



Figure 4: Forest plot showing meta-analysis of odds of HCV antibody in selected HIV-positive populations versus HIV-negative population groups

This study highlights the importance of routine HCV testing in all HIV-infected individuals, but especially in PWID. There is also **a need to improve country level surveillance of HCV prevalence across different population groups in all regions.**

Fattori che contribuiscono alla progressione della fibrosi in pz con epatite C cronica

Established factors ¹	More recently identified risk factors
Duration of HCV infection	Patient age at time of diagnosis
Older age at infection	Genotype 3 infection
Male gender	Insulin resistance
Presence of baseline fibrosis	Gene polymorphisms involved in inflammation and iron metabolism
 HIV coinfection ¹ /CD4 count < 200 cells/mL	Human leukocyte antigen DRB1*1201-3 allele
Long term alcohol consumption (> 20-50 g/d)	Latin ethnicity
HBV coinfection	Daily cannabis use
Metabolic syndrome (steatosis, insulin resistance, type 2 diabetes)	

HCV-HIV coinfection

Clin Infect Dis. 2002 Mar 15;34(6):831-7. Epub 2002 Feb 6.

Hepatitis C Virus prevalence among patients infected with Human Immunodeficiency Virus: a cross-sectional analysis of the US adult AIDS Clinical Trials Group.

Sherman KE¹, Rouster SD, Chung RT, Rajjic N.

⊕ Author information

Abstract

Hepatitis C virus (HCV) has emerged as an important etiologic agent of liver injury and failure in patients infected with human immunodeficiency virus (HIV). The prevalence and characteristics of HCV in a representative cohort of HIV-infected patients have not been described. Therefore, a representative sample of 1687 HIV-infected patients was studied; a 213-sample subcohort was selected by use of risk-based sampling from 2 large prospective US Adult AIDS Clinical Trials Group clinical trials. HCV prevalence,

HCV RNA level, and genotype were determined. The weighted overall estimate of HCV prevalence in the study cohort was 16.1% (95% weighted confidence interval, 14.3%-17.8%), with significant variability depending on risk factors and HIV RNA levels. Among patients defined as being "at risk", 72.7% were HCV positive, whereas, among low-risk patients, the positivity rate was 3.5%.

Genotype 1 was found in 83.3% of infected patients. Median HCV RNA level was 6.08×10^6 IU/mL. High virus loads and genotype 1 prevalence may be important to interferon-based antiviral response rates among coinfecting patients.

Building up a collaborative network for the surveillance of HIV genetic diversity in Italy. A pilot study

(Centro Nazionale AIDS, Istituto Superiore di Sanità, Rome, Italy)



Four hundred and thirty four HIV-infected migrants were enrolled in 9 Italian clinical centers located throughout the Italian territory. Standard Operating Procedures (SOPs) for sample collection were provided by the National AIDS

Center to each clinical center.

In addition, clinical centers were required to fill up a case report form (crf) for each patient, which included demographic, clinical, immunological and virological information.

Italian Network for HIV Characterization

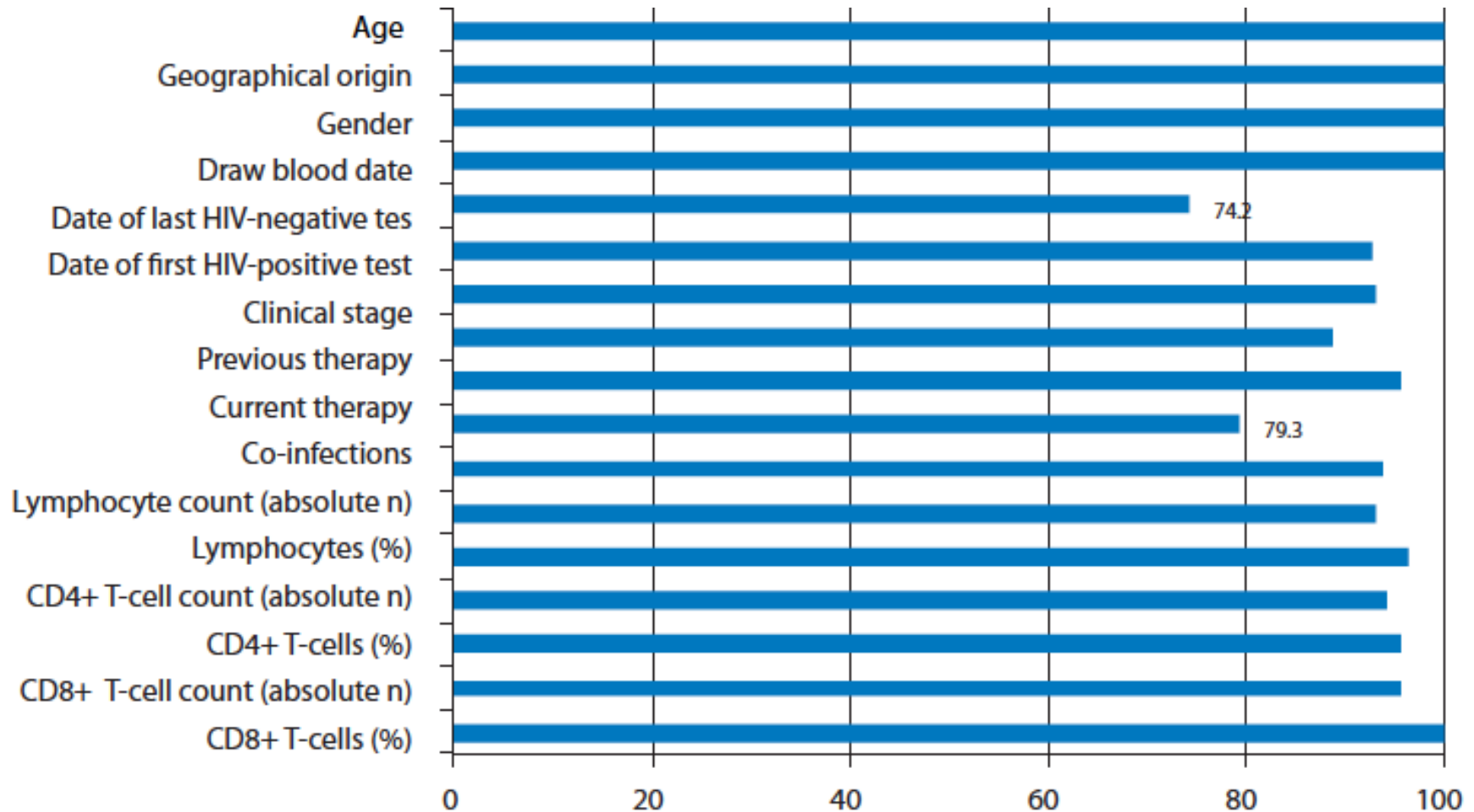
Percent of reported information in the case report form

	Field	All centers (434 pts)	North (263 pts)	Centre (125 pts)	South (46 pts)
General/demographic	Age	100	100	100	100
	Geographical origin	100	100	100	100
	Gender	100	100	100	100
	Draw blood date	100	100	100	100
	Date of last HIV-negative test	<u>74.2</u>	97.7	<u>34.4</u>	<u>47.8</u>
	Date of first HIV-positive test	92.6	100	<u>74.4</u>	100
Clinical	Clinical stage	93.3	100	85.6	<u>76.1</u>
	Previous therapy	88.7	100	<u>70.4</u>	<u>73.9</u>
	Current therapy	95.8	99.2	96.0	<u>76.1</u>
	Co-infections	<u>79.3</u>	100	<u>39.2</u>	<u>44.0</u>
Immunological	Lymphocyte count (absolute n)	93.8	99.2	96.8	<u>54.3</u>
	Lymphocytes (%)	93.3	100	93.6	<u>54.3</u>
	CD4+ T-cell counts (absolute n)	96.5	100	96.8	<u>76.1</u>
	CD4+ T-cells (%)	94.2	100	96.8	<u>54.3</u>
	CD8+ T-cell counts (absolute n)	95.8	99.2	96.7	<u>71.7</u>
	CD8+ T-cells (%)	95.8	99.6	96.6	<u>71.7</u>
Virological	Viral load	100	100	100	100

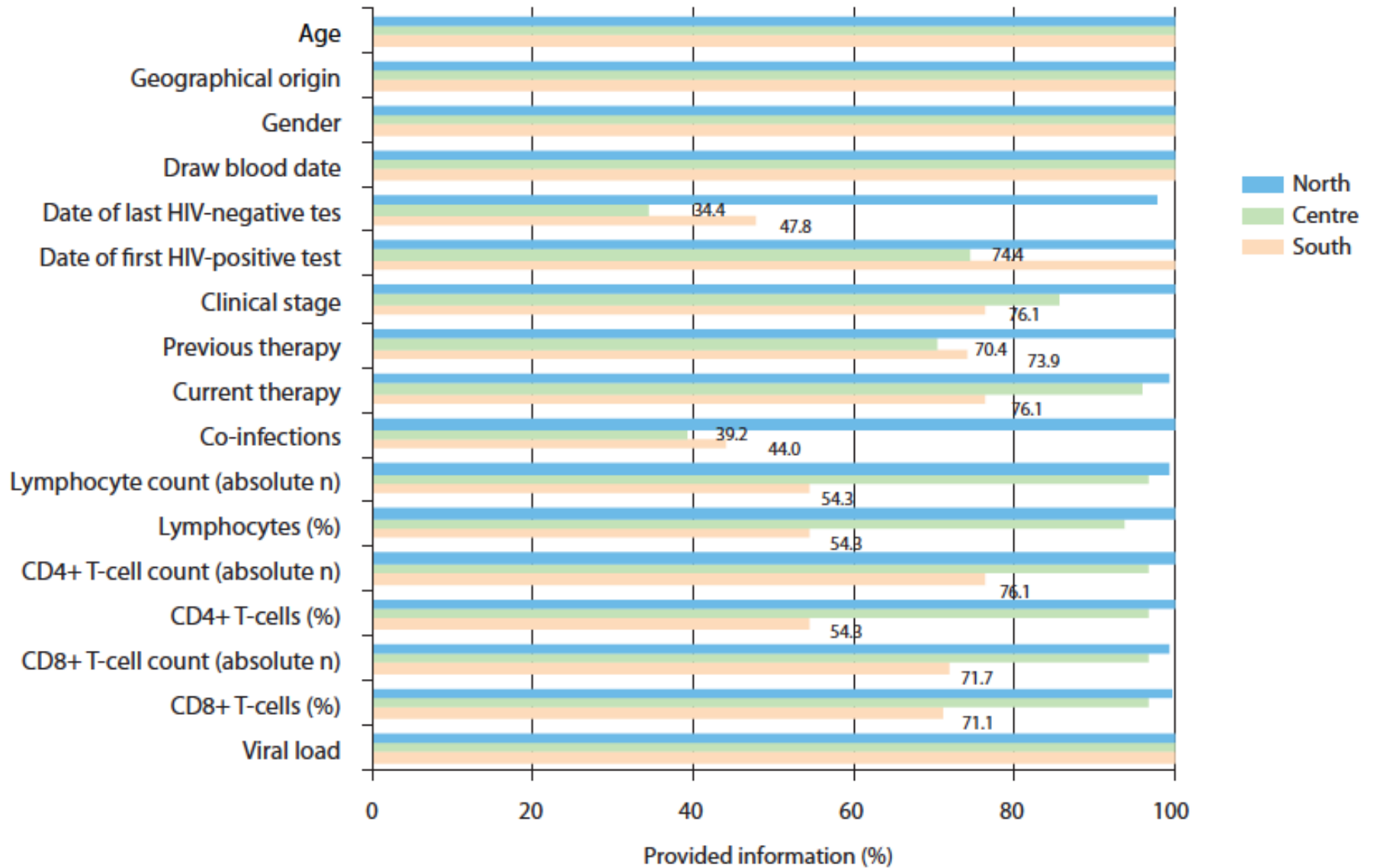
Percent of reported information for each field is indicated. Variables filled in with a frequency < 80% are underlined.

Sanarico N1, D'Amato S1, Picconi O1, Ensoli B1, Buttò S1; Italian Network for HIV Characterization.

Informazioni rese efficientemente dai diversi centri (nord-centro-sud)

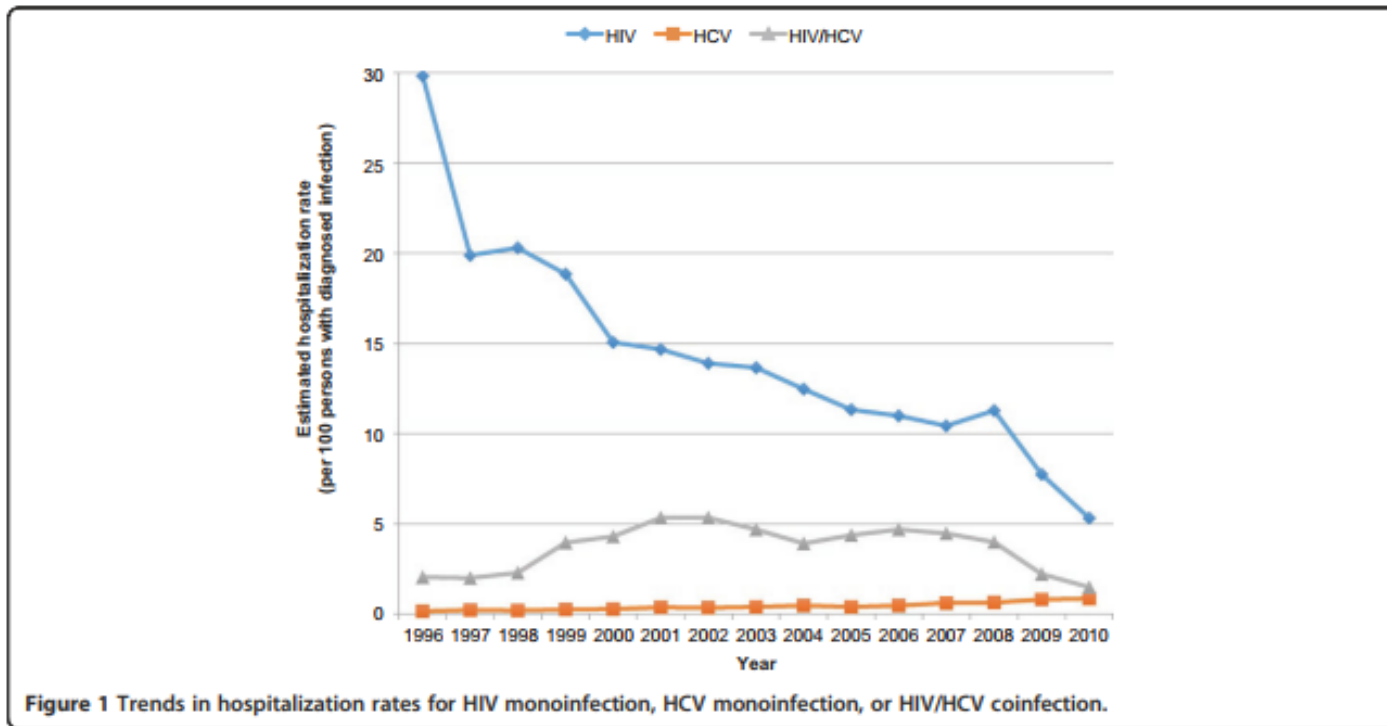


Efficienza variabile nelle informazioni rese dai diversi centri (nord-centro-sud)



Ospedalizzazioni correlate a HCV, HIV e HCV-HIV

National trends in hospitalization and mortality rates for patients with HIV, HCV, or HIV/HCV coinfection from 1996-2010 in the United States: a cross-sectional study



“Hospitalizations have declined more rapidly for HIV infection (including HIV/HCV coinfection) than for HCV infection. This growing disparity between HIV and HCV underscores the need to allocate more resources to HCV care in hopes that similar large-scale improvements can also be accomplished for patients with HCV”.

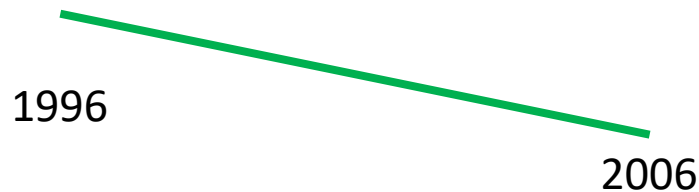
In Italy?



Hepatitis C Virus Infection Trends in Italy

Daniel Lavanchy*

In previous issue of Hepatitis Monthly, La Torre G *et al.* from Sapienza University and the Catholic University of the Sacred Heart located in Rome, Italy, have published their findings on the incidence of hepatitis C virus (HCV) infections in Italy (1). In the Italian general population, they estimate that the overall trend, and also the trends in gender and different age groups, has decreased significantly over the period from 1996 to 2006, with an



(8-10) and in US population groups (11). Estimation of the incidence of HCV infection remains difficult; reporting systems can underestimate the incidence of HCV infection despite well-established surveillance systems, such as that in Italy. Regular population-based surveys should be conducted to confirm these findings.

The notable decrease in the incidence rate seen in the last 2 decades in Italy is mainly attributed to the improvement in the safety of blood supplies and blood products, use of safe injection practices, and implementation of universal precautions in medical settings. Intravenous drug use, other parenteral exposure i.e. ear piercing, tattooing), surgery, hospitalization, and dental treatment remain common risk factors among patients with HCV infection, particularly in resource-limited settings. Therefore, there is still no room for complacency. The public health agenda warrants maintaining surveillance, prevention, and control of HCV infection. The joint-point regression method used in this study may help to assess the impact of public health policies to meet the chal-

Attempt to calculate the prevalence and features of chronic hepatitis C infection in Tuscany using administrative data.

Silvestri C¹, Bartolacci S¹, Pepe P¹, Monnini M¹, Voller F¹, Cipriani F¹, Stasi C¹.

⊕ Author information

Abstract

AIM: To evaluate this prevalence in Tuscan populations that was known and unknown to the Tuscan Regional Health Service in 2015.

METHODS: Tuscan Health administrative data were used to evaluate hepatitis C virus (HCV) infected people known to the Regional Health Service. Residents in Tuscany with a HCV exemption code (070.54) were identified. Using the universal code attributed to each resident, these patients were matched with hospital admission codes identified by the International Classification of Diseases, Ninth Revision (ICD-9), Clinical Modification, and with codes for dispensing drugs to patients by local and hospital pharmacies. Individuals were considered only once. Capture-recapture analysis was used to evaluate the HCV-infected population unknown to the Regional Health Service.

RESULTS: In total, 14526 individuals were living on 31/12/2015 with an exemption code for HCV. In total, 9524 patients were treated with pegylated interferon + ribavirin and/or direct-acting antiviral drugs during the last 10 years, and 13879 total hospital admissions were noted in the last 15 years. After data linkage, the total number was 25918. After applying the Capture-Recapture analysis, the number of unknown HCV-infected people was 23497. Therefore, the total number of chronic HCV-infected people was 38643, excluding those achieved sustained virological response to previous treatment.

CONCLUSION: Our results show a prevalence of HCV infected people of 1%. Tuscan administrative data could be useful for calculating health care costs and health planning in the coming years.

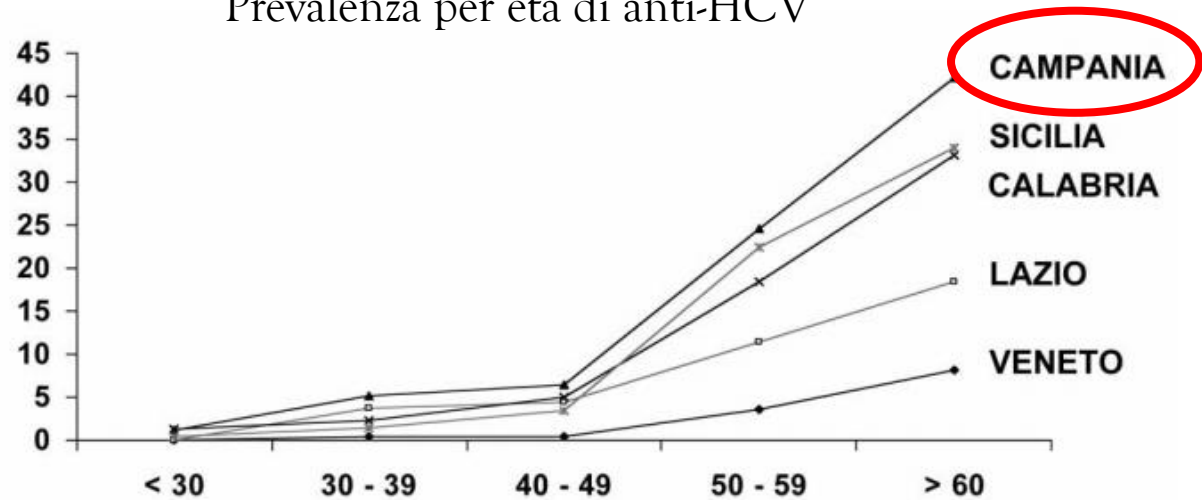
“In conclusion, Tuscan administrative data reveal a prevalence of chronic HCV infection of approximately 1%. Given the high number of chronic HCV-infected patients and the high costs of these drugs, the new regimens will probably remain inaccessible to many patients throughout the world. **Therefore, these data could be useful for calculating health care costs and health planning in the coming years”.**

HCV in Regione Campania

Campania, il «primato» degli ammalati di epatite C



Prevalenza per età di anti-HCV



Si stima che in Campania i soggetti portatori di infezione da HCV siano più di

100mila

PROGETTO IN CORSO IN REGIONE CAMPANIA

“Valutazione dell’impatto epidemiologico ed economico della popolazione con infezioni virali in Regione Campania”