HCV infection in prison. From individual care to viral eradication strategy: a benefit for the community

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Hosted by Jim Gauthier
Senior Clinical Advisor, Diversey

www.webbertraining.com **November 15, 2019**

Key points of the talk

- HCV in community and prisons
- What about Italian and Milano prisons?
- What is the state of art of HCV treatment in prisons?
- Real life experience of our group
- What about reinfection?

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HCV in community and prisons

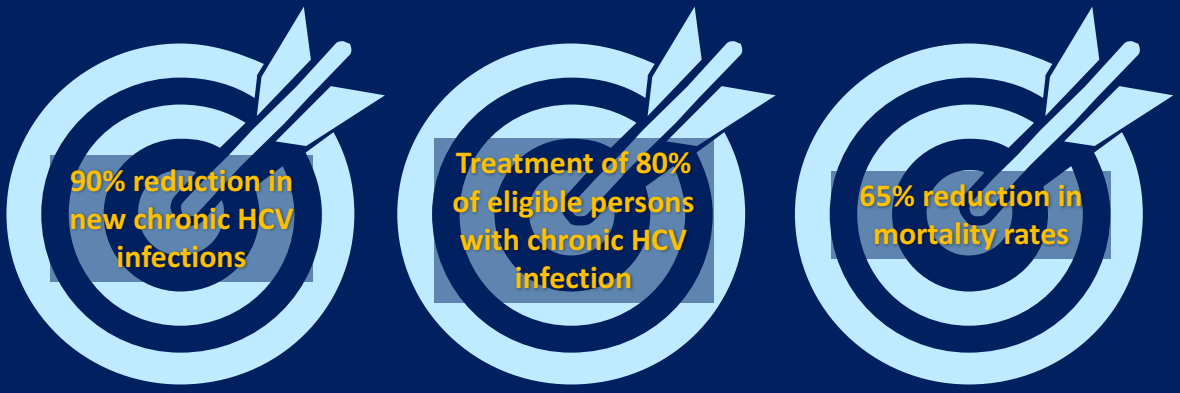
3

WHO Vision: Eliminate Viral Hepatitis as a Major Health Threat by 2030

World Health Organization

"A world where viral hepatitis transmission is halted and everyone living with hepatitis has access to safe, affordable and effective care and treatment services"

at:



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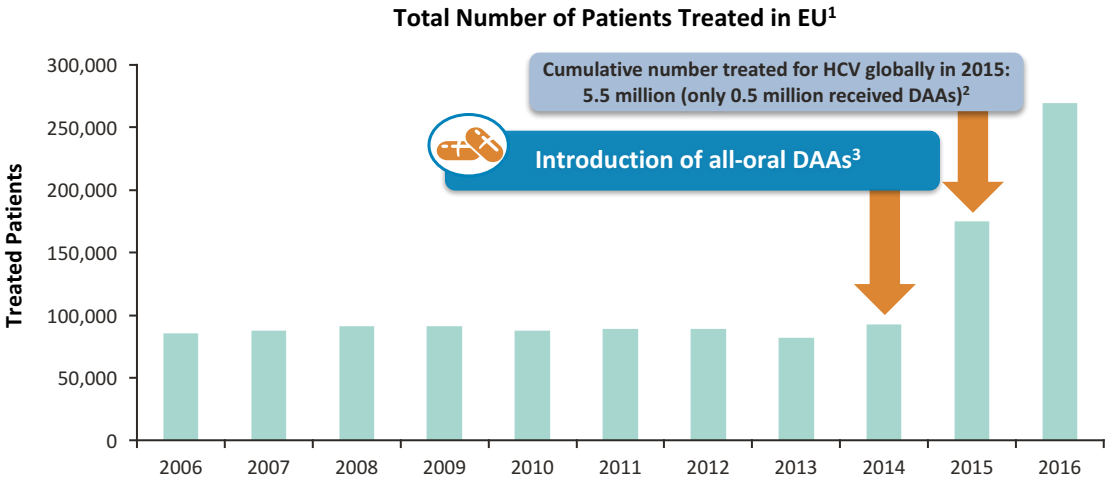
The Changing Paradigm of HCV Treatment Has Led to a Significant Increase in the Number of Patients Being Treated



1. Adapted from the Polaris Observatory. Available at: http://cdafound.org/polaris-hepC-graphs/;
2. WHO Global Hepatitis Report, 2017. Available at: http://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/;
3. CDC Hepatitis C: 25 years since discovery. Available at: https://www.cdc.gov/knowmorehepatitis/media/pdfs/hepc-timeline.pdf.

5

All Patients Are Now Prioritized for Treatment

WHO[1] Last updated April 2016	AASLD[2] Last updated September 2017	EASL[3] Last updated April 2018
Treatment is indicated for:		
All adults and children with chronic HCV infection, including PWID	All patients with chronic HCV infection, except those with short life expectancies that cannot be remediated	All patients with HCV infection must be considered for therapy, including TN patients and individuals that failed to achieve SVR after prior treatment

PWID, people who inject drugs; TN, treatment naïve

1. WHO guidelines for the screening, care and treatment of persons with chronic HCV infection. Available at: http://apps.who.int/iris/bitstream/10665/205035/1/9789241549615_eng.pdf?ua=1;
2. AASLD recommendations for testing, managing and treating hepatitis C. Available at: http://www.hcvguidelines.org/full-report-view

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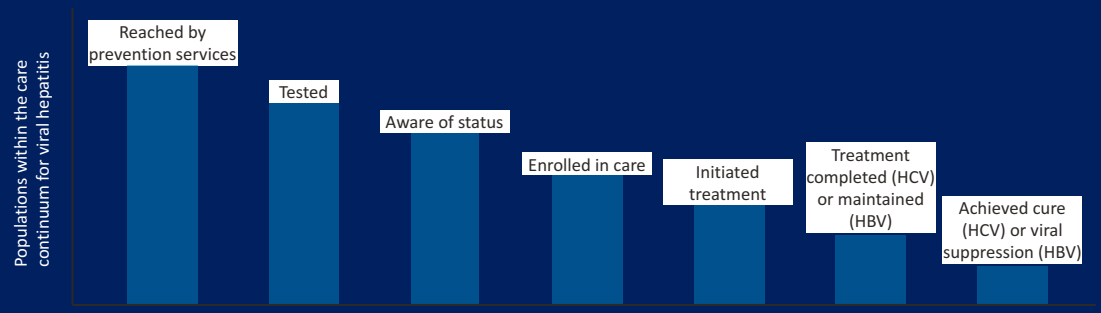
Overview of the WHO Care Continuum for Viral Hepatitis and the Associated Challenges Encountered When Aiming toward WHO Elimination Targets



Care continuum for viral hepatitis	Prevention	Screening and Linkage to Care	Treatments
Current challenges within the care continuum for viral hepatitis with reference to achieving WHO elimination targets	1. Provision of HBV birth-dose vaccination within 24 hours of birth to prevent mother-to-child transmission 2. Expansion of hemovigilance schemes and safe injection practices to reduce iatrogenic transmission	3. Adoption of point-of-care testing to expand diagnostic coverage and strengthen linkage to care 4. Integration of screening into existing care delivery models for at-risk populations to increase their access to and engagement with viral hepatitis care	5. Maintenance of treatment for all cirrhotic HBV-infected patients indefinitely to minimize risk of disease progression 6. Procurement of affordable DAAs to enable universal access to treatment for HCV

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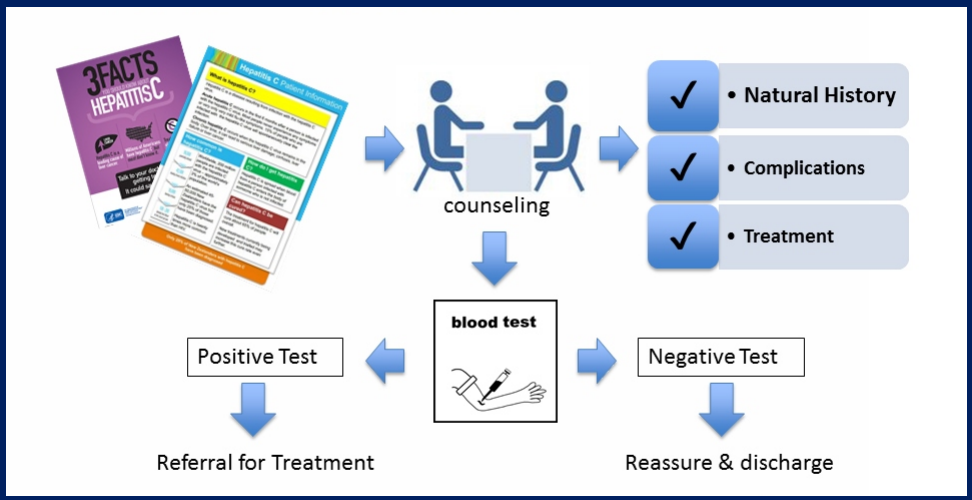
Hofferman A., et al. Open Forum Infect Dis 2015; 2:ofv043

Screening Must Be Linked to Care



CDC. Testing for HCV infection: An update of guidance for clinicians and laboratorians. MMWR 2013; **62**. Available at: https://www.cdc.gov/hepatitis/hcv/pdfs/hcv_flow.pdf

8

High-Risk Populations Face Unique Challenges with Linkage to Care…

- Stigma and discrimination[1–3]
- Substance abuse[1,2]
- Lack of specialists/ coverage of services[1,2]

- Lack of HCV awareness in patients and HCPs[1–3]
- Lack of additional support, i.e. harm-reduction services[2]
- Socioeconomic factors[1,2]

MSM, men who have sex with men; PWID, people who inject drugs

1. Yap L, *et al. PLoS One* 2014; **9:**e87564; 2. Grebely J, *et al. J Int AIDS Soc* 2017; **20:**22146; 3. Sacks-Davis R, *et al. J Int AIDS Soc* 2018; **21**(Suppl 2):e25051

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Benefits of Targeting HCV in Prisons

Prison System
- Decreased risk of HCV transmission within the prison
- Improved health of inmates
- Deceased 'risk' to custodial staff

Incarcerated Individual
- Cured of HCV
- Decreased risk of liver failure and liver cancer

BENEFITS OF HCV TREATMENT

Community
- Decreased risk of HCV transmission by prisoners following release
- Long-term cost savings

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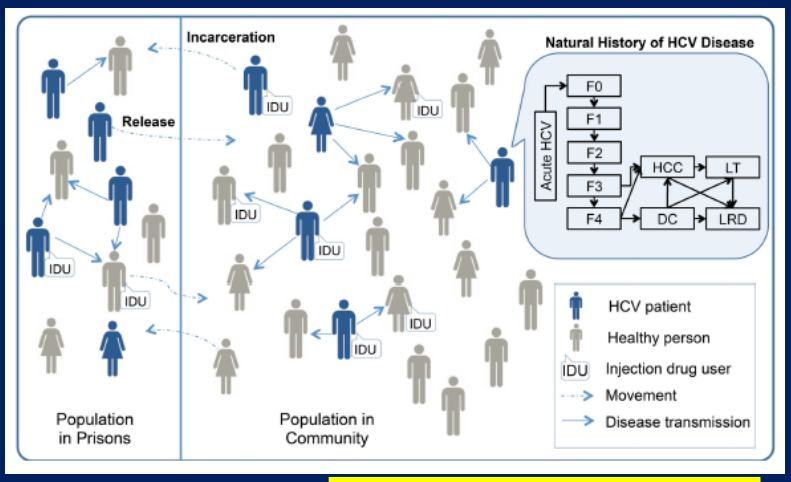
Benefits of Treatment in Prison



- Risk-based and opt-out screening and treatment
- Prevent new infections – 90% in the community!
- Highly cost-effective
- But would require increase in healthcare budget

- Potential to decrease HCV in prison
- And in the community!!

F0, no fibrosis; F1, portal fibrosis without septa; F2, portal fibrosis with few septa; F3, numerous septa without cirrhosis; F4, compensated cirrhosis; DC, decompensated cirrhosis; HCC, hepatocellular carcinoma; LT, liver transplants; LRD, liver-related deaths.

He T, *et al. Ann Intern Med* 2016; **164**:84–92

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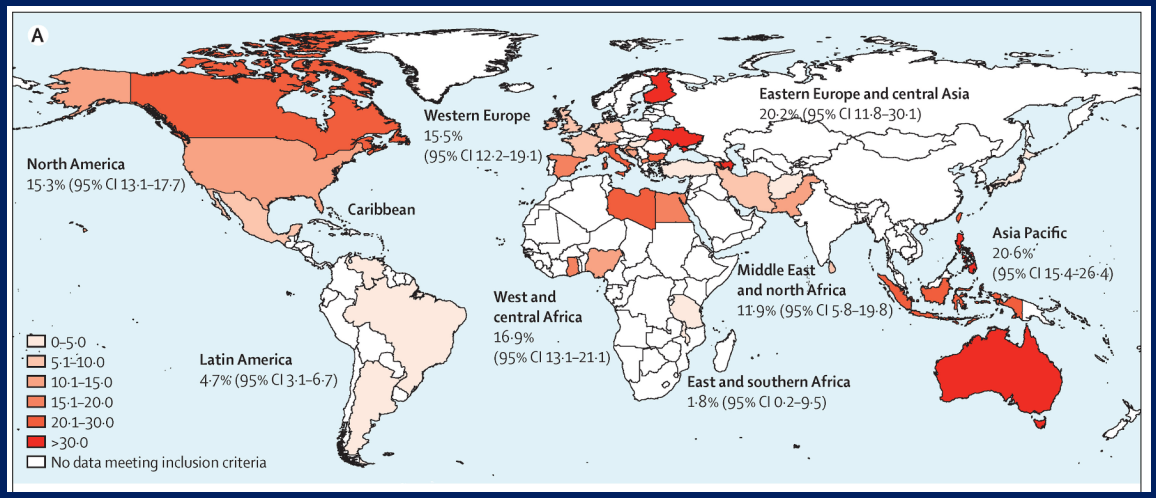
Global and Regional Prevalence of Hepatitis C in Prison Inmates Published Between 2005 and 2015

Percentage unware of HCV infection :25% to 35%



Dolan K, *et al*. Lancet 2016; **388**:1089–1102

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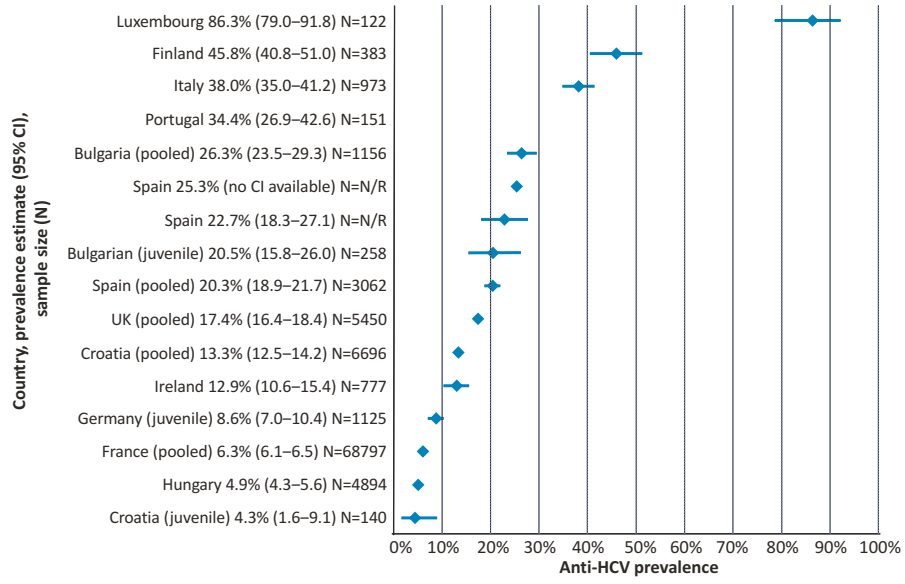
Anti-HCV Prevalence among People in Prison across the EU/EEA



All but 4 estimates (Germany, France, Hungary, Croatia) were above 10% prevalence

EU/EEA, European Union/European Economic Area.

Falla AM, *et al. BMC Infect Dis* 2018; **18**:79.

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14

Bielen *et al. Harm Reduction Journal* (2018) 15:25
https://doi.org/10.1186/s12954-018-0230-1

Harm Reduction Journal

RESEARCH Open Access

Harm reduction and viral hepatitis C in European prisons: a cross-sectional survey of 25 countries

Rob Bielen[1,2], Samya R. Stumo[3], Rachel Halford[4], Klára Werling[5], Tatjana Reic[6], Heino Stöver[7], Geert Robaeys[1,2,8†] and Jeffrey V. Lazarus[3,9*†]

Background: Current estimates suggest that 15% of all prisoners worldwide are chronically infected with the hepatitis C virus (HCV), and this number is even higher in regions with high rates of injecting drug use. Although harm reduction services such as opioid substitution therapy (OST) and needle and syringe programs (NSPs) are effective in preventing the further spread of HCV and HIV, the extent to which these are available in prisons varies significantly across countries.

Conclusion: Despite the existence of evidence-based recommendations, infectious disease prevention measures such as harm reduction programs are inadequate in European prison settings. Harm reduction, HCV testing/screening, and treatment should be scaled up in prison settings in order to progress towards eliminating HCV as a public health threat.

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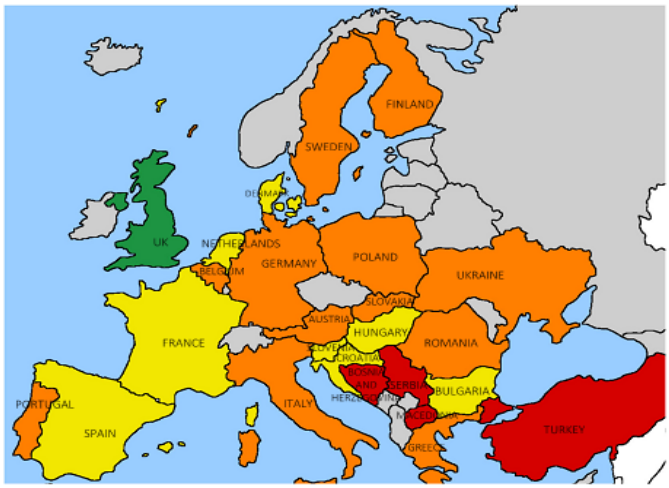

Fig. 1 Availability and coverage of HCV testing/screening in European prisons. *Green*: universal screening in prison upon entry, opt-out procedure; *yellow*: testing/screening for HCV available in prison, extent unknown, but highlighted as an at-risk population for HCV; *orange*: testing/screening available in prison, extent unknown, not highlighted as an at-risk population for HCV; *red*: no data available from the literature, prisoners not highlighted as an at-risk population for HCV; *gray*: not part of the Hep-CORE dataset

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What about Italian and Milano prisons?

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Italian Penitenciary System september 2018

[www.giustizia.it]

- N. of correctional houses → 190
- Total capacity → 50.544 p/l
- Total presents → 58.087 p/l
- Overcrowding → +15%
- Foreigners → 19.818 = 34%
- Women → 2.441 = 4,2%
- PWUD → 19.752 = 34,1%
- Pris. in Lombardia → 8.527 = 14.3%

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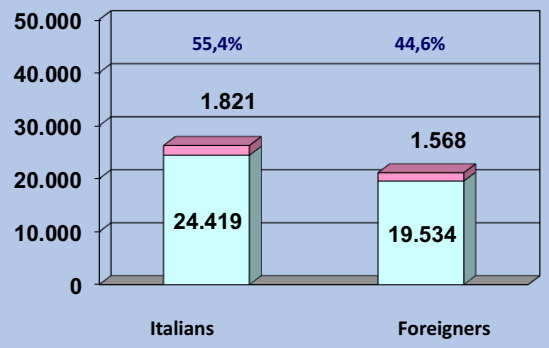
New comers in 2017 (47.342) High turnover and short stay

[www.giustizia.it]



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In 2008 penitenciary health management was transferred from Ministry of Justice to Ministry of Health.

Every region adopted its own way: most have choosen territorial management through Local Health Authorities.

Lombardia has attributed health care activities to local hospitals.

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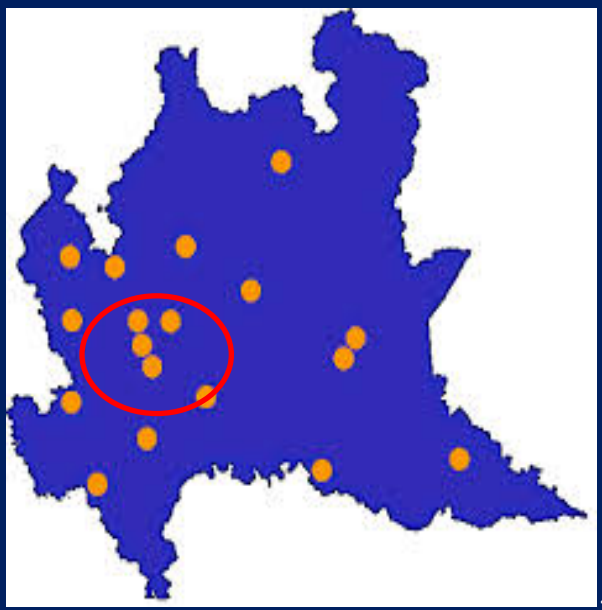
Distribution of the 19 correctional houses in Lombardia

RegioneLombardia



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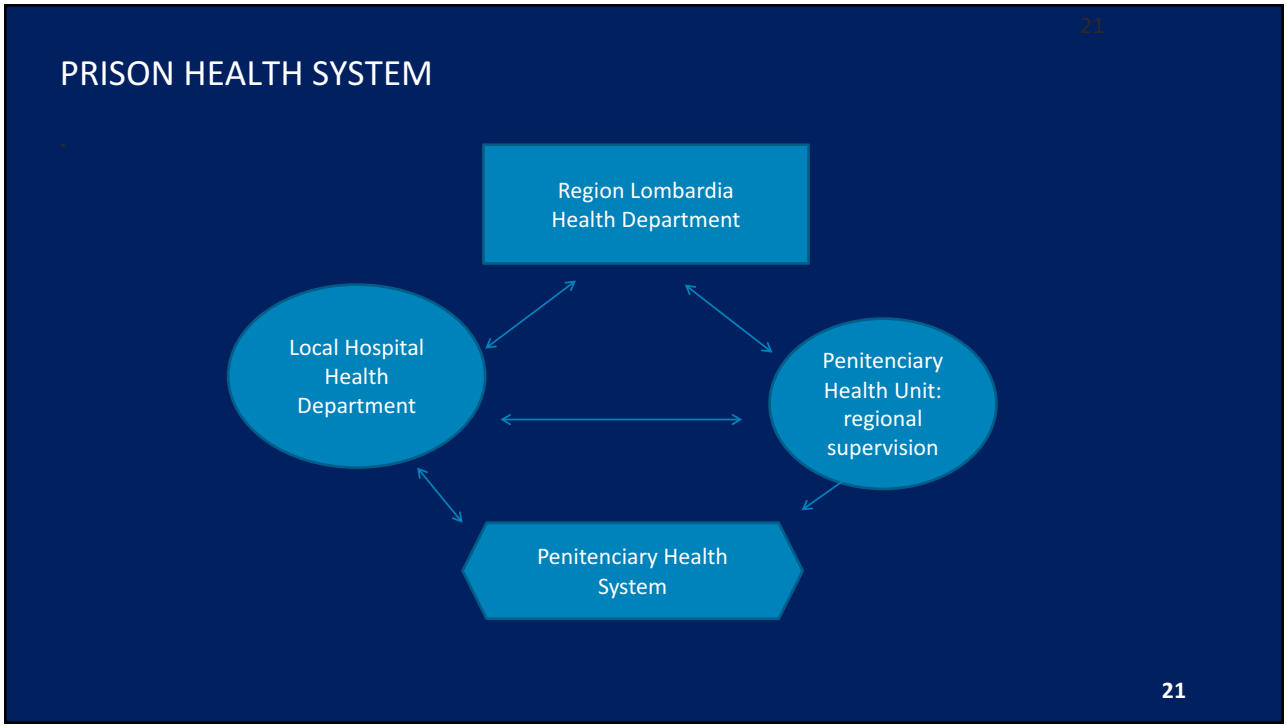
PRISON HEALTH SYSTEM
Region Lombardia Health Department
Local Hospital Health Department
Penitenciary Health Unit: regional supervision
Penitenciary Health System
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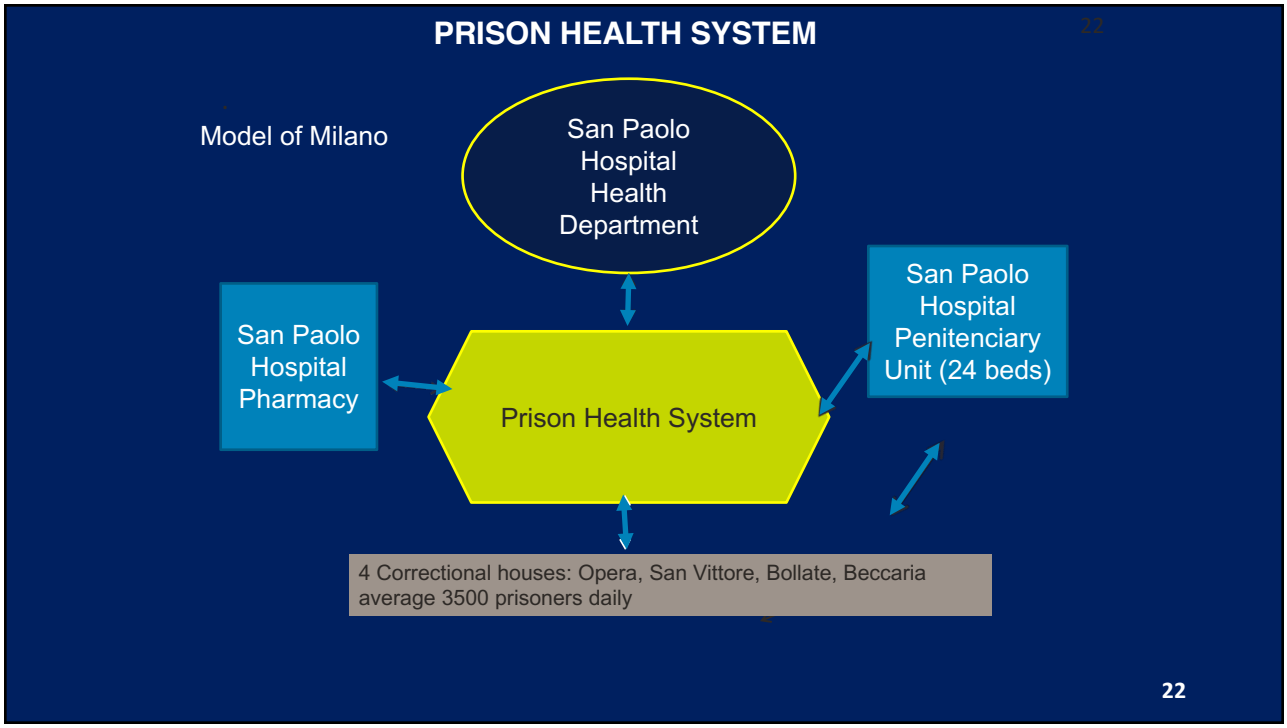
PRISON HEALTH SYSTEM
Model of Milano
San Paolo Hospital Health Department
San Paolo Hospital Pharmacy
Prison Health System
San Paolo Hospital Penitenciary Unit (24 beds)
4 Correctional houses: Opera, San Vittore, Bollate, Beccaria
average 3500 prisoners daily
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Casa Circondariale Milano San Vittore (VIT) is the remand Prison for the metropolitan area of Milan. It has a capacity of 1100 beds, hosts male and female population mostly of foreign origin and is the first place of incarceration, including people awaiting trial. It is characterized by high turnover (monthly average of entrants: 270) with frequent releases to community or transfers to other prisons, mainly to Milano Opera prison (OPE). Inmates usually have sentences less than 2 years; there is a dedicated new comers service where all arrested people are evaluated for infectious diseases including TB and blood borne infections. The facility has a blood sample collection room, radiological services and a fully equipped pharmacy. Psychiatric, Drug addiction and Infectious Disease services are integrated and provided on site. Nursing care is guaranteed 24h/7d.

There is a attenuate surveillance section dedicated to mothers and children

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Casa di Reclusione Milano Opera (OPE) is a detention house hosting high security and long sentenced male prisoners mostly Italians; it has a capacity of 1300 beds and a monthly average of entrants of 30; the majority of prisoners are coming from other Italian prisons. It is equipped with a medical center for most severe patients cases requiring continuous assistance. Laboratory and radiological facilities are functioning on site. All transferred prisoners are re-evaluated for TB and blood borne infections and receive a dedicated individual counseling and group sessions for infectious diseases with a specific focus on HCV treatment options. Psychiatric, Drug addiction and Infection Disease services are integrated and provided on site. Nursing care is guaranteed 24h/7d.

All services and specialists are provided by San Paolo University Hospital under the coordination of the Public Health Unit. Pharmacy, Infectious Diseases consultants (ID) and laboratory services are linked one another and the same staff operates in both structures.

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CR Bollate, is similar to Opera, has a capacity of 1100 beds, hosts both males and females, generally at the end of their sentences and on the way of social rehabilitation (programs for jobs, study, ecc)

Istituto Beccaria is a juvenile prison for male adolescents and young adults (until 26 years), has a capacity of 50 beds.

Cesare Lari

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Based on the characteristic of each facility there are different levels of health assistance:
Milano Opera, San Vittore, Bollate provide a multispecialistic integrated assistance:

General physicians 24 h/daily
Nurses 24 h/daily
Radiology (daily): chest, skeleton , abdomen, ultrasound (visceral and vascular)
Laboratory for analysis (daily)
New comers service (24 h/daily)
First aid service (24 h/daily)
Digestive Endoscopy service
Drug addiction Service
Pharmacy (depending on Central Pharmacy)
Multispecialistic service: psychiatrics, psycologists, infectious diseases consultants, otolaryngologists, ophthalmologists, pneumologists, orthopaedics, endocrinologists, dentists, surgeons, dermatologists, pediatricians, gynecologists, neurologist, cardiologists, physioterapists

Outside services: es. CT, NMR, hospital admissions are provided by San Paolo Hospital

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Opera and San Vittore host a Clinical Center for admissions of patients affected by serious diseases (i.e. decompensated diabetes, cardiomiopathy, COPD, AIDS, cirrhosis).

Overall 120 beds with 24 h/daily assistance
4 beds for infectious isolation (i.e. TB)
Opera is considered an italian hub for complex pathologies and particularly for infectious diseases monitoring and treatment.

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What is the state of art of the HCV treatment in prisons?

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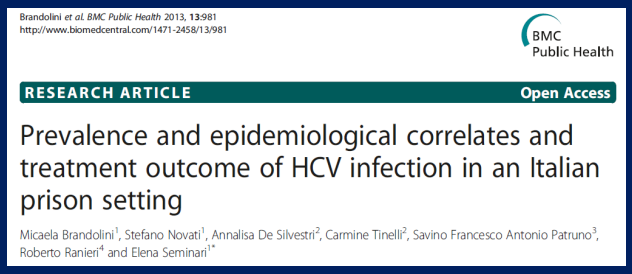
HCV Treatment in Prisons in the Interferon era

Study site	N	Male, %	Mean age	Treatment	Completed Rx, %	Overall SVR, %
Rhode Island	90	96	38	IFN/RBV	46	29
Virginia	59	83	41	IFN/RBV	NR	36
Canada	114	100	38	IFN/RBV	NR	52
Italy	39	98	36	PegIFN/RBV	26	13
Connecticut	68	85	41	PegIFN/RBV	69	47
Rhode Island	71	100	41	PegIFN/RBV	46	28

Chew KW, et al. J Clin Gastrenterol. 2009;43:686-691.

What's our experience


Brandolini *et al. BMC Public Health* 2013, **13**:981
http://www.biomedcentral.com/1471-2458/13/981

BMC Public Health

RESEARCH ARTICLE Open Access

Prevalence and epidemiological correlates and treatment outcome of HCV infection in an Italian prison setting

Micaela Brandolini[1], Stefano Novati[1], Annalisa De Silvestri[2], Carmine Tinelli[2], Savino Francesco Antonio Patruno[3], Roberto Ranieri[4] and Elena Seminari[1*]

RESULTS:

- 2012 HCV + prevalence: 22%
- HCV-RNA positivity: 86%
- Eligible for treatment: 26%
- Overall SVR 48: 43%
- Main causes for ineligibility or treatment discontinuation: judiciary concerns

1. Brandolini M, *et al*. BMC Public Health 2013; **13**:981

Hepatitis C Management in Prisons in the era of DAAs

Hepatology / Volume 64, Issue 5

Correspondence

Hepatitis C management in prisons: An insight into daily clinical practice in three major Italian correctional houses

Antonella Foschi M.D., Maddalena Casana M.D., Anna Radice M.D., Roberto Ranieri M.D., Antonella d'Arminio Monforte M.D., Ph.D.

DAA regimens are a safe, short duration treatment strategy in prisons. We need to dedicate further efforts to strengthen the continuity of care and improve HCV management in prisons for both individual and public health.

Foschi A, *et al. Hepatology* 2016; **64**(5)

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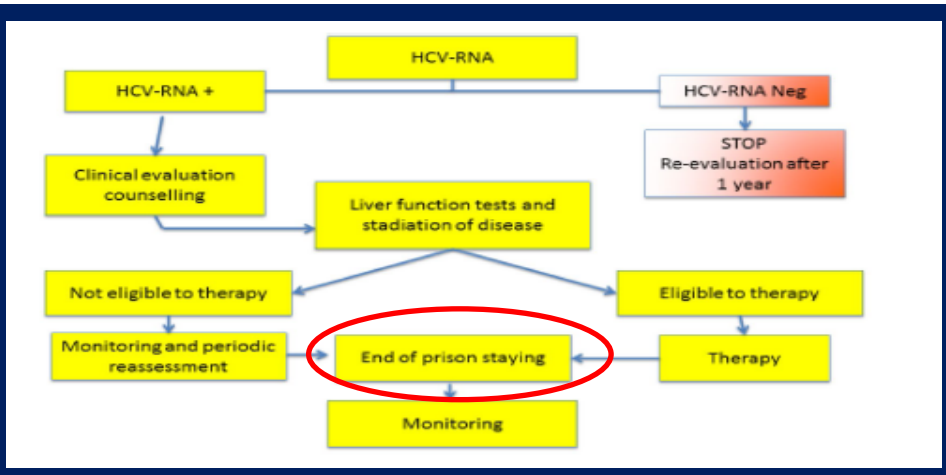
Infection
DOI 10.1007/s15010-016-0973-0

REVIEW

Management of HCV infection in the penitentiary setting in the direct-acting antivirals era: practical recommendations from an expert panel

Ranieri Roberto[1,2] · Starnini Giulio[2,3] · Carbonara Sergio[2,4] · Pontali Emanuele[2,5] · Leo Guido[2,6] · Romano Antonio[7] · Panese Sandro[8] · Monarca Roberto[2,9] · Prestileo Tullio[10] · Barbarini Giorgio[11,12] · Babudieri Sergio[2,13] · on behalf of the SIMSPe Group



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Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Short Report

Treatment with direct-acting antivirals in a multicenter cohort of HCV-infected inmates in Italy

Emanuele Pontali[a], Vito Fiore[b], Anna Maria Ialungo[c], Roberto Ranieri[d], Oscar Mollaretti[e], Giorgio Barbarini[f], Daniele Marri[g], Tullio Prestileo[h], Serena Dell'Isola[c], Elena Rastrelli[c], Guido Leo[e], Giulio Starnini[c], Sergio Babudieri[b,*], Giordano Madeddu[b], Gruppo Infettivologi Penitenziari

[a] Infectious Disease Unit, Galliera Hospital, Genoa, Italy
[b] Unit of Infectious Diseases, Department of Clinical and Experimental Medicine, University of Sassari, Sassari, Italy
[c] Medicina Protetta-Unit of Infectious Diseases, Belcolle Hospital, Viterbo, Italy
[d] Penitentiary Infectious Diseases Unit, A.O. Santi Paolo e Carlo, University of Milan, Milan, Italy
[e] Infectious Disease Unit, Ospedale Amedeo di Savoia, Turin, Italy
[f] 2nd Division of Infectious Diseases, Policlinico San Matteo Hospital, Pavia, Italy
[g] Infectious Diseases Unit, A.O. Santa Maria alle Scotte, Siena, Italy
[h] ARNAS, Ospedale Civico-Benfratelli Palermo, Palermo, Italy

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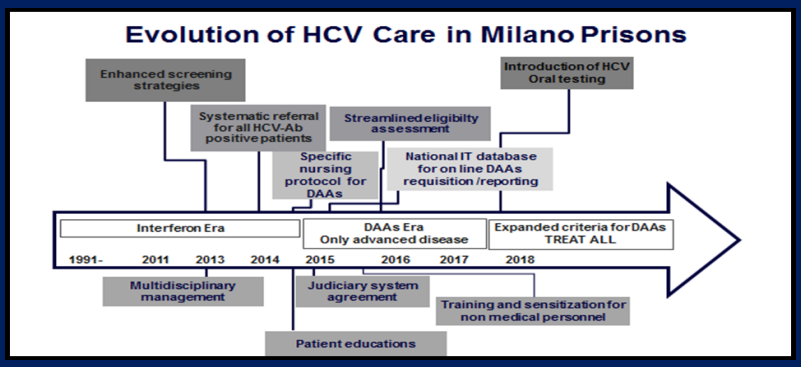

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Clinical Infectious Diseases

BRIEF REPORT

Demonstration of Near-Elimination of Hepatitis C Virus Among a Prison Population: The Lotus Glen Correctional Centre Hepatitis C Treatment Project

Sofia R. Bartlett,[1] Penny Fox,[2] Harris Cabatingan,[3] Anissa Jaros,[3] Carla Gorton,[4] Rhondda Lewis,[4] Eugene Priscott,[4] Gregory J. Dore,[1,a] and Darren B. Russell[4,5,6,a]

[1]Kirby Institute, UNSW Sydney, [2]Department of Medicine, Cairns Hospital, [3]Lotus Glen Correctional Centre, Mareeba, [4]Cairns Sexual Health Service and [5]James Cook University, Cairns, and [6]Melbourne University, Australia.

Micro-elimination of hepatitis C virus (HCV) infection through rapid uptake of government-funded direct-acting antiviral therapy within an Australian prison setting is demonstrated. During a 22-month period, 119 patients initiated treatment for chronic HCV infection, with HCV in-prison viremic prevalence declining from 12% to 1%.

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Clinical Practice Guidelines

JOURNAL OF HEPATOLOGY

EASL Recommendations on Treatment of Hepatitis C 2018☆

European Association for the Study of the Liver*

- Treatment with new pangenotypic regimens can be initiated without knowledge of the genotype and subtype in areas where genotype determination is not available and/or not affordable, or to simplify treatment access (**B1**).

- Treatment should be considered without delay in incarcerated individuals) (**A1**).

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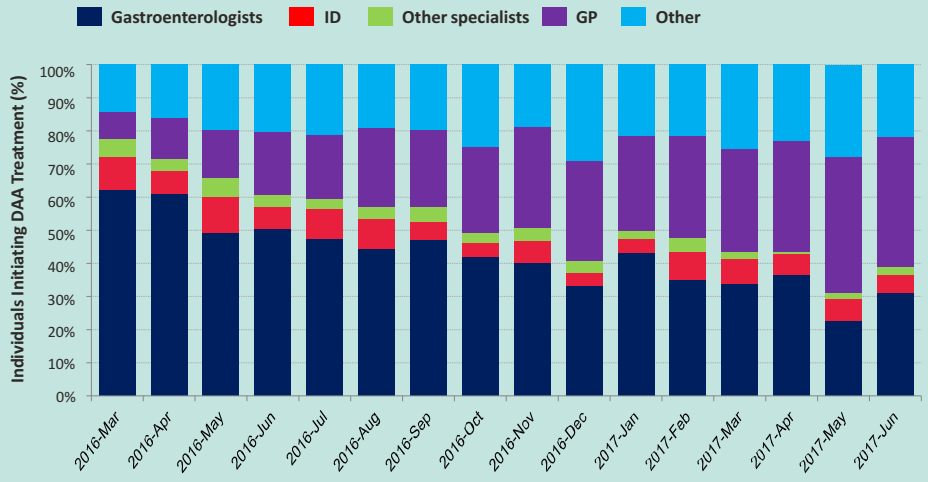
- In patients with socioeconomic disadvantages and in migrants, social support services should be a component of HCV clinical management (**B1**).
- Peer-based support and patient activation assessment are recommended to improve HCV clinical management (**B2**).
- Patients with harmful alcohol consumption during treatment should receive additional support during antiviral therapy (**B1**).

Recommendations

- HCV treatment should be delivered within a multidisciplinary team setting, with experience in HCV assessment and therapy (**A1**).
- HCV-infected patients should be counselled on the importance of adherence for attaining an SVR (**A1**).

Increasing Involvement of Non-specialists

MERCK & CO., INC.
Kenilworth, N.J., U.S.A.



GP, general practitioners; ID, infectious diseases physicians.

1. Hajarizadeh B, *et al. J Viral Hepat* 2018; **25**;
2. Dore GJ & Hajarizadeh B. *Infect Dis Clin North Am* 2018; **32**:269–279.

39

- Drug-drug interactions are a key consideration in treating HIV-HCV coinfected patients, and close attention must be paid to anti-HIV drugs that are contraindicated, not recommended or require dose adjustment with particular DAA regimens (**A1**).

Table 4D. Drug-drug interactions between HCV DAAs and central nervous system drug

		SOF	SOF/ LDV	SOF/ VEL	OBV/ PTV/r + DSV	GZR/ EBR	SOF/ VEL/ VOX	GLE/ PIB
Anti-depressants	Amitriptyline	◆	◆	◆	■	◆	◆	◆
	Citalopram	◆	◆	◆	◆	◆	◆	◆
	Duloxetine	◆	◆	◆	◆	◆	◆	◆
	Escitalopram	◆	◆	◆	◆	◆	◆	◆
	Fluoxetine	◆	◆	◆	◆	◆	◆	◆
	Paroxetime	◆	◆	◆	◆	◆	◆	◆
	Sertraline	◆	◆	◆	■	◆	◆	◆
	Trazodone	◆	◆	◆	■	◆	◆	◆
	Venlafaxine	◆	◆	◆	■	◆	◆	◆
Anti-psychotics	Amisulpiride	◆	◆	◆	◆	◆	◆	◆
	Aripiprazole	◆	◆	◆	■	■	◆	■
	Chlorpromazine	◆	◆	◆	■	◆	◆	◆
	Clozapine	◆	◆	◆	■	◆	◆	■
	Flupentixol	◆	◆	◆	■	◆	◆	◆
	Haloperidol	◆	◆	◆	■	◆	◆	◆
	Olanzapine	◆	◆	◆	■	◆	◆	◆
	Paliperidone	◆	■	◆	◆	◆	■	■
	Quetiapine	◆	◆	◆	●	■	◆	■
	Risperidone	◆	◆	◆	■	◆	◆	◆
	Zuclopentixol	◆	◆	◆	■	◆	◆	◆

Table 4E. Drug-drug interactions between HCV DAAs and cardiovascular drugs.

		SOF	SOF/ LDV	SOF/ VEL	OBV/ PTV/r + DSV	GZR/ EBR	SOF/ VEL/ VOX	GLE/ PIB
Anti-arrhythmics	Amiodarone	●	●	●	●	■	●	■
	Digoxin	◆	■	■	■	◆	■	■
	Vernakalant	◆	◆	◆	■	◆	◆	◆
	Flecainide	◆	◆	◆	■	◆	◆	◆
Beta-blockers	Atenolol	◆	◆	◆	◆	◆	◆	◆
	Bisoprolol	◆	◆	◆	■	◆	◆	◆
	Carvedilol	◆	■	■	■	◆	■	■
	Propranolol	◆	◆	◆	◆	◆	◆	◆
Calcium chanal blockers	Amlodipine	◆	■	■	■	◆	◆	◆
	Diltiazem	◆	■	■	■	◆	■	■
	Nifedipine	◆	◆	◆	■	◆	◆	◆
Hypertension and heart failure agents	Aliskiren	◆	■	■	●	◆	●	●
	Losartan	◆	◆	◆	◆	◆	◆	◆
	Doxazosin	◆	◆	◆	■	◆	◆	◆
	Enalapril	◆	◆	◆	■	◆	■	■

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The real life experience of our group

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HCV-free prisons : Real life experience towards micro-elimination in Milano penitentiary services.

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We present our experience of almost eradicating HCV infections in Milano prisons and coming close to the 2030 WHO targets of diagnosis and treatment.

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Intervention to scale up HCV care in prison

In 2014 San Paolo University Hospital decided to strengthen the Hepatology services offered in the prisons with the objective to reach and maintain high coverage of HCV screening among newly admitted prisoners and to allow fast HCV treatment with DAA in HCV infected inmates. The program included i) strategies to achieve universal HCV screening, ii) broadened treatment eligibility criteria, iii) provision of continuous treatment across and outside prison and iv) information and education for inmates and health care staff.

HCV Screening. In VIT all newly admitted inmates were offered opt out HCV screening along with other STI tests. HCV antibody testing was performed on venous blood with a turn-around time of 48 hours. From March 2017 onwards, prisoners opting-out screening at admission were counseled by Infectious Disease (I.D.) specialists and offered rapid oral test. All positive oral tests were confirmed by HCV serology testing. In OPE availability of previous screening results were checked at the time of transfer from other prisons; if results were not accessible or older than 2 years old, counseling and testing was offered by health professionals within a month of transfer. Regular HCV testing catch-up campaigns were conducted to increase coverage targeting patients who had previously refused the test.

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Eligibility

During the pre-DAAS era (until 2013) less than one third of inmates were eligible for treatment with depression being on the main reason for ineligibility. For this reason, integration of infectious diseases and psychiatric services with joint clinical consultation and strengthened psychiatric support was offered to patients in need. In 2014, when the first generation DAAs (telapravir) became available, nurses underwent intensive training on administration of directly observed therapy, early identification and management of side effects together with motivational counseling. Initially DAAs were only available for individuals with advanced disease (liver fibrosis staged F3 F4 with metavir score). The national health care system changed the eligibility criteria in April 2017. All HCV viremic individuals regardless of the stage of disease and co-morbidities became eligible for DAAs resulting in a massive increase of eligible individuals. To cope with the new demand eligibility assessment was streamlined . All inmates with HCV antibodies underwent HCV RNA and HCV genotype testing as well as ultrasounds and elastometry to study severity of the liver disease. Regular multidisciplinary case discussions were implemented to optimize treatment for HCV infected inmates with co-morbidities taking into account potential drug interactions and switching concomitant treatment towards safer regimens. Staff from the justice system was invited to attend these meetings to discuss judicial aspects that could hamper the treatment, like duration of sentence, possibility of transfer to other prisons or allocation in correctional regimes alternative to detention)

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Information and education

OPE introduced specific informative session for newly admitted prisoners on risk of transmission of HCV and prevention, HCV diagnosis and treatment options, as well as more general information about infectious diseases and risk of transmission during detention, perception of risk and consequences on mental health Training and sensitization sessions were also offered to the detention officers and non-medical staff at risk for infection at work.
Provision of continuous treatment. In 2014 a national IT database was introduced to monitor and guide prescription of DAAs.The database strengthened the link between correctional facilities, hospitals and prison pharmacy guarantying prompt supply and delivery of medications. The judiciary system agreed to postpone when possible transfer of HCV infected inmates to correctional facilities where treatment was not available once treatment was completed. A list of inmates on HCV treatment was thus regularly shared between medical and administrative staff within prisons. In case of unexpected release, proper written referral to specific ID clinic in town was ensured and individuals were counselled about the following steps to be taken by the patient. Collaboration with the local centers for treatment of substance and ID clinics in town was strengthened.

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A cross-sectional survey based on chart reviews was performed among all inmates on the in October-November 2017. Information was collected regarding HCV screening, prevalence of HCV antibody positivity, HCV RNA prevalence, HCV treatment history and outcome. The following variables were recorded: demographic data (sex, country of origin, pre-incarceration drug use, duration of detention), HCV testing offered, HCV virological testing (HCV RNA and Genotype), HBV or HIV co-morbidities, eligibility data. For inmates who initiated HCV treatment pre-treatment fibrosis, previous treatment history, type of regimen (DAAs vs IFN based regimens), location (prison vs community) and date of treatment initiation were recorded. For HCV-infected inmates who did not start treatment reasons for ineligibility were reported. Data was extracted and entered into an access database.
The survey was performed on request of Ministry of Health at local level. Ministry of Justice approved the study and granted a waiver on informed consent. Data were collected in accordance with the national ethical standards. No specific consent was required since data were collected in anonymous and aggregate form.

Statistical analysis
All analysis was performed using Stata version 14 (Stata-Corp, TX, USA). Proportions were calculated for categorical variables and median and interquartile ranges for continuous variable. Associations between not undergoing HCV testing and HCV antibody positivity and explanatory variable such as age, gender, pre-incarceration drug use, country of origin and duration of detention were investigated using univariate and multivariate logistic regression.

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Characteristics of Inmates tested and not for HCV Antibodies

	Total	HCV -Ab tested	HCV - Ab Not tested	Univariate Odds Ratio (95% CI)	Multivariate Odds ratio (95% CI)
		N (%)	N (%)		
PRISON (OPE)	1335	1234 (92.4%)	101 (7.6%)	1	1
JAIL (VIT)	1031	861 (83.5%)	170 (16.5%)	2.41 (1.86-3.13)	2.05 (1.53-2.74)
Men	2261	1996 (88.3%)	265 (11.7%)	1	1
Women	105	99 (94.3%)	6 (5.7%)	0.46 (0.20-1.05)	0.27 (0.12-0.63)
Non Italian	1017	856 (84.2%)	161 (15.8%)	1	1
Italian	1349	1239 (91.9%)	110 (8.2%)	0.47 (0.36-0.61)	0.73 (0.54-0.99)
<35 years	772	640 (82,9%)	132 (17,1%)	1	1
>35 years	1594	1455 (91,3%)	139 (8,7%)	0.46 (0.36-0.60)	0.62 (0.46-0.83)
No Drug Users	1266	1098 (86.7%)	168 (13.3%)	1	1
Drug Users	1100	997 (90.6%)	103 (9.4%)	0.68 (0.52-0.88)	0.62 (0.47-0.80)

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Association between HCV-Ab positivity and risk factors

	Total	HCV antibody negative	HCV antibody positive	Univariate Odds Ratio (95% CI)	Multivariate Odds Ratio (95% CI)
		N (%)	N (%)		
PRISON (OPE)	1234	1104 (89.5%)	130 (10.5%)	1	
JAIL (VIT)	861	779 (90.5%)	82 (9.5%)	0.89 (0.67-1.20)	
Men	1996	1794 (89.9%)	202 (10.1%)	1	
Women	99	89 (89.9%)	10 (10.1%)	1.00 (0.51-1.95)	
Non Italian	856	820 (95.8%)	36 (4.2%)	1	1
Italian	1239	1063 (85.8%)	176 (14.2%)	3.77 (2.61-5.46)	2.19 (1.46-3.28)
Age group					
<35 years	640	628 (98.1%)	3 (1.9%)	1	1
>35 years	1455	1255 (86.3%)	200 (13.8%)	8.34 (4.62-15.05)	7.40 (4.03-13.59)
No Drug users	1098	1047 (95.4%)	51 (4.6%)	1	1
Drug users	997	836 (83.9%)	161 (16.2%)	3.95 (2.85-5.49)	4.92 (3.52-6.89)
HIV-Ab negative	1941	1781 (91.8%)	160 (8.2%)	1	
HIV-Ab positive	66	22 (33.3%)	44 (66.7%)	22.26 (13.02-38.08)	
HIV not done	88	80 (90.9%)	8 (9.0%)	1.11 (0.53-2.34)	

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Characteristics of patients with HCV RNA available

	N (%)	N	
HCV RNA NEGATIVE pts	151		
Treated with DAAs	77 (51%)	15	Treatment on going
		22	Reached EOTR
		40	Reached SVR12
Previously treated with IFN	36 (24%)		
No treatment history	38 (29%)		
HCV RNA POSITIVE pts	41 (21%)		
Eligibility on going	8 (20%)		
Eligible for DAAs	21(51%)	14	DAAs Treatment initiated
		7	DAAs Treatment requested
Relapse to DAAs	1 (2%)		
No treatment (relevant co-morbidities, refusals)	11 (27%)		

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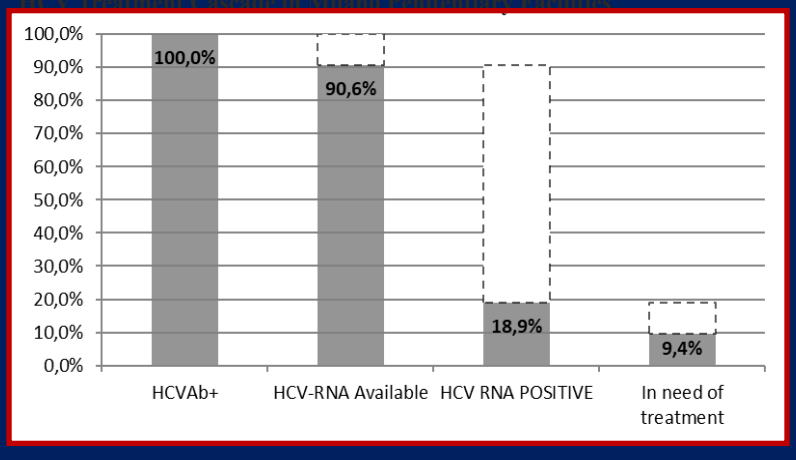
Milano prisons HCV cascade of care



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Discussion

This survey was conducted to evaluate the impact of a bundle of interventions aimed at enhancing and expanding HCV care in prison considering it a strategic venue for treatment of affected individuals otherwise neglected with overall benefits for the general community. As shown by Martin N.K. et al. elimination of HCV in PWID could be very effective to reduce HCV in the general community.

High HCV testing coverage (88%) was achieved by using a combined approach of offering opt-out HCV testing, either blood or oral tests , repeat individual counseling for those who did not want to test and education and information to increase awareness both among inmates as well as staff. Opt-out testing HCV testing in prison has been proven to be a cost-effective strategy to reduce transmission in the community, nevertheless special care must be taken when running universal program within a community of individuals whose liberty has been restricted often with stressing effects on mental condition that might lead to refusal to test at first entrance. In our experience additional strategies were needed to ensure also “difficult” and marginalized patients would adhere to the screening offer and overcome distrust towards medical personnel, e.g. young offenders with behavioral disorders, long course drug users with concomitant psychiatric problems and homeless. A tailored approach around the patients who opt out need to be developed to ensure to reach high coverage and included one to one counseling, repeat contact with the same person along the detention period and counselling from different providers, as well as less invasive methods. In our experience oral tests were found to be more acceptable among illegal immigrants of African origin and young offenders and led to identification of new cases.

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The prevalence of HCV infection in our cohort was 10,1%, slightly lower than previously reported in a similar cohort in Italy and Spain [18,19], that might be explained by improved access to rehabilitation program in the community for offenders with substance abuse problems that are sentenced for minor crimes. Over 90% of HCV positive inmates underwent further evaluation to determine their eligibility, with very few that missed this opportunity due to judicial issues, like unexpected transfer or quick release. Such high proportion of onward referral and linkage to HCV care was possible because all HCV positive inmates were referred to ID specialist by the general practitioners or straight by the laboratory in case of new infections. This in turn enabled post-test counseling, rapid eligibility assessment, prompt start of treatment and completion within a short period of time.

Among the patients with undetectable viral load the majority was as such as a result of a previous treatment received while in prison. DAAs, that were used in our experience in 75% of the cases, are indeed particularly suitable to the prison setting due to easy administration, lack of side effects and short duration of treatment that overcome the possibility of interrupt treatment due to unexpected transfers and release Besides, several trials had shown similar efficacy among active drug users receiving DAAs who were on substitution therapy and who had admit concomitant substance abuse .Up to date in our experience, till now *over 200* only one patient had relapsed, that was started on treatment while in the community before entering the prison. Results were similar in short and long-stay facilities because of the prompt treatment of all eligible individuals as soon as identified.

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Comparing our experience to a recently published HCV test and treat trial conducted in a Spanish prison (18) that were able to reach 0 prevalence of viremic infection, the main practical challenges were the continuous new admission from the community of new HCV positive inmates often unaware of their condition and the refusal to treat especially in case of asymptomatic infections or due to their mental condition or psychological/emotional situation.
In relation to our experience the main limitation in term of exportability to other Italian prisons and other countries is the availability of specialists within the prison, as well as ultrasounds service, while pharmacy orders and laboratory results are easily available by web from inside the prison. Treatment as prevention program in the prison have been already found to be cost [23] effective: despite the extra cost for having specialist care inside the prison might not have been considered in such calculation, it is unlikely to change the overall benefit and such availability appears more linked to political endorsement of a HCV elimination program. Regarding the survey main limitations concern the method: data were extracted retrospectively from clinical files so that some variables, in particularly the counseling approach was not properly recorded and the concomitant psychiatric condition and diagnosis was not always clear, when present. Also variable such as substance abuse was self-reported and didn't always differentiate between endo-venous or oral abuse. Lastly, it was not possible to compare the intervention with a baselines assessment, in particular the prevalence of viremic infection before the treatment thus it is difficult to assess how much of the effect was due to the intervention bundle.

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Conclusions

Implementation in prison of test and treat program offer an unique possibility of detection and cure of HCV
in a special at risk population that is often suffering from reduced access to care once free in the community, with benefits that go beyond the individual and reach the overall community.
Our program based on systematic screening of all new inmates followed by fast track and prompt treatment of eligible cases is the result of an elimination strategy that has been tailored to respond to the specific characteristic and challenges of our setting and that has been built over the time with a multidisciplinary approach and strong coordination between health and non-health professionals, including patients and judiciary system .
Despite the positive impact of this strategy, still it remains a small group of persons difficult to engage in care due to important co-morbidities, especially psychiatric conditions or diseases, that require a dedicated individual strategy.

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Case Study – 1

- DM, 49 years old italian male
- IDU (heroin & cocaine). Followed by a Drug Addiction Service since 1987 and taking opioid substitution treatment (methadone)
- Alcohol abuser (daily alcohol intake 3lts)
- Heavy cigarette smoker (40 c. a day)
- Never submitted to blood borne diseases screening
- 1989: Admitted in hospital for pneumonia. Diagnosis of PCP AIDS (C3 Atlanta) : CD4 cell count nadir 1/mmc
- Referred to Infectious Disease Unit of San Paolo Hospital
- Started on dual and then triple drug regimen therapy according to guidelines. Throughout the years an optimal virological status was achieved (January 2018 CD4 1248/mmc, 24% HIV-RNA undetectable)
- 1991: Diagnosis of HCV genotype 1b infection
- 1992: Liver biopsy Chronic HCV Hepatitis Ishak score: 7
- Comorbidities: COPD, arterial hypertension, ischemic heart disease (MI due to cocaine abuse with PTCA), epilepsy treated with phenobarbital

DM, demographic; IDU, injection drug use; PCP, pneumocystis pneumonia; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty.

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Case Study – 2

- 2001: first detention in Milano prison due to a three year sentence
- ALT 96 IU, AST 88 IU, HCV-RNA 1,288,000 IU, PT INR 0.97, albumin 4.5 g/dl, total bilirubin 0.7 mg/dl CD4 count 720/mmc HIV RNA undetectable
- Liver biopsy: Ishak 7 (same as before)
- Liver ultrasound: fatty liver, neither signs of portal hypertension or hepatic nodules
- Treatment started in March 2003
- 2004 NEJM increased treatment efficacy in coinfected people is shown

ALT, alanine transferase; IU PT INR, international units prothrombin time international normalized ratio; RVR, rapid virologic response; EVR, early virologic response

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Case Study – 3

- July 2003 - unexpected release in freedom, without being referred in time to Service for Drug Addiction and Infectious Disease Unit
- Relapsed in drug and alcohol abuse
- August 2003 therapy was discontinued with HCV breakthrough
- In spite of drug abuse, the patient keeps the link with the Infectious Disease Unit and goes on taking antiretroviral therapy. HIV-RNA always suppressed. No further treatment for HCV is started.
- July 2017: new detention with a two-year sentence
- August 2017: ALT 91 UI, AST 68 UI, tot bilirubin 1.1 mgs/dl, PT INR 0.95, albumin 4.7 g/dl, HCV-RNA genotype 1b, HCV-RNA 1801568, CD4 1248/mmc, 24% HIV-RNA undetectable
- Current ART: Elvitegravir + cobicistat + TAF + emtricitabine
- Liver elastography (fibroscan): grade 2 fibrosis
- Liver ultrasonography: fatty liver, no signs of portal hypertension or hepatic nodules
- Patient eligible for treatment with DAAs

ALT, alanine aminotransferase; ; ART, antiretroviral therapy; PT INR, prothrombin time international normalized ratio; TAF, tenofovir alafenamide; DAA, direct acting antiviral

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Case Study – 4

What issues should be considered? What is your opinion?

Issues to be considered:

- Duration of treatment
- Duration of sentence
- Other judiciary concerns: transfer to other prison, unexpected release
- Drug–drug interactions (antiretroviral, cardiovascular, anti-epyleptic, psichiatric)
- Linkage to care after release

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Case Study – 5

What did we do? Short-duration HCV treatment

- An agreement with judiciary system was achieved to ensure treatment completion avoiding transfer before end of the schedule
- Treatment started in early December 2017 and ended in early February 2018
- Both EOTR and SVR 12 were reached
- At the end of treatment a document including diagnosis, drug regimen, outcome and indication for medical facility was given to the patient aiming to ensure linkage to care when released

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EASL recommendations

- Patients with no to moderate fibrosis (METAVIR score F0-F2), with SVR and no ongoing risk behaviour should be discharged, provided that they have no other comorbidities (**A1**).
- Patients with advanced fibrosis (F3) or cirrhosis (F4) with SVR should undergo surveillance for HCC every 6 months by means of ultrasound (**A1**).

- The risk of reinfection should be explained, to positively modify risk behaviour (**B1**).
- Following SVR, monitoring for HCV reinfection ideally through bi-annual, at least annual HCV RNA assessment should be undertaken in PWIDs or men who have sex with men with ongoing risk behaviour (**A1**).
- Retreatment should be made available, if reinfection is identified during post-SVR follow-up (**A1**).

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A Matched Comparison Study of Hepatitis C Treatment Outcomes in the Prison and Community Setting, and an Analysis of the Impact of Prison Release or Transfer During Therapy

J Viral Hepat. 2016 Dec;23(12):1009-1016. doi: 10.1111/jvh.12580. Epub 2016 Aug 11.

A matched comparison study of hepatitis C treatment outcomes in the prison and community setting, and an analysis of the impact of prison release or transfer during therapy.

Aspinall EJ[1,2], Mitchell W[3], Schofield J[4], Cairns A[5], Lamond S[5], Bramley P[3], Peters SE[6], Valerio H[1,2], Tomnay J[7], Goldberg DJ[1,2], Mills PR[6], Barclay ST[8], Fraser A[9], Dillon JF[10], Martin NK[11,12], Hickman M[12], Hutchinson SJ[1,2].

2009 and 2012 were eligible for inclusion. 291 prison initiates were matched with 1137 community initiates: SVRs were 61% (95% CI 55%-66%) and 63% (95% CI 60%-66%), respectively. Odds of achieving a SVR were not significantly associated with prisoner status (P=.33). SVRs were 74% (95% CI 65%-81%), 59% (95% CI 42%-75%) and 45% (95% CI 29%-62%) among those not released or transferred, transferred during treatment, or released during treatment, respectively. Odds of achieving a SVR were significantly associated with release (P<.01), but not transfer (P=.18). Prison-based HCV treatment achieves similar outcomes to community-based treatment, with those not released or transferred during treatment doing particularly well. Transfer or release during therapy should be avoided whenever possible, using anticipatory planning and medical holds where appropriate

Aspinall EJ, et al. J Viral Hepatology 2016;23(12):1009–1016.

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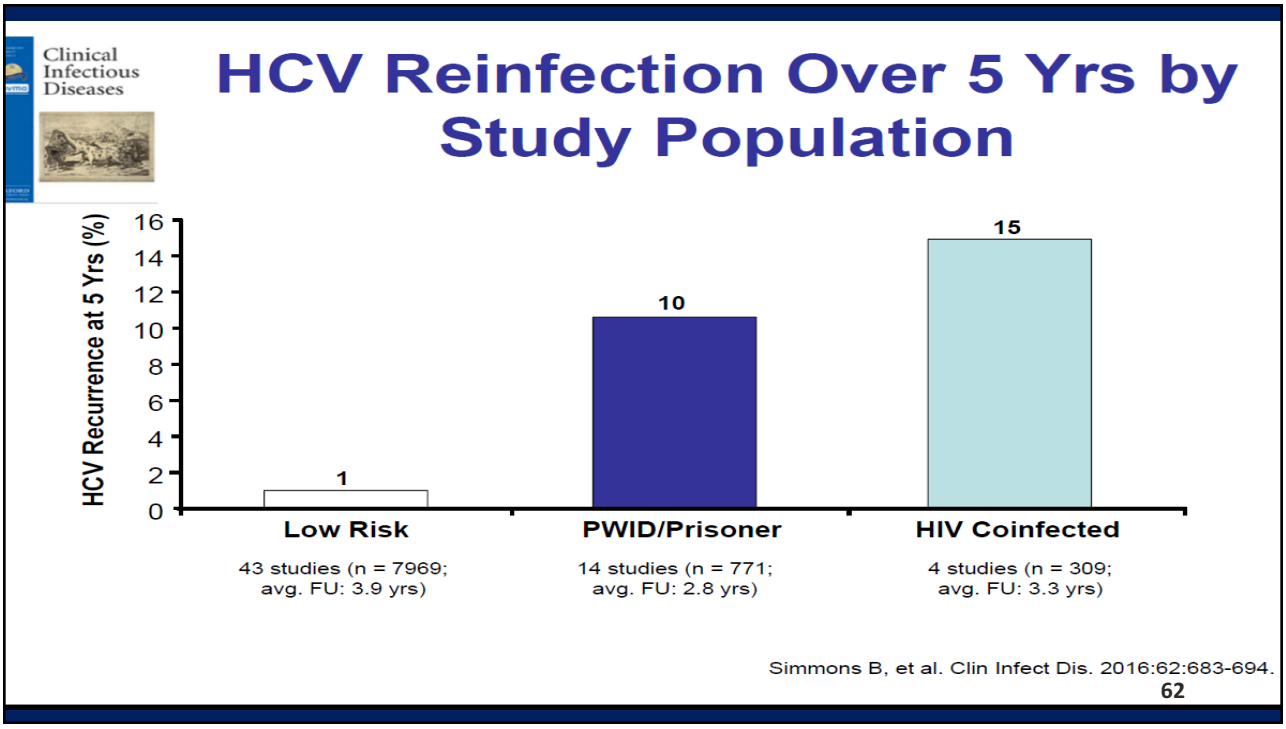

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Conclusions and Recommendations

- Detention is an opportunity for testing, diagnosis and care for HCV infected inmates, mainly if unaware of this infection
- Extensive blood borne disease screening is strongly recommended in high risk populations
- Eligibility path and treatment could be entirely performed inside prison by a multi-specialist team with a nurse protocol
- An agreement with judiciary system has to be reached in order to keep the patients in the same institution for the whole duration of treatment
- A document including diagnosis, drug regimen, outcome and indication for medical facility has to be given to the patient aiming to ensure linkage to care after release
- Inmates have to be referred to Infectious Diseases/Gastroenterology Unit for follow-up and to prevent liver complications or reinfections

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- **Prison officers**
- **Magistrates**
- **San Paolo Hospital Health Department**

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HCV Infection in Prison. From Individual Care to Viral Eradication Strategy
Dr. Roberto Ranieri & Dr. Ruggero Giulliani, Penitenciary Regional Health Unit
San Paolo University Hospital, Milano, Italy
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