

CORSO DI AGGIORNAMENTO ECM

**BUONE PRASSI E NETWORKING NELLA
GESTIONE DELL' EPATITE C IN SOGGETTI
CON DISTURBO DA ADDICTION, AL TEMPO
DEL CORONAVIRUS**

Il Progetto HAND

5 novembre 2020

Quadro epidemiologico dell'HCV
nei pazienti utilizzatori di sostanze:
dalla realtà nazionale a quella
locale.

Impatto dell'infezione da Covid-19
sul testing per HCV nei Serds

Dr. Alberto Chiesa

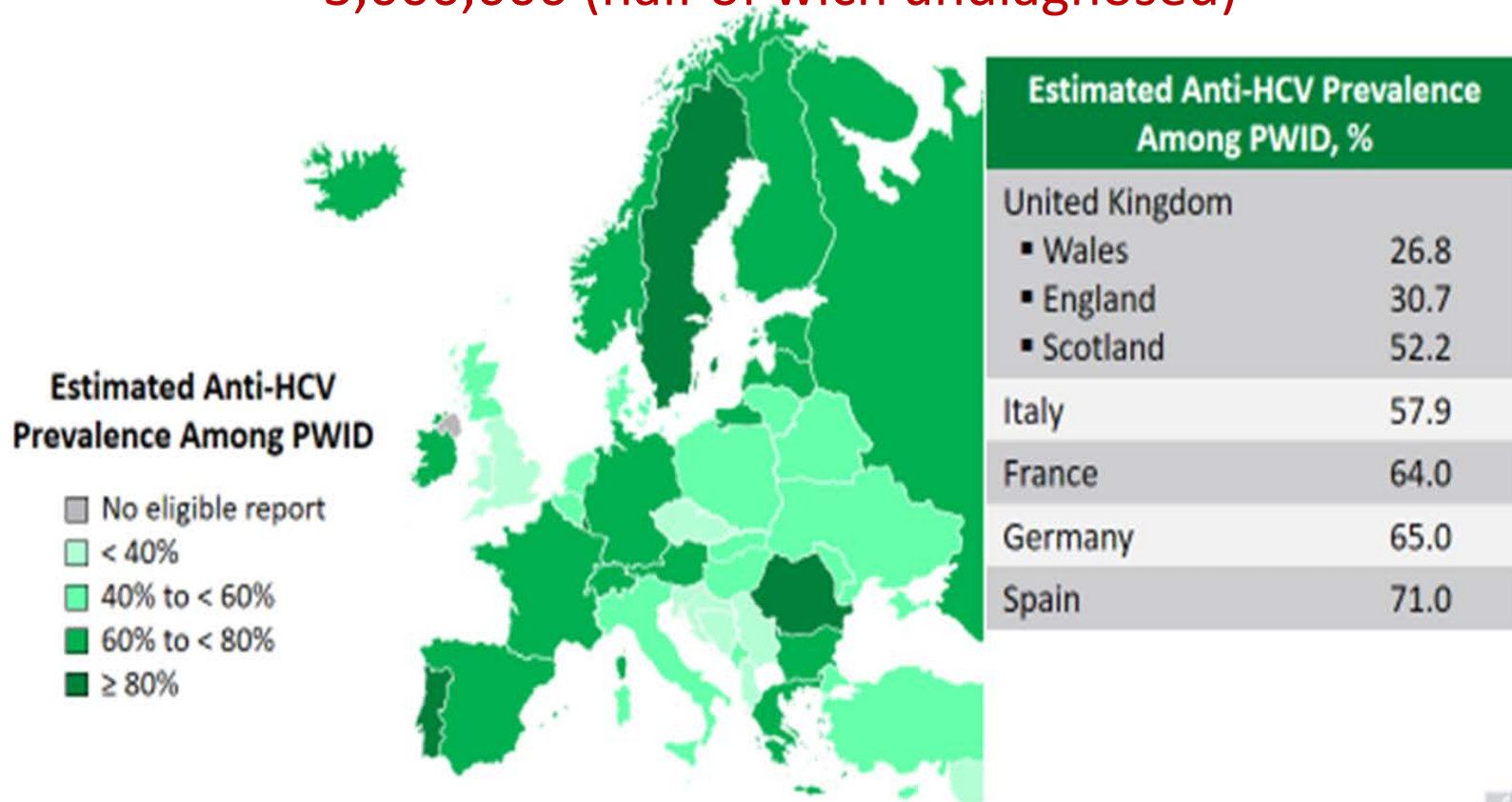
Dirigente Medico 1 Livello - SerD Vizzolo Predabissi

of 15,6 million global PWID 6,000,000 PWID HCV + in the world

About 1,7 million new infection/year

How Common Is HCV Infection Among PWID in Europe?

3,000,000 (half of wich undiagnosed)










Degenhardt. Lancet Glob Health. 2017;5:e1192.

Slide credit: clinicaloptions.com

Stima della popolazione infetta in Italia 500.000 soggetti

IQVIA Sept 2018

More than 100k patients are estimated to be drug related, while 230k were infected by glass syringes of trasfusions

Transmission route	Pre DAA	Pre cured	New infection	Actual infected ⁴
 Drug related	113.960	12.004	441	101.871
 MSM with sexual risk practices	39.458	7.990	454	31.922
 Tattoo & piercing	91.120	15.729	497	75.888
 Blood transfusion	151.368	34.004	0	119.345
 Vertical transmission	16.730	3.415	43	13.365
 Glass syringe	142.961	32.003	0	109.958
 Unknown risk factor	120.300	31.001	607	105.306
Total	881.871	136.316	2.100	557.654

1. Epidemiological model output
2. Data from Region's AIFA split by risk factor using model output fitness distribution by transmission route
3. Analysis based on bollettino SCIEVA data and expert opinion
4. Column 1 = column 2 + column 3 = current HCV/HIV+ population

Italian PWID

450,000 high-risk users

150,000 attending the Drug Dependence Services

(Serds - over 580 in Italy),

mean age **30-54 yrs**,

delay of presentation 6 yrs.

300,000 unknow

20% tested

HCV prevalence in general population
unknown due to the lack of an universal screening program:

Estimated prevalence -> 1-2%

Same figure in **PWID population:**

Parliament 's annual Report shows a value of **more than 40%** (64% Stroffolini 2012) but this value is not accurate (mainly tested historical patients with higher prevalence).

Most likely to be **1/3 of patients**

E.V. drug use is responsible of about **23% of new infections.**

- **In the first 5 year of «activity» over the 50% of PWID became infected** with an incidence rate of 1000 time more respect the general population.
- **Each PWID infected 20 other subjects within the first three years** of the beginning of the dependence (Magiorkinis 2013)

Progress Toward HCV Elimination Goals

2030 WHO Goals^[1]

90% ↓ in HCV incidence

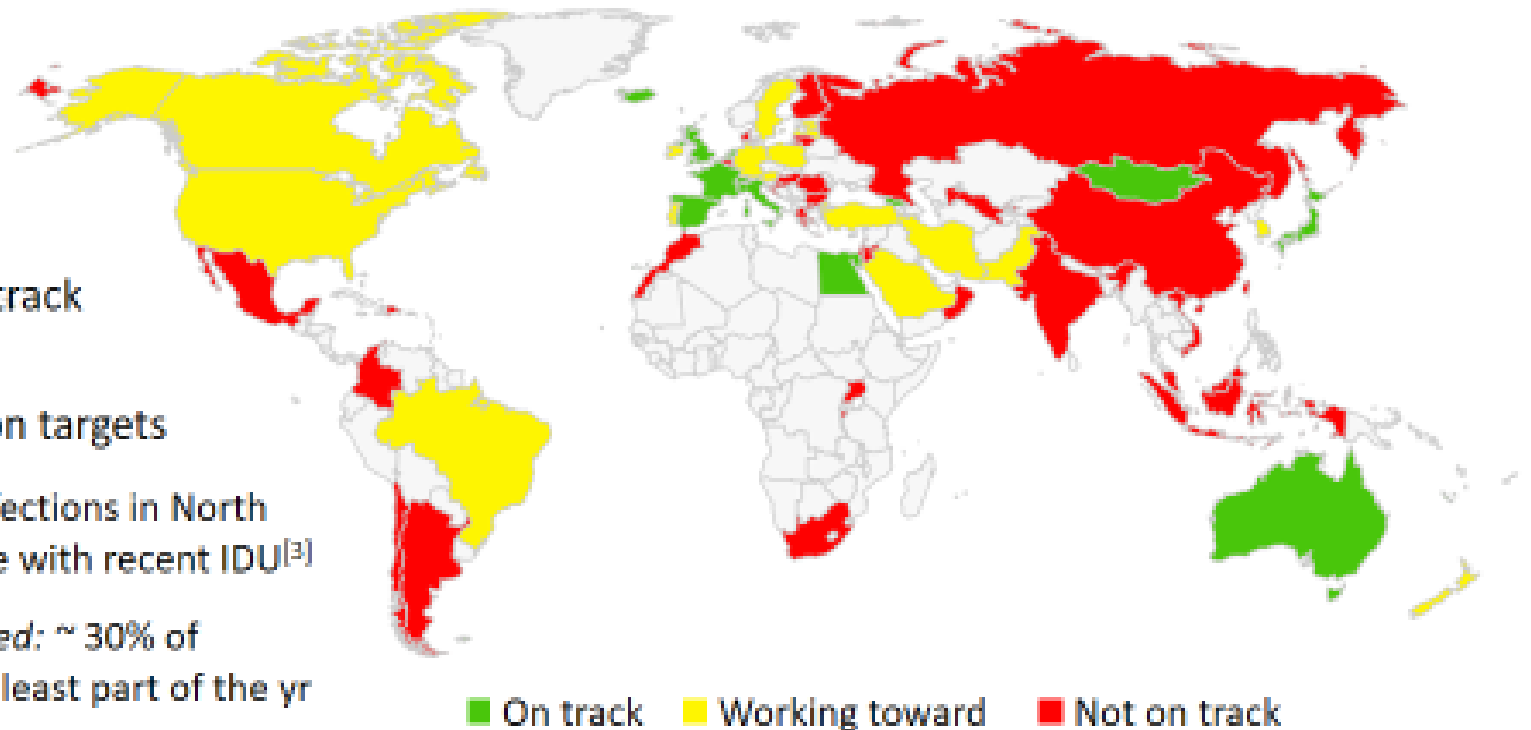
65% Reduced mortality

90% Diagnosed

80% Treated

- US *not* among countries on track to eliminate HCV^[2]
- Missing important population targets
 - PWID: 30.5% of all HCV infections in North America are among people with recent IDU^[3]
 - People who are incarcerated: ~ 30% of people with HCV spend at least part of the yr in a correctional facility^[4]

HCV Elimination Targets: 2017^[2]



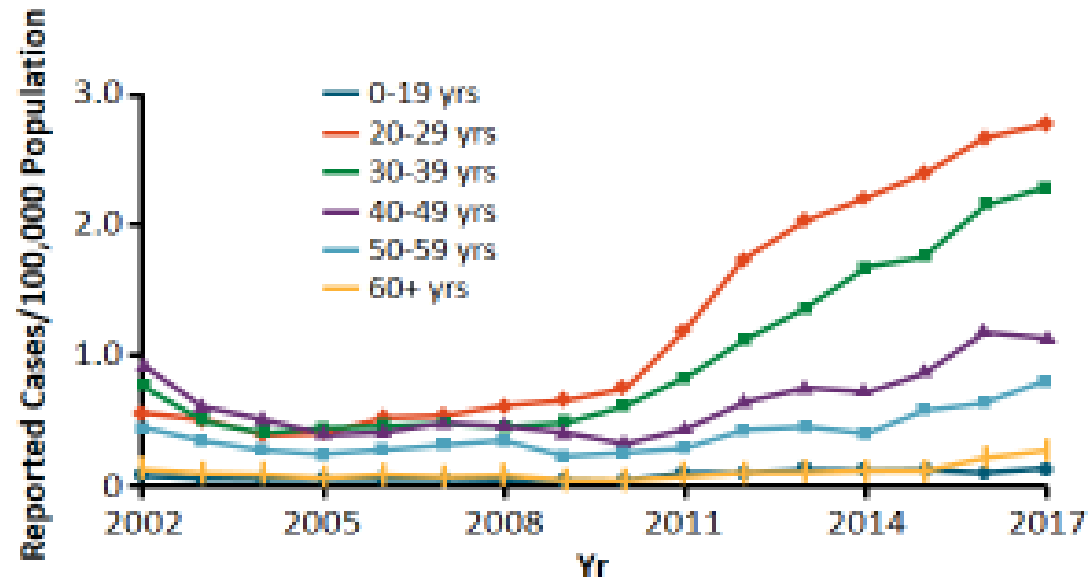
1. WHO. Global Health Sector Strategy on Viral Hepatitis, 2016-2021. 2. http://polarisobservatory.org/polaris_view/hapC.htm.
3. Grebely. *Addiction*. 2019;114:150. 4. Varan. *Public Health Rep*. 2014;129:187.



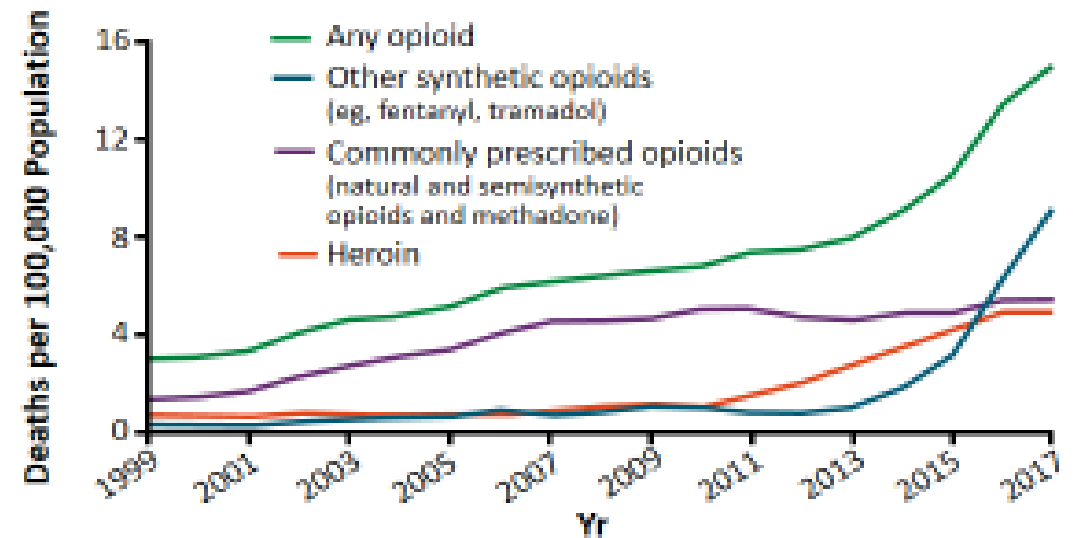
- In the three years 2017-2019 we **did not reach the target** of 240,000 patients treated (~200,000).
- Italy has been downgraded from **«on track»** to **«working toward elimination»** country by the CDA's Foundation Polaris Observatory in Lafayette»
- ...For the eradication of hepatitis C virus there **is no real national plan** and no coordinated actions at regional level although some more virtuous regions have shown considerable capacity of initiative...
- ...We've made a lot of investment in drugs, but nothing about the **de-shadowing of the underground** or the **strengthening of centres to increase the capacity of care** and the reception of patients who do not know where to turn...

Twin Epidemics of HCV and Injection Drug Use

Rising Rates of Incident HCV^[1]



Rising Rates of Overdose Death^[2]



1. CDC. Viral Hepatitis Surveillance, 2017. 2. CDC. Opioid Data Analysis and Resources.

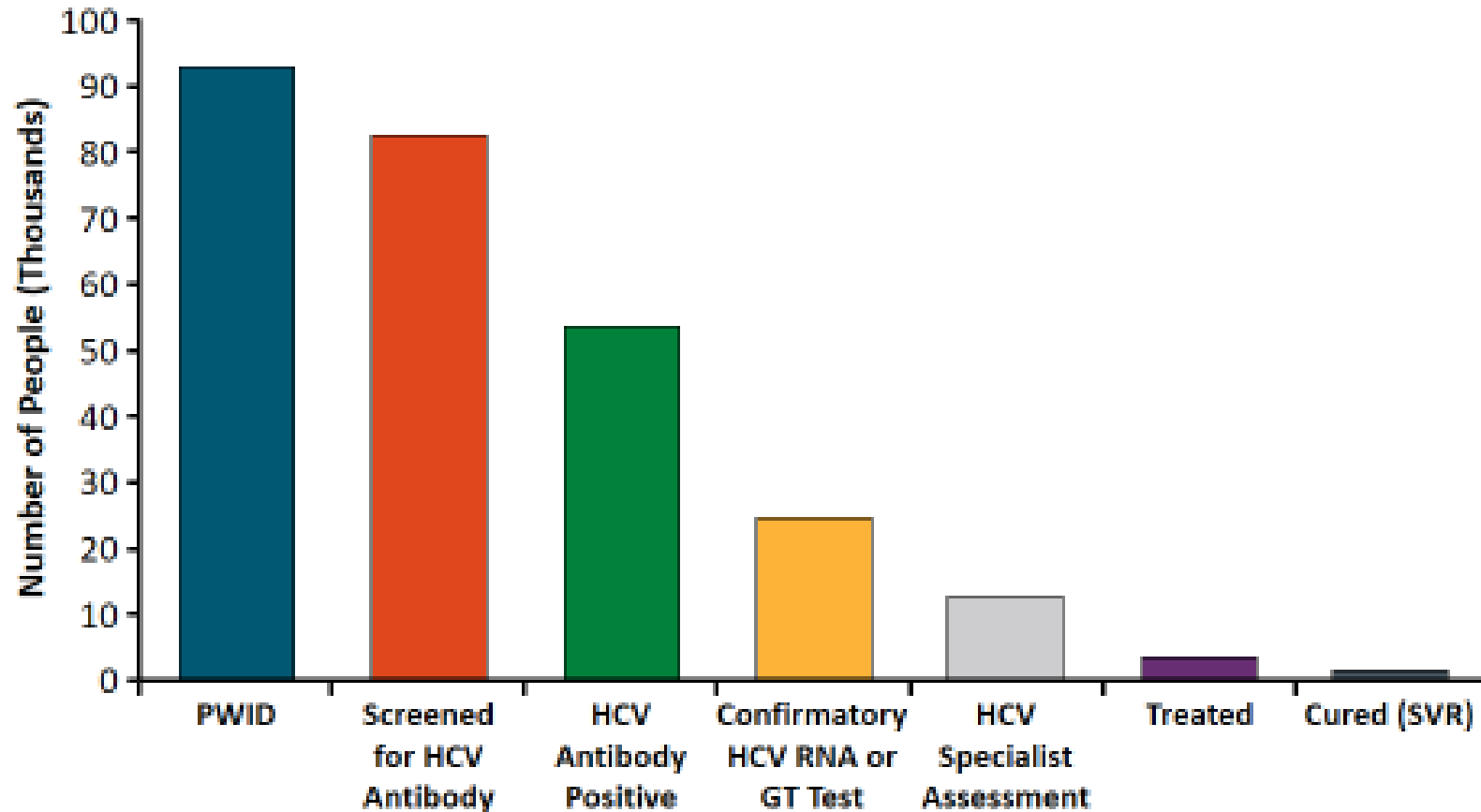


Slide credit: clinicaloptions.com

Starting Down the Road: Linking and Maintaining PWID in HCV Care



The Vast Majorities of PWID Are Not Coming to the Clinics: Example PWID HCV Care Cascade From Australia

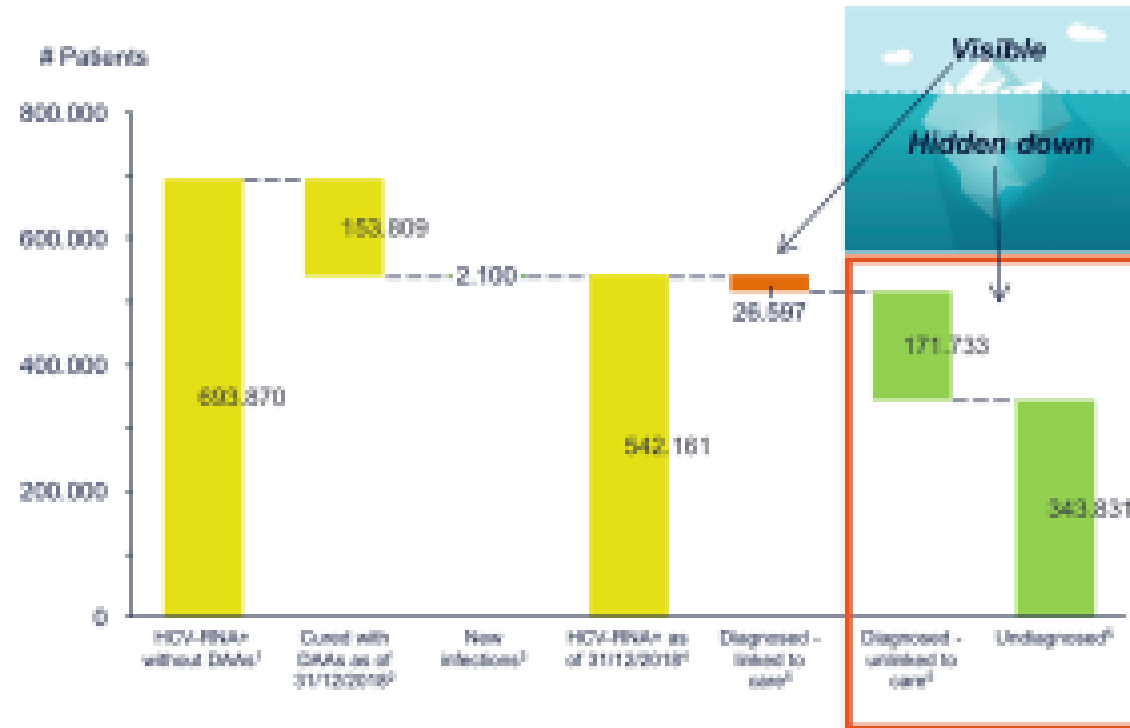


Grebely. Nat Rev Gastroenterol Hepatol. 2017;14:641. Iversen. Int J Drug Policy. 2017;47:77.

Slide credit: clinicaloptions.com

IQVIA dati al 31/12/2018

Italian Care Cascade: there are around still 542k HCV patients untreated but only 26K are diagnosed & linked to care



1. Epidemiological model output
2. The 93% of DAAs treated patients (165,386) is considered cured
3. Projection based on SEI-EVA bulletin data and expert opinion
4. Column 1 - column 2 + column 3 = current HCV-RNA+ population as of 31/12/2018
5. Epidemiological model output & estimates based on expert opinion

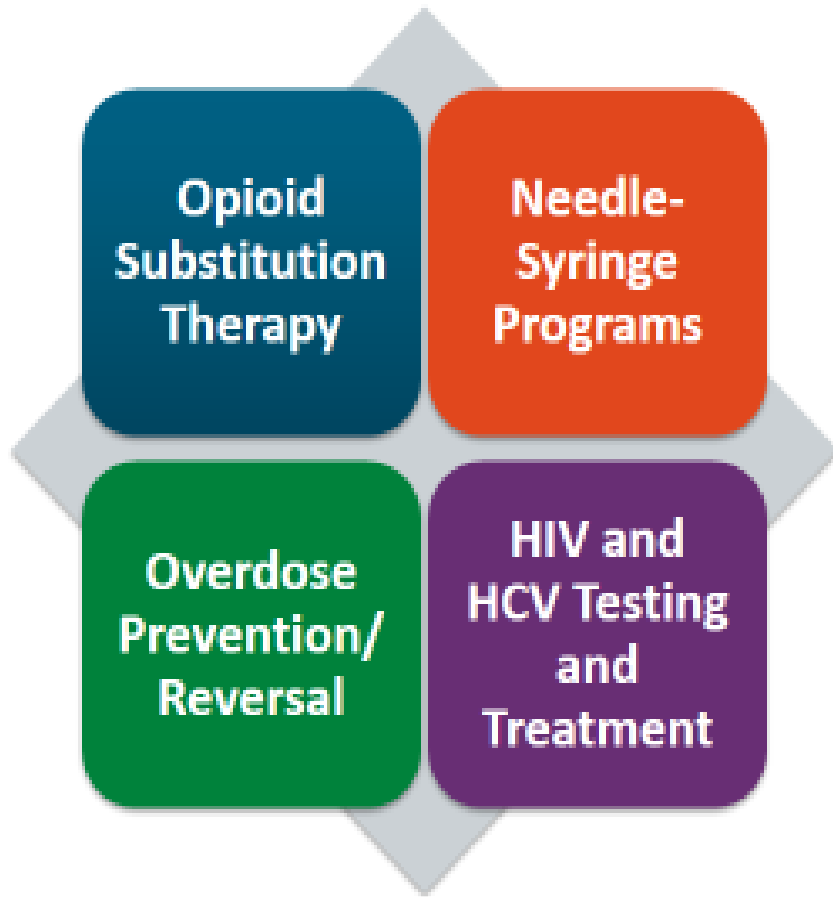
Progetto Scudo

(Survey condotta su 8 Serds Italiani in 5 aree geografiche)

Criticità nel referral and linking to care:

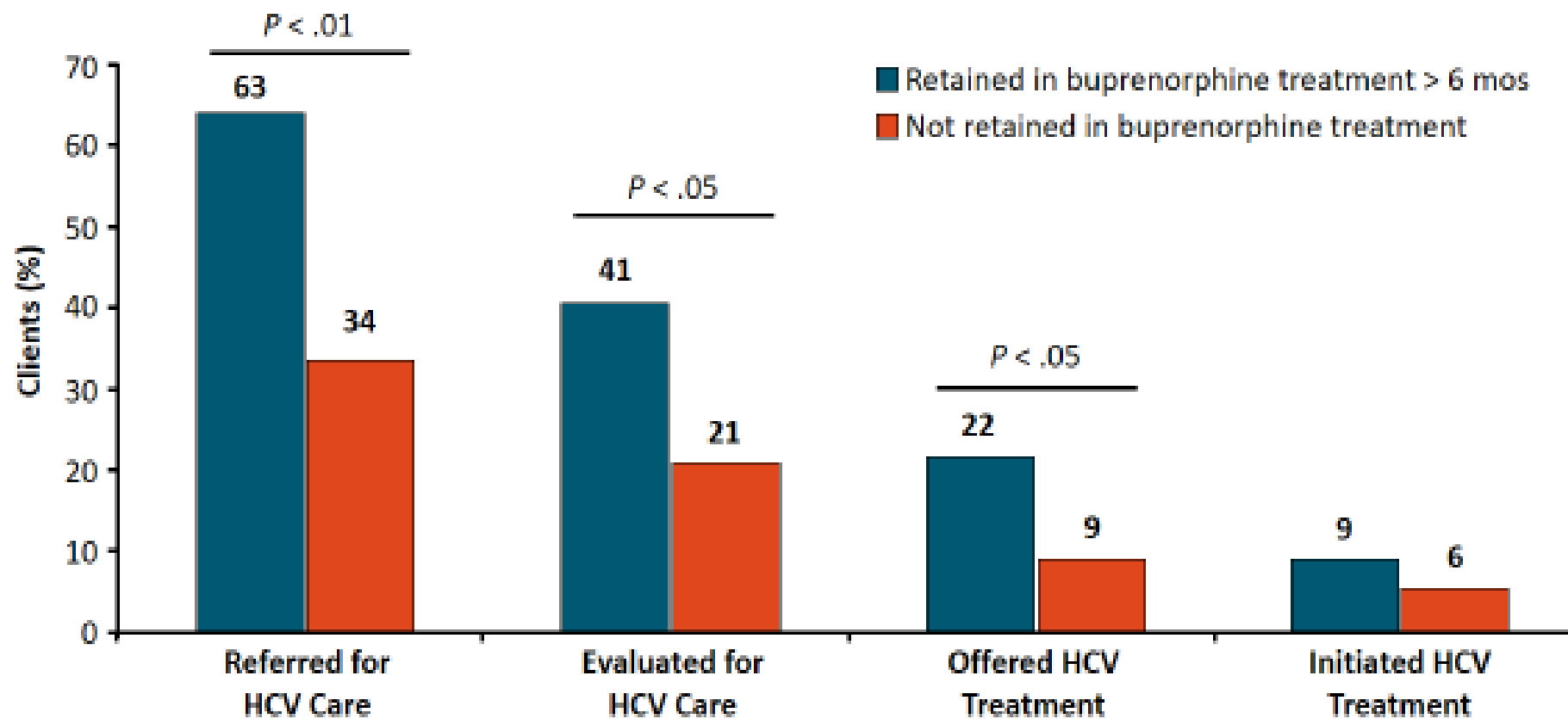
- Ridotta percentuale di soggetti testati e quindi riferiti per il trattamento
- Ridotta percentuale di soggetti trattati con DAA
- Mancata offerta di azioni di riduzione del danno in grado di ridurre malattia e reinfezione

Harm Reduction: What It Is and What It Does



- Harm reduction **goals**: decrease medical, social, economic harms resulting from drug use
- Harm reduction **outcomes**:
 - Reduces HIV, HCV transmission
 - Prevents overdose death
 - Improves health, social service uptake

Colocalized Drug and HCV Treatment: Buprenorphine Treatment Retention May Improve Cascade of HCV Care



Norton. J Subst Abuse Treat. 2017;75:38.

Slide credit: clinicaloptions.com

HCV Prevention Among PWID: Harm Reduction and Drug User Health

OAT (Methadone/Buprenorphine)

Country or Region	No. of Studies	RR	95% CI
Australia	3	0.42	0.25-0.72
North America	4	0.57	0.42-0.77
Europe	5	0.43	0.27-0.68
Overall	12	0.51	0.40-0.63

50% reduction in risk

OAT + High Coverage NSP

Study	Unadjusted RR	95% CI
Bruneau 2015	0.63	0.37-1.07
Hope 2011	0.17	0.02-1.54
Palmateer 2014	0.24	0.10-0.59
Van Den Berg 2007	0.15	0.06-0.40
Overall	0.29	0.13-0.65

71%
reduction
in risk

OAT + Low Coverage NSP

Study	Unadjusted RR	95% CI
Hope 2011	1.08	0.31-3.82
Palmateer 2014	0.48	0.24-0.95
Van Den Berg 2007	1.04	0.53-2.05
Overall	0.76	0.44-1.33

24%
reduction
in risk

Studio Delphi

(Survey condotta sui medici dei Serds)

Criticità nel referral and linking to care:

- Mancanza di risorse ed investimenti su personale e strutture
- Assenza di protocolli e raccomandazioni per il trattamento

Patient-Centered Model of HCV Care for PWID: Hepatitis C Real Options (HERO) Study

- On-site HCV treatment at community health centers or methadone treatment programs (16 sites in 8 states)
 - Treatment: 12 wks SOF/VEL

Patients with any GT HCV
infection, IDU in previous 3 mos,
± current OAT, DAA naive,
± HIV coinfection
(N = 600)

Modified Directly Observed Therapy (mDOT)
(methadone maintenance program: n = 150;
community health center: n = 150)*

Standardized Intervention: Patient Navigation
(methadone maintenance program: n = 150;
community health center: n = 150)

*Patients in mDOT arm treated at methadone maintenance programs receive SOF/VEL daily with daily methadone and those treated in community health centers video record themselves taking SOF/VEL each day using app on their mobile device.

Evolution of HCV Guidelines

AASLD^[1]
Last updated Nov 2019

WHO^[2]
Last updated July 2018

EASL^[3]
Last updated April 2018

Treatment is indicated for:

All patients with acute or chronic HCV infection, except those with short life expectancies that cannot be remediated

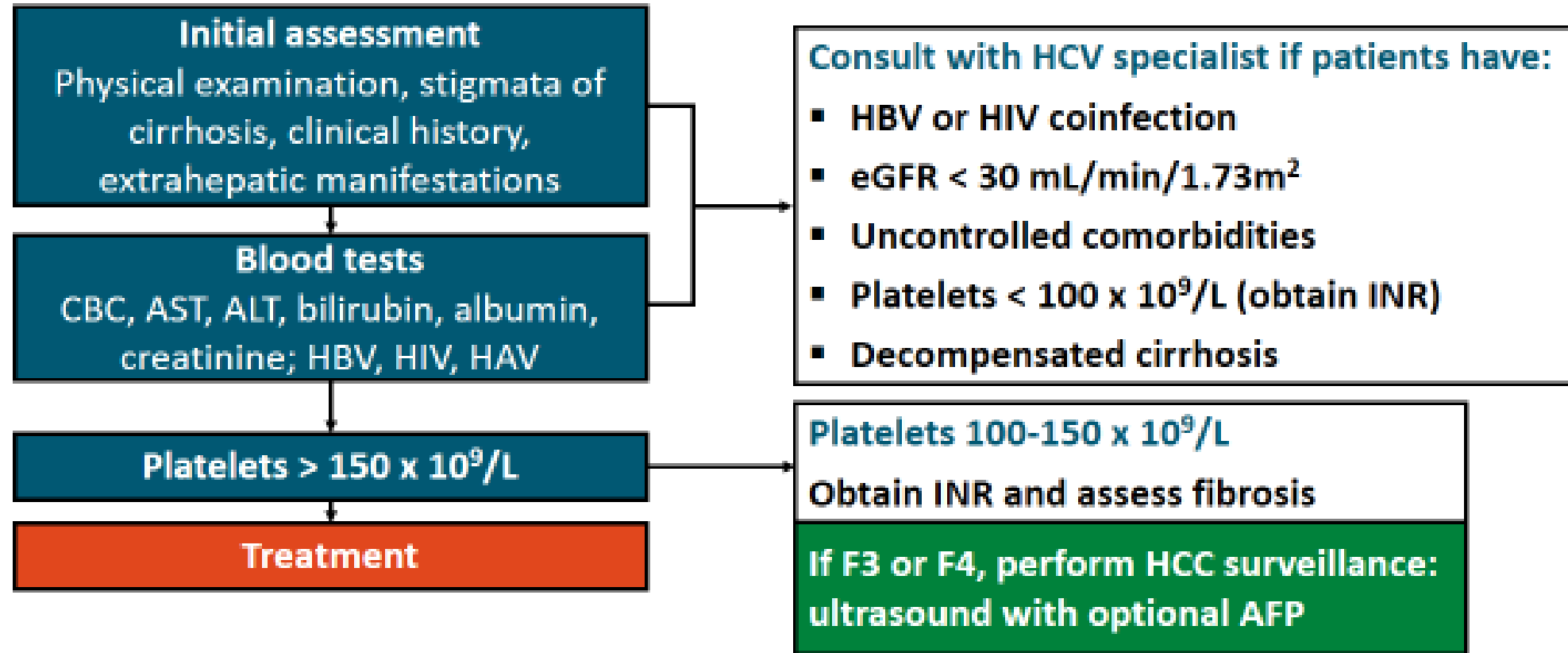
All individuals diagnosed with HCV infection who are 12 yrs of age or older (with the exception of pregnant women), regardless of disease stage

All patients with HCV infection, including treatment-naive patients and individuals with prior treatment failure

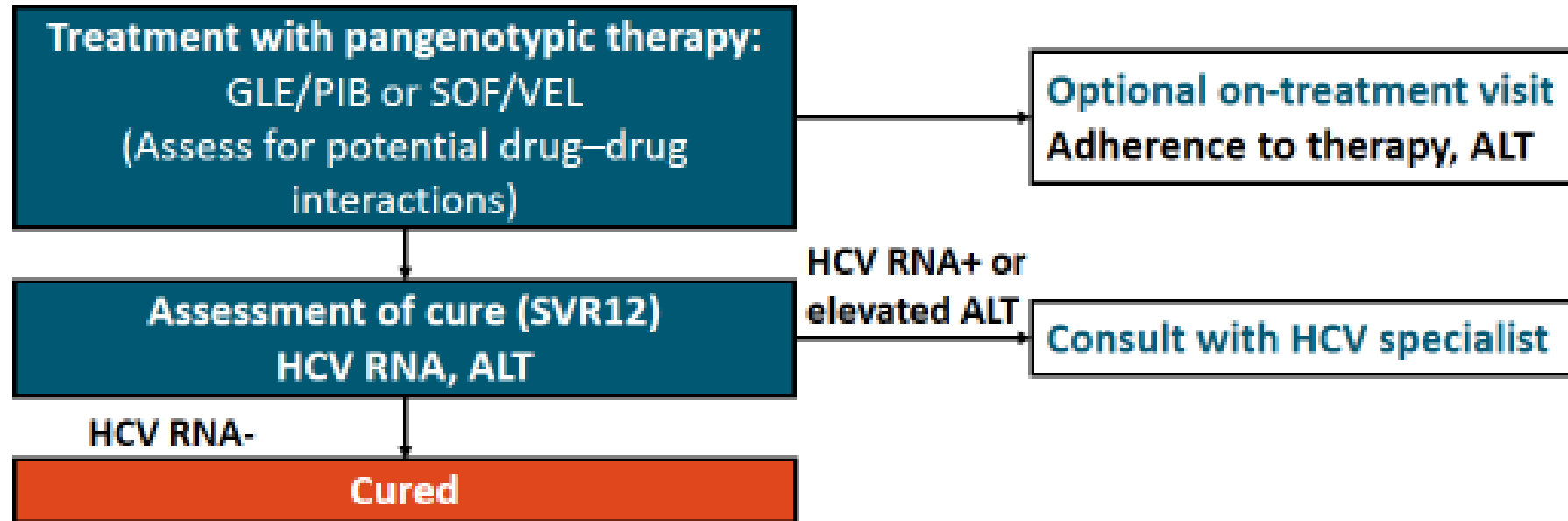
1. AASLD Guidance, November 2019, 2. WHO Guidelines, July 2018, 3. EASL Guidelines, April 2018.



Simplified Algorithm for HCV Pretreatment Assessment



Simplified Algorithm for HCV Treatment and Monitoring

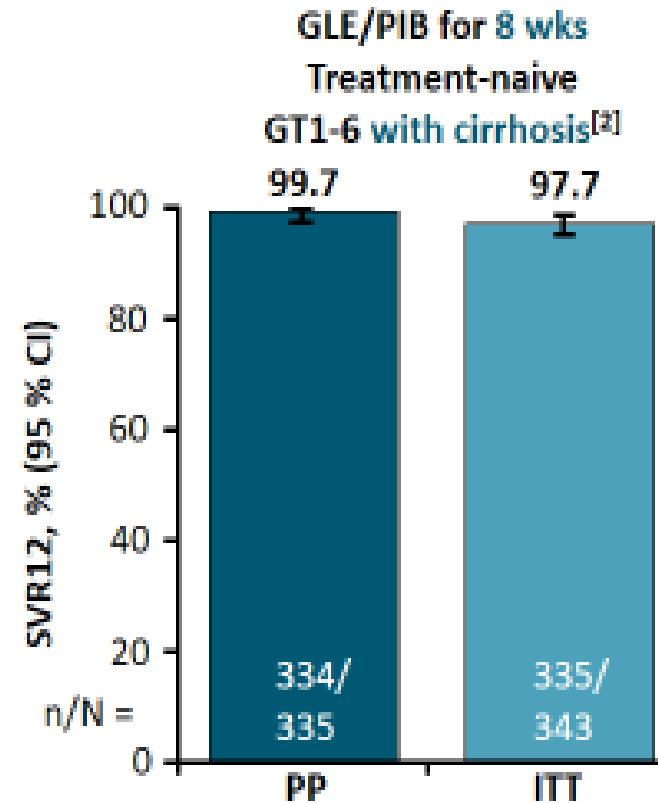


EXPEDITION-8: High SVR12 for 8-Wk GLE/PIB in Treatment-Naive Patients With Compensated Cirrhosis

- Based on paradigms used in phase III trials, GLE/PIB originally approved in treatment-naive patients for 8 wks if no cirrhosis, 12 wks if cirrhosis

On 9/26/2019, FDA expanded approval of 8-wk GLE/PIB to:

Treatment-naive adults and pediatric patients ≥ 12 yrs or weighing ≥ 45 kg with chronic HCV GT1-6 and compensated cirrhosis^[1]



1. GLE/PIB PI. 2. Brown. J Hepatol. 2019:[Epub].

San Francisco DeLIVER Care Van

- Converted a UCSF shuttle bus into the DeLIVER Care van



- Phlebotomy station
- Clinical exam table
- *FibroScan* 430 Mini+

- HCV screening and staging
 - *OraQuick* HCV rapid antibody test
 - Venipuncture for confirmatory HCV RNA and genotype
 - *FibroScan* fibrosis staging
- Linkage to HCV care
 - Linkages to local HCV providers
 - On-site treatment at select locations: telehealth consultation, treatment initiation, follow-up visits, and prescription pick up

Slide courtesy of Jennifer C. Price, MD.

Slide credit:  clinicaloptions.com

Who Should Be Tested for HCV?

- All adults born between 1945 and 1965 should be tested once!

Risk Behaviors

- Drug use: injection or intranasal

Risk

Exposures

- Long-term dialysis
- Failure of facility to follow health department guidelines leading to percutaneous/parenteral exposure
- Healthcare workers exposed to HCV-infected blood
- Children born to HCV-infected mothers
- Persons who received transfusions or organ transplants (those notified they received blood from HCV+ donor, blood product prior to 1992, clotting factor concentrate prior to 1987)
- Incarcerated persons

Other

Circumstances

- Individuals infected with HIV
- Individuals who are sexually active prior to starting PrEP for HIV
- Unexplained chronic liver disease
- Individuals who donated solid organs
- All pregnant women



Studi recenti suggeriscono che concentrare le strategie di cattura nei PWID HCV infetti, sia di primaria importanza per ridurre il pool di HCV nella popolazione generale introducendo il concetto di

«treatment as prevention»

Conventional treatment vs Treatment as prevention

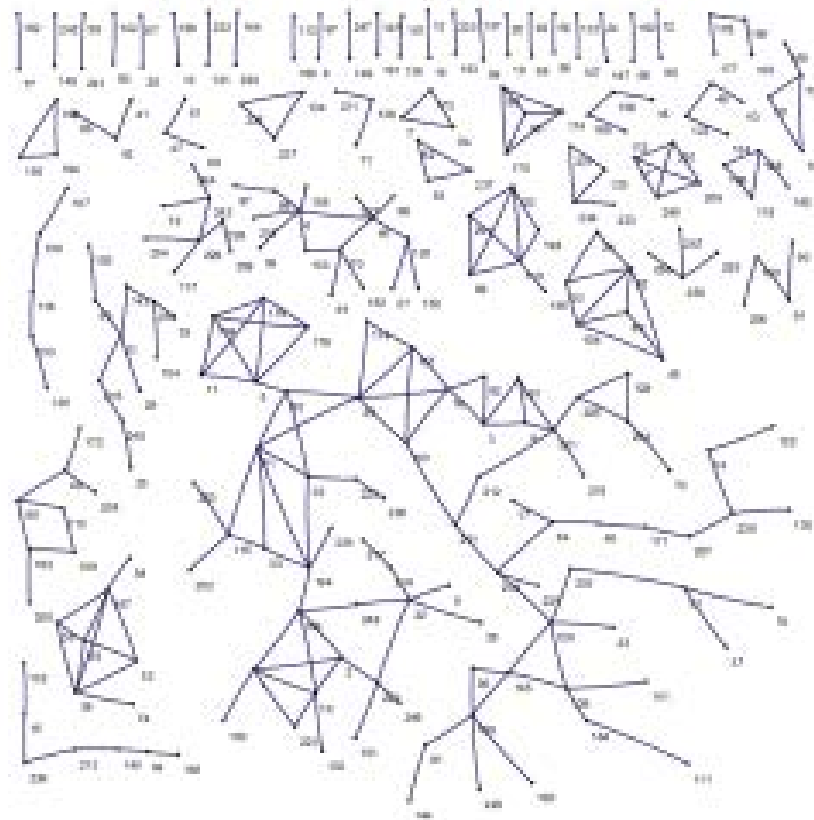
In the first case the decision for treatment is taken largely by the patient for their individual benefit (**individual health**)

In the second concept, the benefit of treatment is much less for the patient but for society as a whole (**public health**)

HCV Treatment as Prevention: Why should PWID be treated?

Modeling HCV Transmission Among PWID

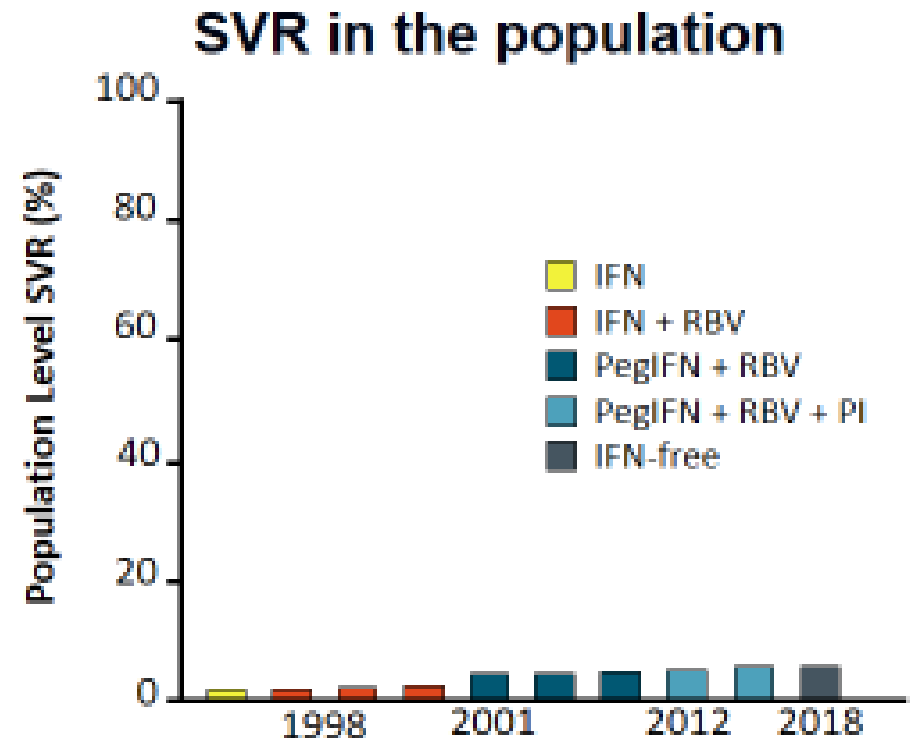
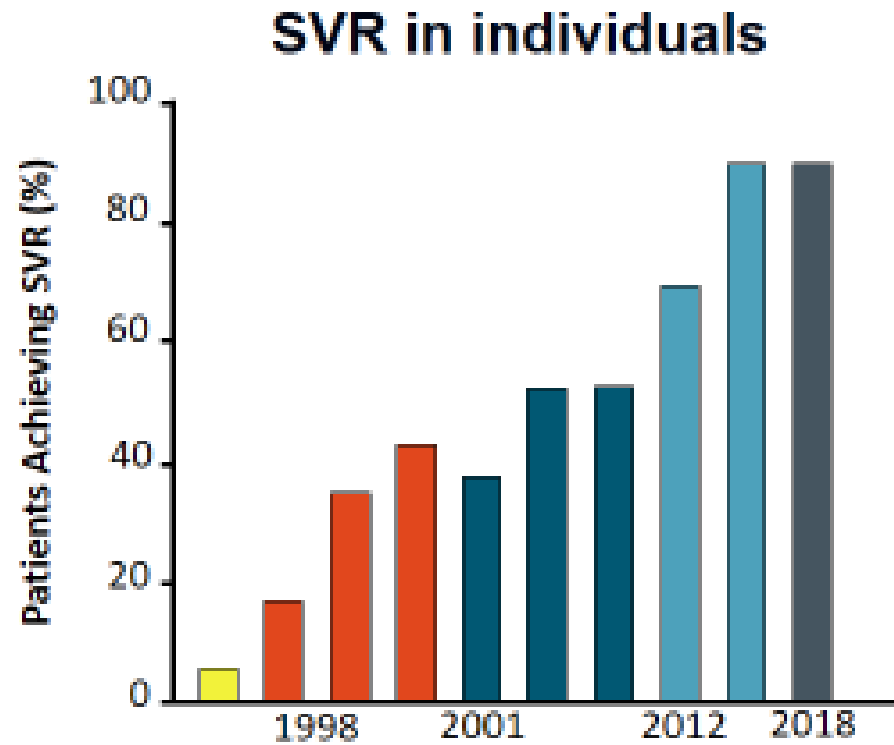
Empirical Social Network of PWID



Rolls, J Theor Biol. 2012;297:73.

Slide credit:  clinicaloptions.com

HCV Elimination Requires More Than Good Drugs



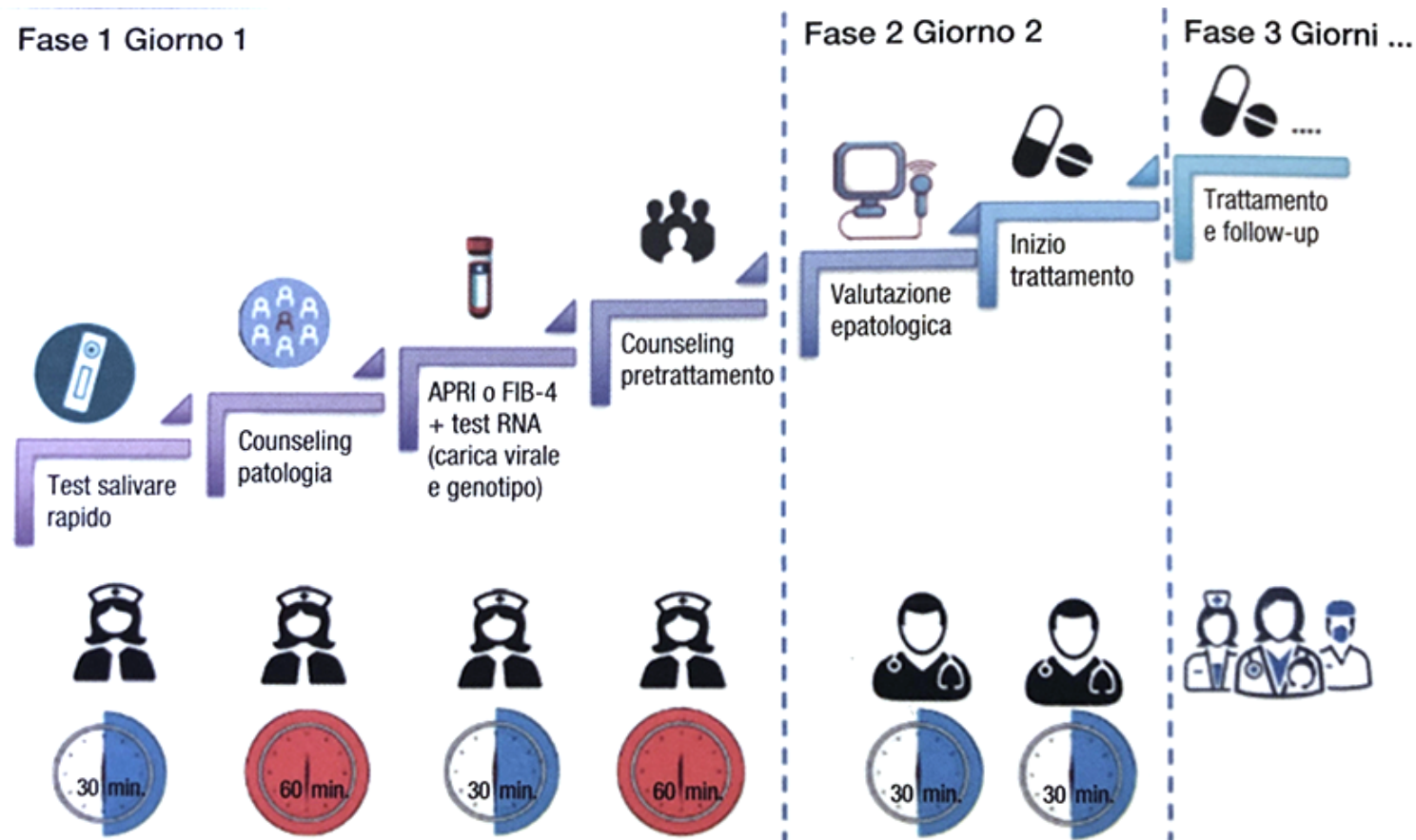
Il modello Point of Care

Le fasi della presa in carico del consumatore di sostanze con HCV



Modello di point of care nei Ser.D.

Inside phase

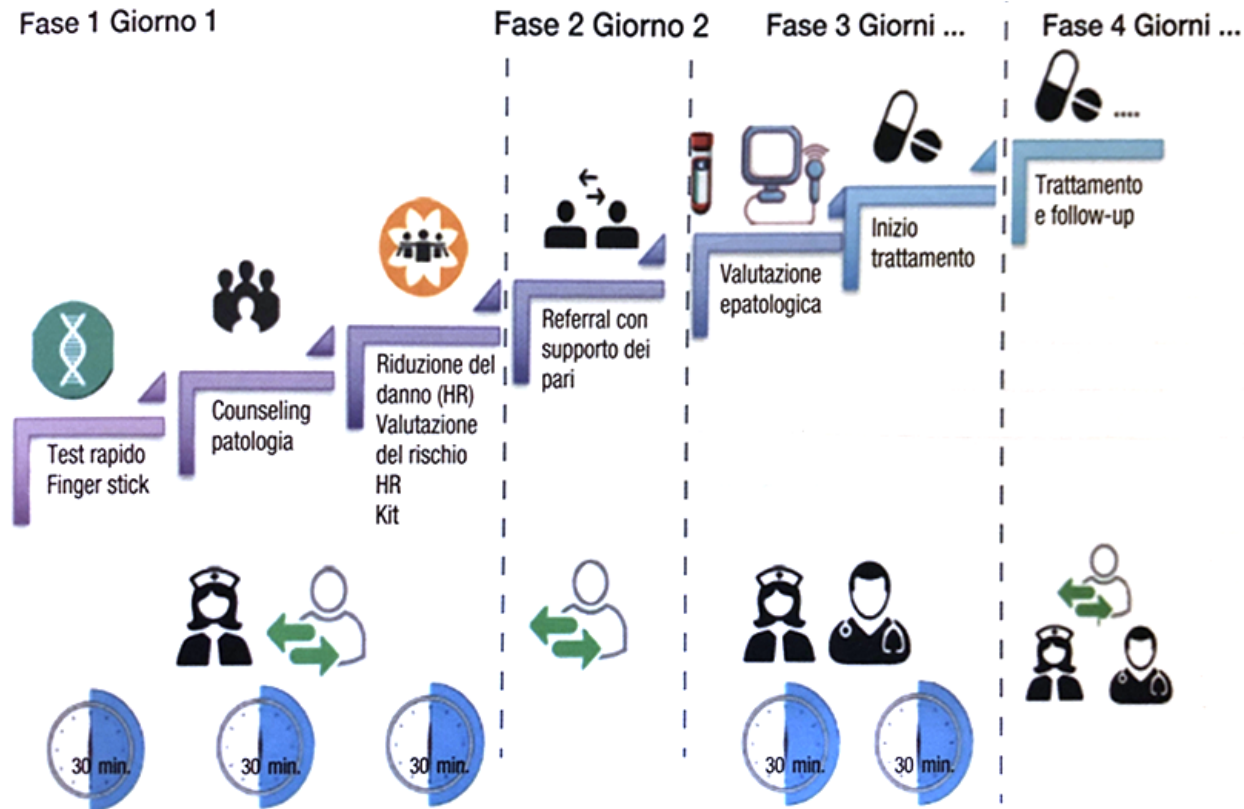


La presa in carico è nurse-based e si sviluppa in tre fasi. La prima (giorno 1) consiste nella fase di screening, di valutazione e di counseling; la seconda (giorno 2) prevede la valutazione epatologica e l'inizio del trattamento; la terza consiste nel follow-up.

Modello di check point

Il modello check point è funzionale all'emersione di HCV tra i soggetti presenti nella popolazione generale, che il consumo occasionale di sostanze rende poco riconoscibili ed esposti al rischio elevato

Outreach phase



La presa in carico è peer e nurse-based e si sviluppa in quattro fasi. La prima (giorno 1) consiste nella fase di screening, di counseling e di valutazione del rischio; la seconda prevede il referral peer-supported; la terza consiste nella valutazione epatologica e l'inizio del trattamento; la quarta consiste nel follow-up.

ICAR Milano, 2019

The health saving costs of HCV treatment of drug users:
evidence from the real practice of Drug Dependence Services (SerDs)

Aims:

The main aims of this study were to evaluate in HCV positive patients attending the Drug Dependence Services (Ser.D.s) of the metropolitan area in Milan (Italy): 1) the efficacy and the effectiveness of **patients' journey** of the treated patients; 2) the public health costs and the **economic benefits** in term of health cost saved for each PWID treated.

Methods:

We performed a retrospective study including **1,333 PWID** took in charge by Ser.D.s in Milan of the area Martesana-Melegnano, over one year (January – December 2017). The data were collected using the electronic clinical database of the public health service of Martesana-Melegnano (ASST-Martesana-Melegnano) able to register for each patient every medical benefits received during the year (including specialist, hospital admissions, diagnosis processes, etc.).

Results:

In the cohort of the patients included the study we found 274 HCV-positive PWIDs, 65 of which were treated. The mean of the health direct costs per each treated patient (excluding the cost of the drug) was € 1,418. The above costs may be further reduced of 12% if the patient is included in a more effective patients' journey, including harm reduction measures able to reduce the re-infection rates.

COST SAVING ABOUT 30000 euros IN THREE YEARS.

Conclusion:

The study shows that the HCV treatment in PWID can significantly reduce over the years not only the individual health costs but also the health community costs. Moreover, our study shows that an integrated and effective patient's journey, together with harm reduction measures, can be further effective and cost saving for the health care system.

PWID Treated vs PWID not treated

Euro 1500
STOP

Euro 250

x20

= Euro 30000

Point of care model

Euro 575
STOP

Modello organizzativo di integrazione
Ospedale/Territorio
Asst Melegnano e Martesana

Divisione di Medicina Generale
DSMD - Serd
Farmacia Ospedaliera

1. Screening e diagnosi di infezione da HCV

- nel contesto degli accertamenti di presa in carico del paziente (approfondimenti diagnostici in collaborazione con la Divisione di Medicina. Slots aperte per FS c/o HSR).
- Test rapidi.

2. Prescrizione DAA da parte del medico epatologo del Sert (con autorizzazione di medico prescrittore).

- 3. Erogazione dei farmaci** da parte del Servizio farmaceutico dell'Ente.
- 4. Esami di controllo e follow-up** eseguiti al Sert che, per le caratteristiche operative proprie (quotidianità di contatto col paziente, équipe multidisciplinare) può tempestivamente rispondere ad eventuali bisogni del paziente.

Pazienti trattati (Maggio 2018 - Maggio 2020): **57**

in definizione: **15**

CARATTERISTICHE PAZIENTI	
Maschi, n (%)	43 (76%)
Età media, anni (IQR)	45 (20-67)
Cirrosi, n (%)	9 (16%)
G1,G2,G3,G4	26 , 1, 20 , 8
T.D. Attiva, n (%)	6 (11%)
Coinfetti HBV/HIV	1 (2%)/2 (4%)
Poliassunzione, n (%)	7 (13%)
Experienced, n (%)	4 (7%)

ADERENZA	
W 4	100%
W 8	100%
W 12	100%
1 MESE POST	96%
6 MESI POST	96%

RISULTATI	
SVR 24	96%
Fallimenti	0
Persi al follow-up	1
Recidive t.d.	2
Reinfezioni	0
Decessi*	1

Call to Action Toward HCV Elimination: Focus on Simplified Testing and Cure

- **Simplification:**

- One clinic visit with rapid antibody screening and a single reflexive viral load test
- Standardized treatment regimens with pangenotypic DAAs eliminate delay associated with genotype test
- Confirm SVR at Wk 12 with second viral load test

- **Integration** with primary care and other disease programs (eg, TB, HIV) and outreach settings (harm reduction)

- **Decentralization** of services from referral hospitals to local level care

- **Task sharing** of uncomplicated cases with primary care clinicians, medical officers, advanced practice clinicians, nurses, pharmacists, and trained community care workers

Signatories: AASLD, EASL, APASL, ALEH

Impatto del Covid-19 sul testing per HCV

- 12,43% -> riduzione visite di controllo ambulatoriali nei pazienti con Epatite C cronica
- 27,81% -> sospensione
- 40,24% -> gestione da remoto
- 23,7% -> sospensione prescrizione antivirali
- 40% -> tasso di letalità per Covid-19 in pazienti con cirrosi

Criticità

Piano di eliminazione di HCV completamente da ridefinire

Febbraio: emendamento **Decreto Milleproroghe**

stanziamento di **71,5 milioni di euro** per favorire

screening gratuito HCV

ma

fondi bloccati per mancanza di decreti attuativi specifici

Studio coordinato da Prof. Galli Università Studi Milano

Testing combinato Sars Cov2/HCV nei comuni di Sordio(Lo) e San Pellegrino Terme (Bg)

Risultati:

In soggetti over 40 prevalenza HCVAb del 2% metà dei quali **non consapevole**.

Ace propone screening HCV:

- per soggetti nati tra 1969 e 1989,
- seguiti dai Serd,
- detenuti

(in concomitanza con screening per Covid-19)

COVID-19-Related Opportunities to Advance Hepatitis Elimination Goals

Testing and Contact Tracing	<ul style="list-style-type: none">▪ Increase testing capacity in many countries▪ Combine COVID-19 testing and care referral with testing for HCV and HBV▪ Improve health equity: target populations with shared health risks and disparities in access▪ Potentially decrease stigma and increase acceptability▪ Hepatitis programs can deliver culturally competent testing and referral services for COVID-19 and HBV, HCV testing
Public Health Surveillance	<ul style="list-style-type: none">▪ Increase awareness of importance among the public and providers▪ Improved IT capacity▪ Building staff with skills for data collection and analysis
Service Delivery	<ul style="list-style-type: none">▪ Increase awareness of benefits of infection detection and treatment; seize opportunity to eliminate an infectious disease▪ Telehealth can increase access▪ Diversify sources of care in clinical and community settings

MSM ?

Migranti?

Incremental viremic infections in 2030, missed diagnoses and treatments (2020-2030), and cumulative (2020-2030) excess incident HCV, HCC and LRDs, by WHO region and World Bank Income Group, 1-year delay scenario

REGION	Incremental, 2030	Missed Interventions, 2020-2030		Excess Cases, 2020-2030		
	Viremic infections	New Diagnoses	Treatment Starts	Incident HCV	Incident HCC	LRDs
WHO REGION						
AFRICAN (AFR)	12,300	-47,100	-15,700	2,600	850	4,700
EASTERN MEDITERRANEAN (EMR)	117,000	-221,000	-242,000	47,900	9,800	15,800
EUROPEAN (EUR)	96,900	-142,000	-130,000	15,800	8,700	13,800
AMERICAN (AMR)	68,300	-105,000	-103,000	4,500	10,200	14,800
SOUTH-EAST ASIA (SEAR)	73,100	-104,000	-81,600	20,300	3,600	7,900
WESTERN PACIFIC (WPR)	155,000	-285,000	-174,000	30,000	11,700	18,200
WORLD BANK INCOME GROUP						
HIGH INCOME (HIC)	150,000	-131,000	-209,000	18,100	20,000	29,900
UPPER-MIDDLE INCOME (UMIC)	174,000	-406,000	-196,000	33,700	10,200	15,400
LOWER-MIDDLE INCOME (LMIC)	185,000	-317,000	-322,000	66,200	13,700	25,100
LOW INCOME (LIC)	14,400	-51,400	-18,300	3,200	920	1,800
GLOBAL	623,000	-906,000	-746,000	121,000	44,800	72,200

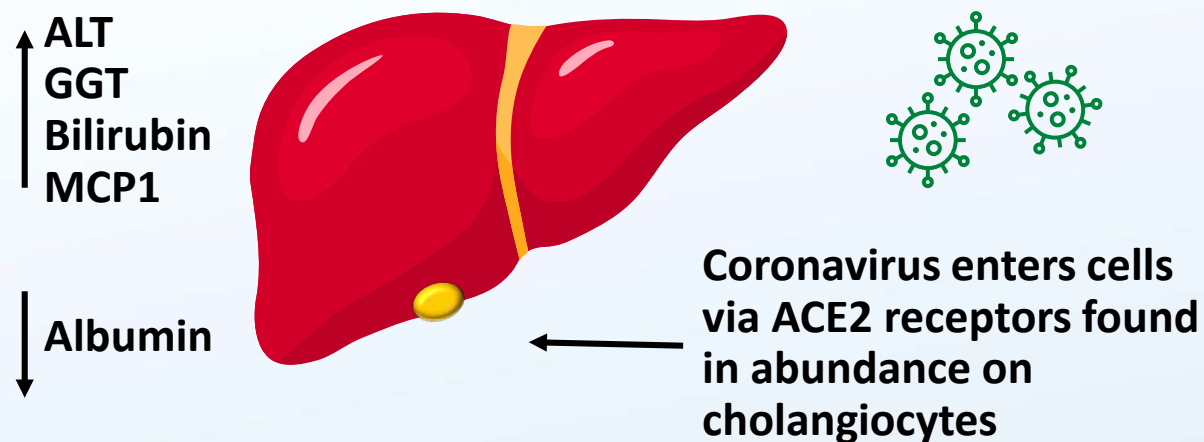


Grazie per l'attenzione

SARS-CoV-2 Infection and the Liver

- Possible causes of liver injury in SARS-CoV-2 infection:
 - Severe inflammatory response/sepsis
 - Hypoxic injury
 - Drug-induced liver injury
 - Microthromboses of hepatic sinusoids
 - SARS-CoV-2–direct damage
 - Multifactorial?

Liver Injury in SARS-CoV-2–Infected Patients



Liver Injury in SARS-CoV-2-Infected Patients

↑
ALT
GGT
Bilirubin
MCP1

↓
Albumin

← Coronavirus enters cells
via ACE2 receptors found
in abundance on
cholangiocytes