HCV micro-elimination

Stanislas Pol, MD, PhD

Université de Paris
Liver Department, Hôpital Cochin
Inserm U-1223 & Immunology of dendritic cells
Institut Pasteur, Paris, France

stanislas.pol@aphp.fr

PHC
13 January 2020

Université de Paris

ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

Institut Pasteur

anrs France REcherche Nord & sud Sida-hiv Hépatites
Agence autonome de l'Inserm

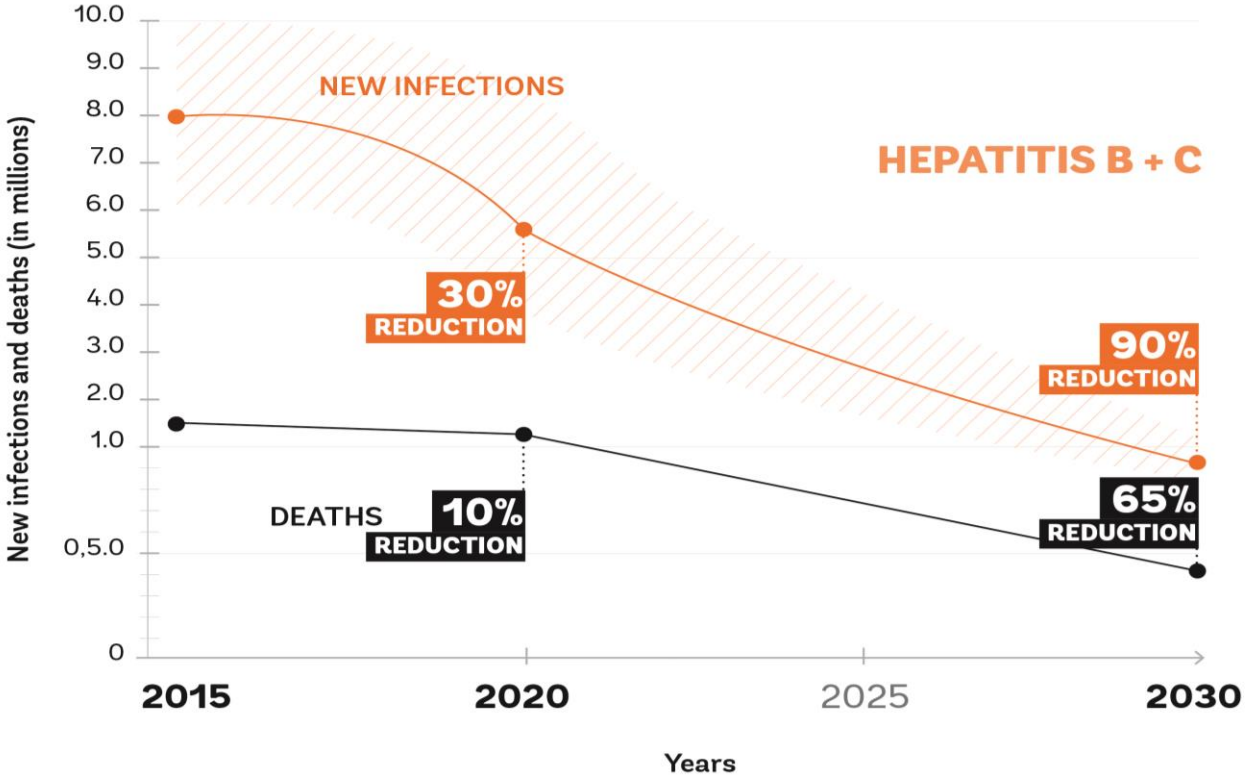
Instituts thématiques Inserm
Institut national de la santé et de la recherche médicale

Disclosures

Speaker or **Board member** : BMS, Biotest, Shiniogi, Janssen, Gilead, Roche, MSD, Abbvie

Grants : BMS, Gilead, Roche, MSD

Elimination of viral hepatitis: the WHO plan for 2030

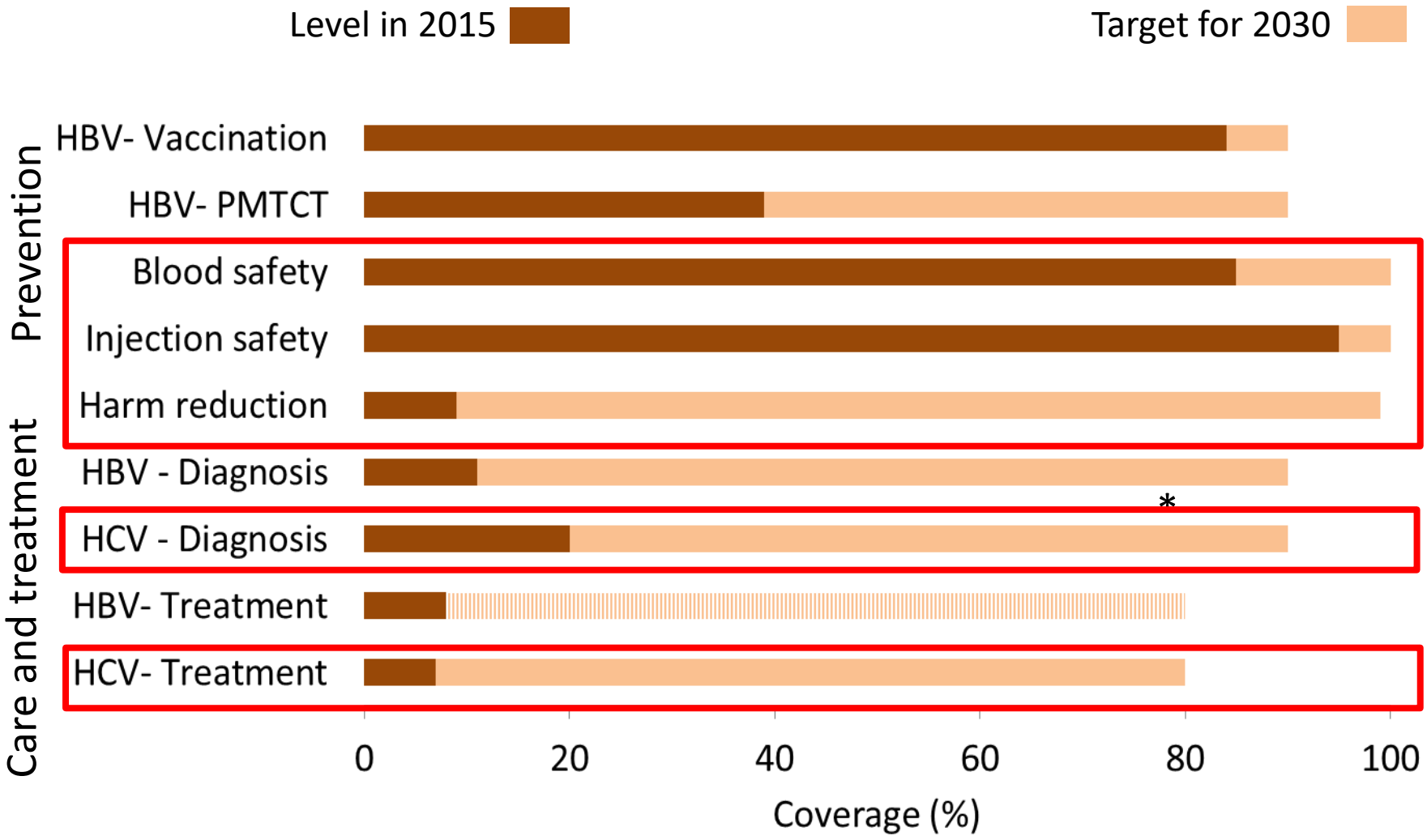


By 2030:

1. **90% aware of HCV infection by 2030**
2. **80% of people treated**
3. **1.4 million deaths (in 2015) to under 500,000 deaths (by 2030)**
4. **6-10 million infections (in 2015) to 900,000 infections (by 2030)**

Global Report on Hepatitis, WHO, 2017

Interventions and targets



Global Report on Hepatitis, WHO, 2017

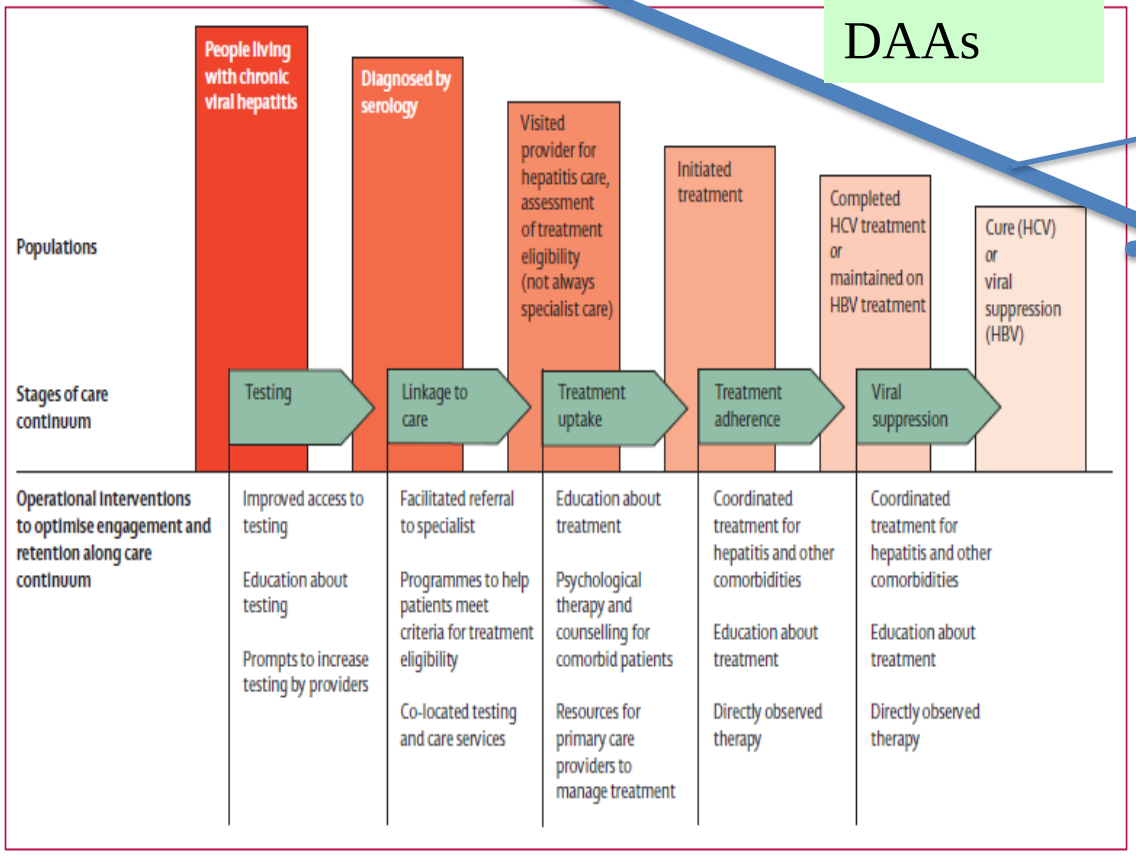
HCV elimination

Screening

Access to care & DAAs

- Drug-drug interaction
- Adherence
- Safety

Follow-up of cured patients and prevention of re-infection

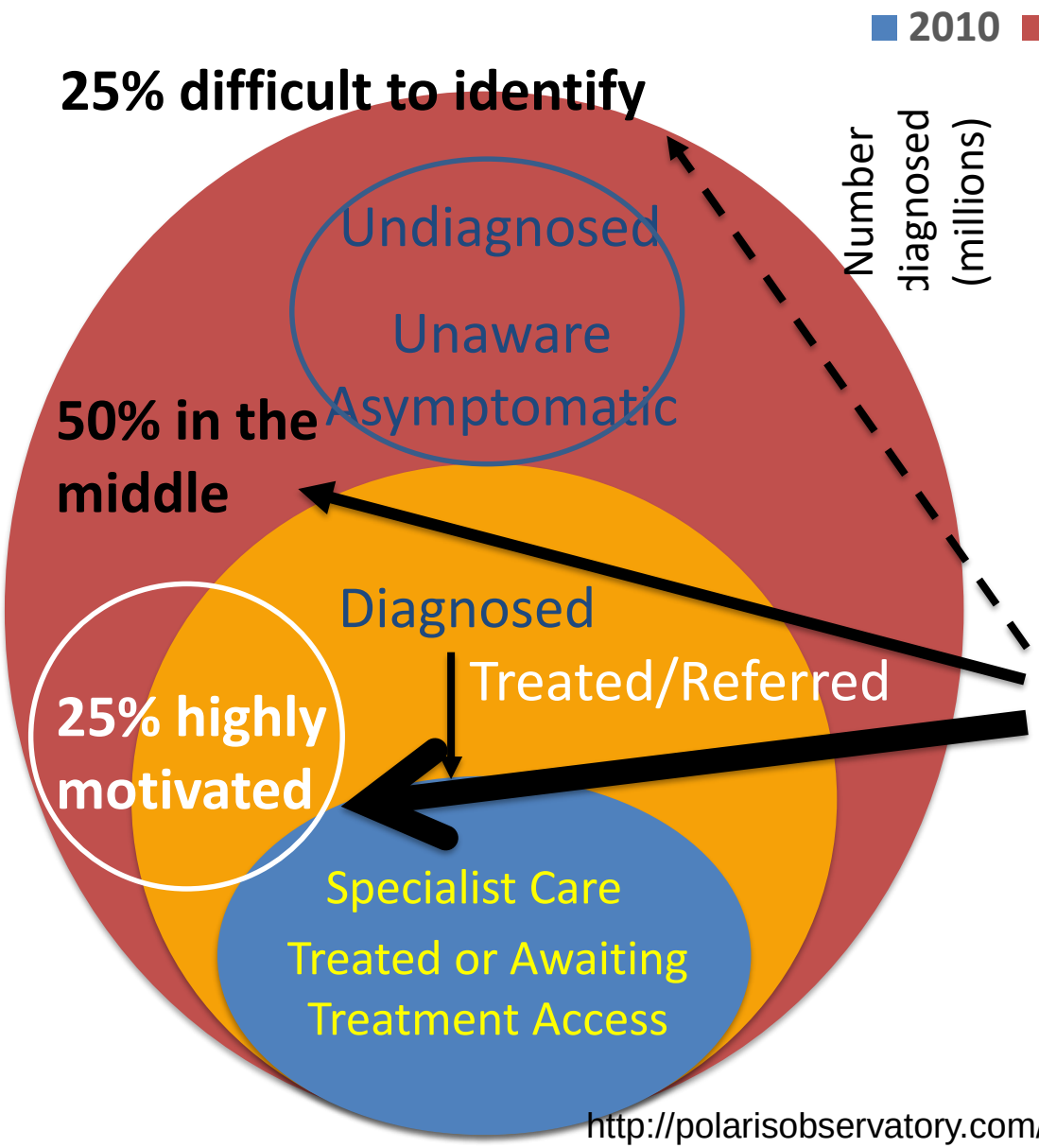


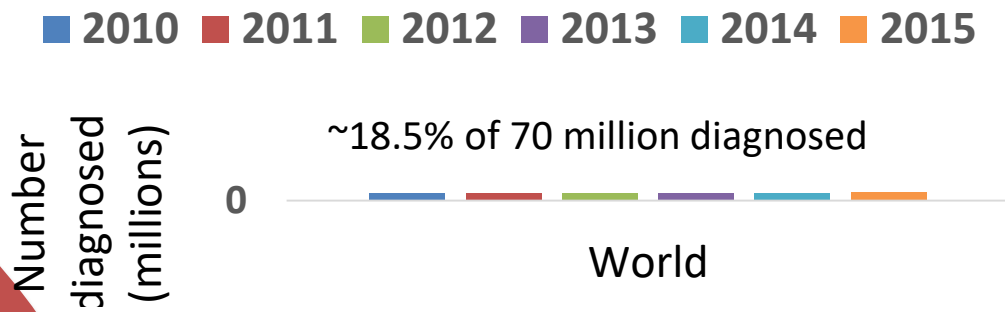
Limitations to HCV elimination :

- screening
- access to care
- cost of drugs

Zhou, Lancet Infect Dis 2016

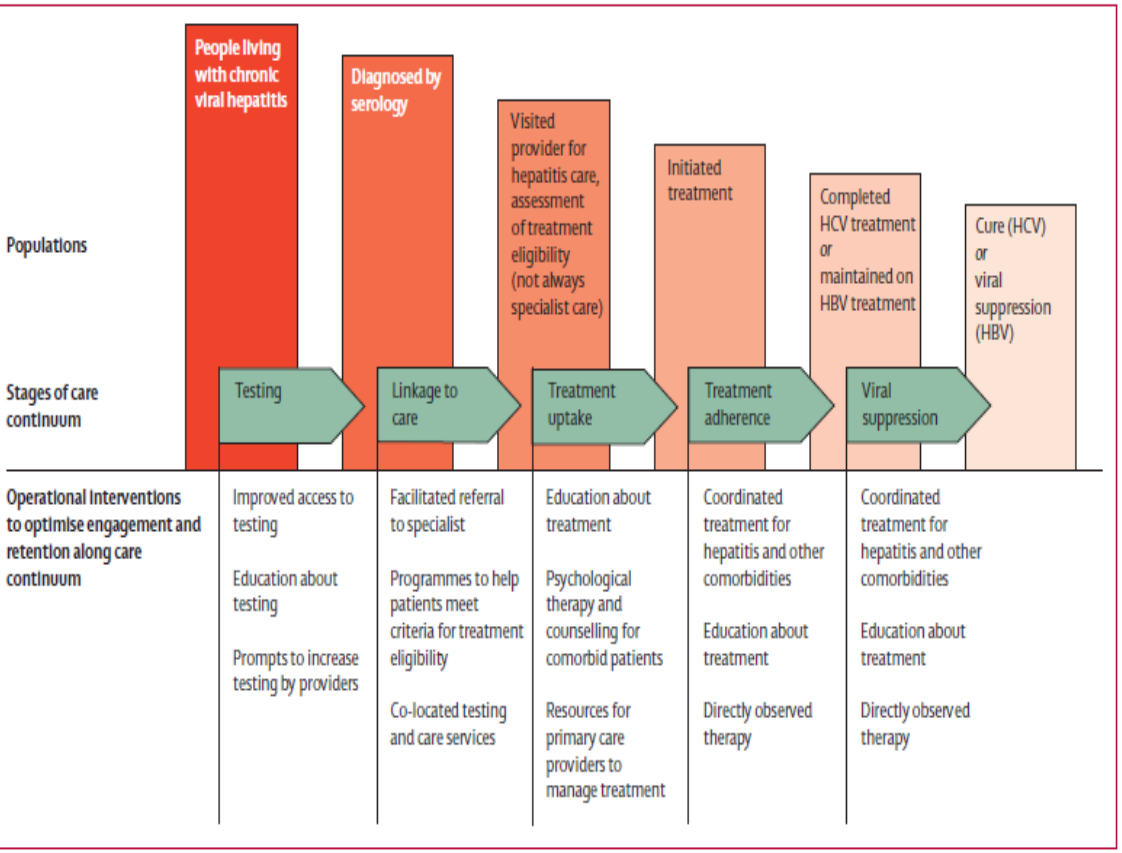
Different populations to screen





http://polarisobservatory.com/polaris/datasheet.htm downloaded 9/18/2016

HCV micro-elimination in “easy-to-screen” patients



- Micro-elimination = SVR in « well-defined » populations

- Decompensated cirrhosis
- US Veterans
- Nephrology
- Hematology
- Oncology

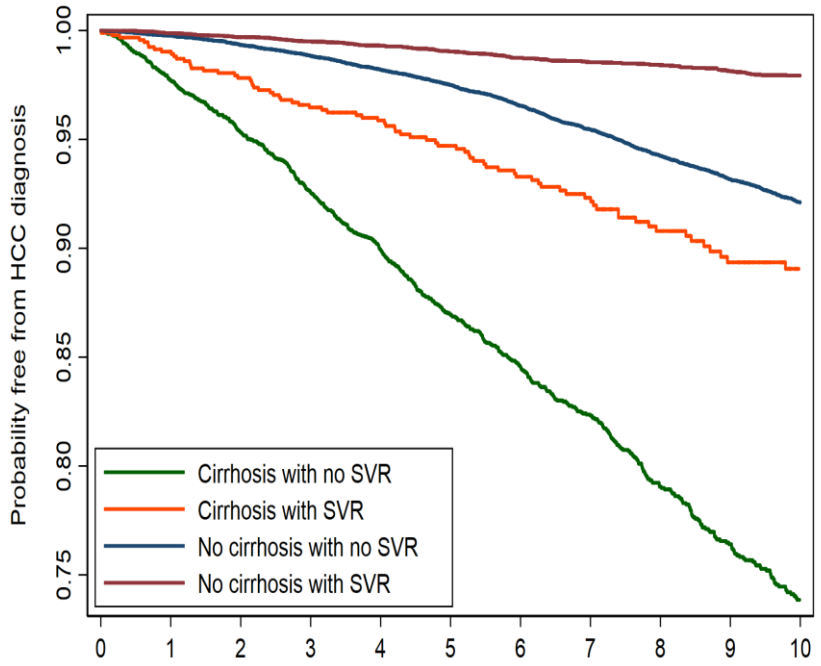
Addition of micro-eliminations will help in macro-elimination

Zhou, Lancet Infect Dis 2016

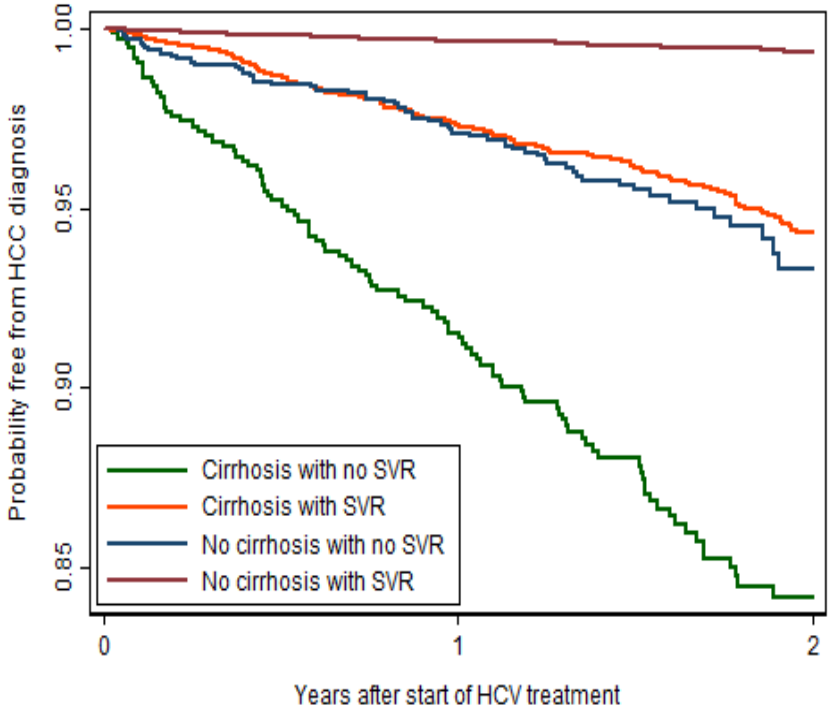
HCV Micro-elimination in easy-to-screen population

Cohort study in Veterans treated from 1999 to 2015

Survival free of HCC by cirrhosis and SVR status after **INF- regimens**



Survival free of HCC by cirrhosis and SVR status after **DAA-only**



Ioannou et al, Hepatol 2017

62,354 HCV pts without detectable HCC in 2015

More than 100,000 cured in August 2019: 25,000 remain to treat

HCV Micro-elimination in easy-to-screen population

Identification of untreated HCV RNA+ patients

Hepather: around 14500 HCV patients in 32 motivated centers

- **Decrease in the number of untreated patients:**
  - 1st october 2018 : 1 882 patients
  - 18st march 2019 : 1 309 patients
  - 2nd december 2019 : 1 143 patients

- **Around 10% of untreated patients**

Fibrosis stage	N (%)
F0 à F1	527 (52%)
F1/2 à F2	208 (21%)
F2/3 à F3	74 (7%)
F3/4 à F4	195 (19%)
Missing data	139
Total	**1 143**

- **No major difference in the profile of treated and untreated patients**

France REcherche Nord & sud Sida-hiv Hépatites
Agence autonome de l'Inserm
CO22
HEPATHER

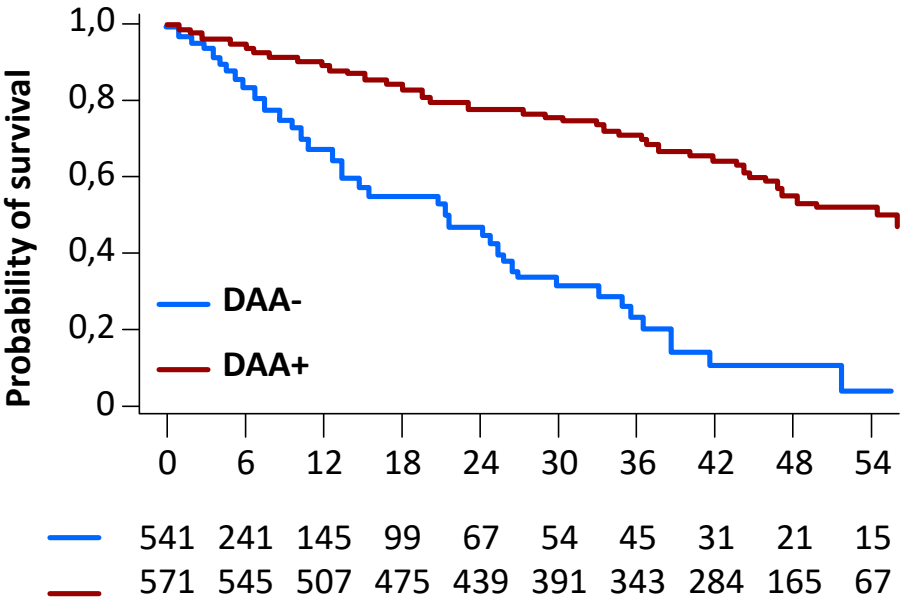
Unpublished Hepather data

CO22
HEPATHER

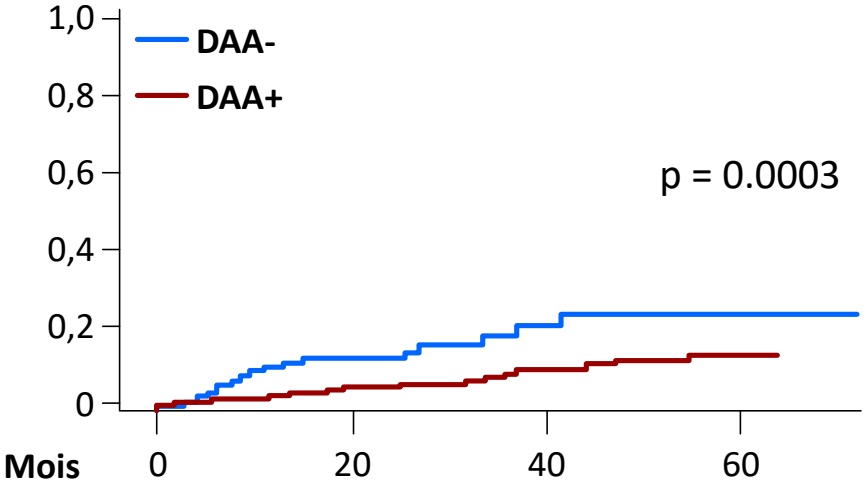
HCV Micro-elimination in easy-to-screen population: decompensated cirrhosis

- HEPATHER : prospective cohort including 699 patients prior decompensation of HCV cirrhosis with a median follow-up of 37 months
- SVR : 86 % (84 % in patients with CP-C and/or MELD > 20)

Mortality



Cumulated incidence of events



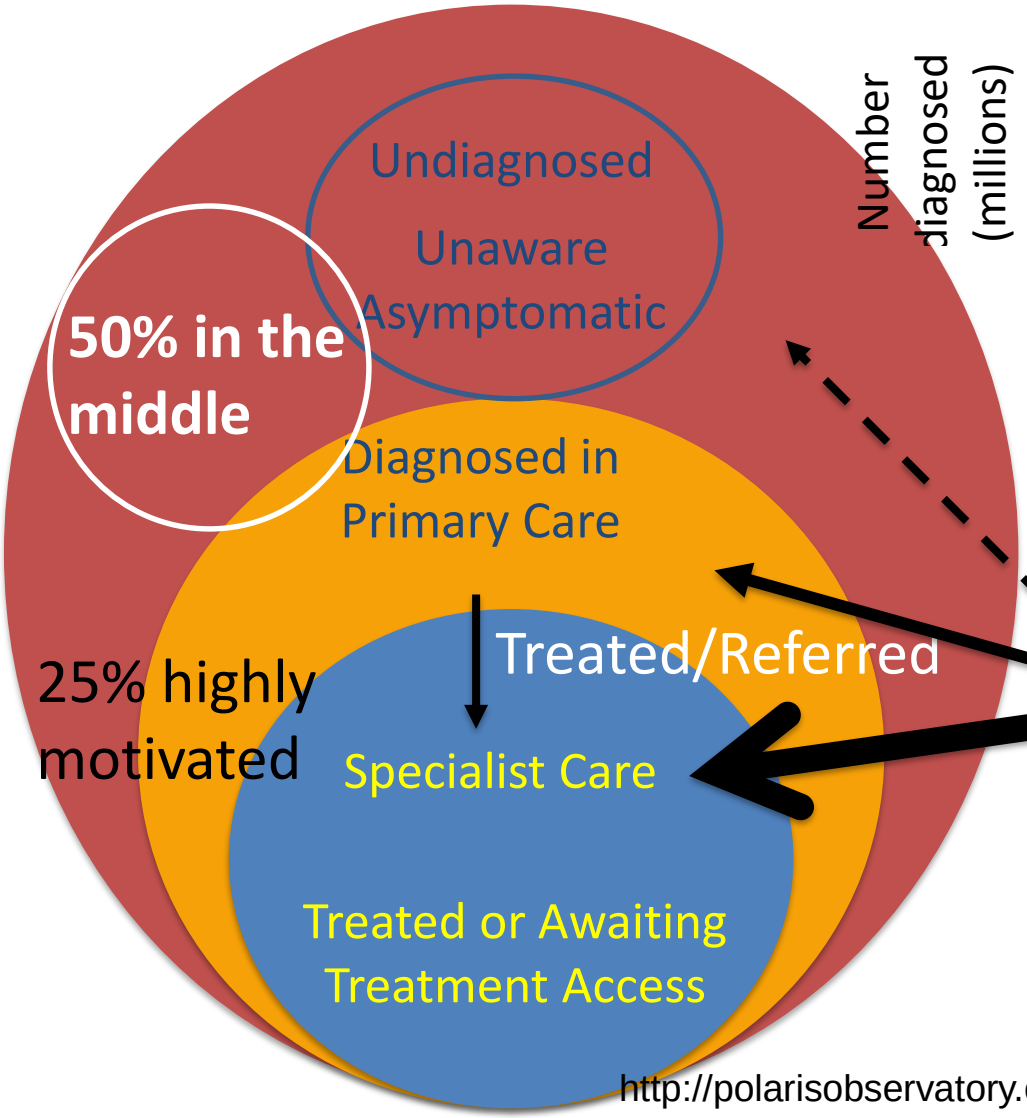
Mortality: adjusted HR 0.44, 95% CI 0.26-0.74 p=0.002

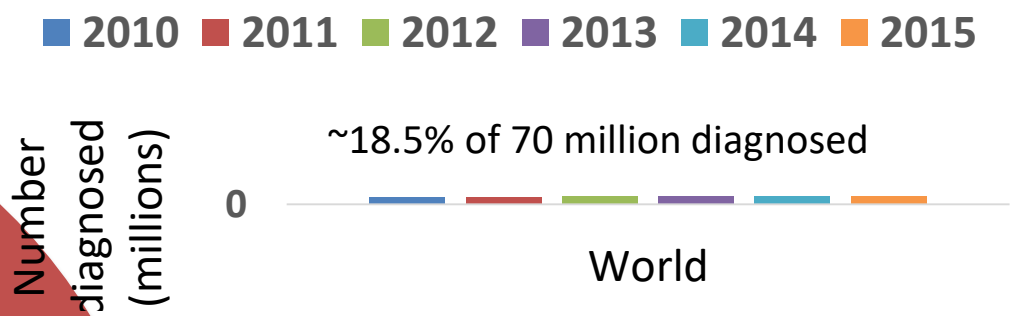
- **571 DAA+ and 128 (18.3%) untreated patients (DAA-)**

Pageaux GP et al. AASLD 2019; A1524

Micro-elimination in “high risk” patients

25% difficult to identify

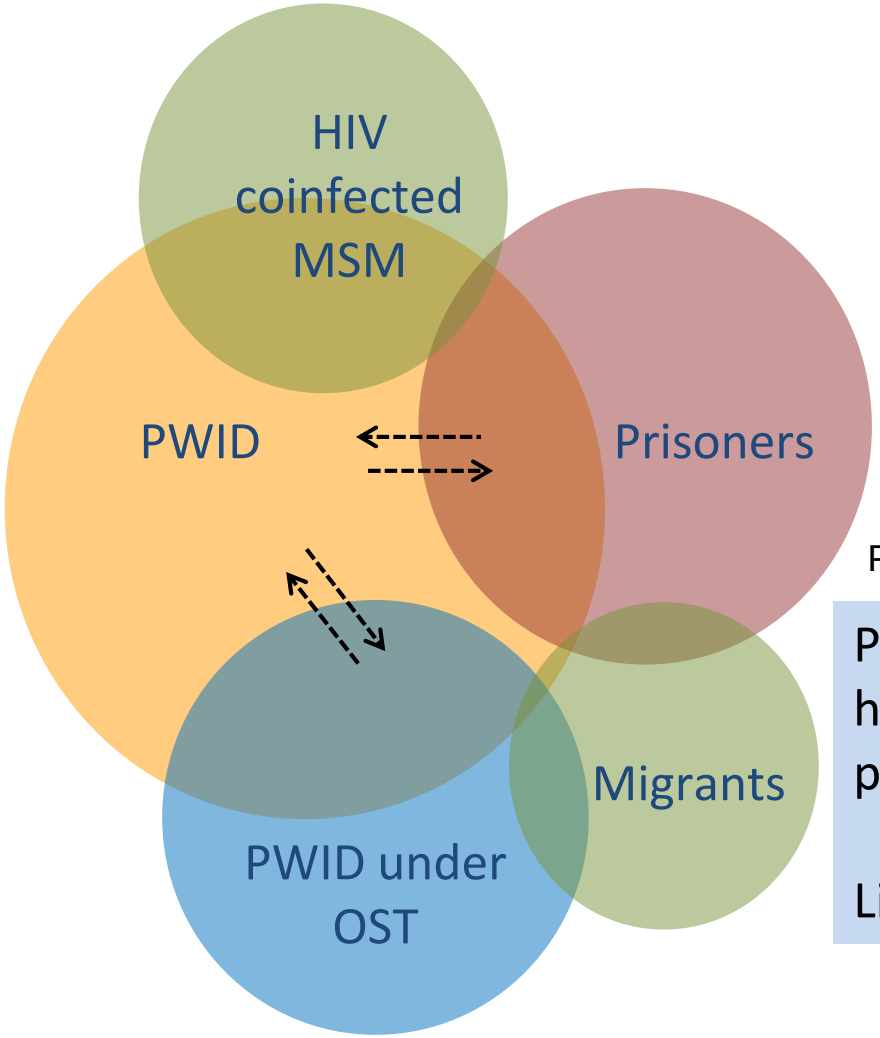




Increased Treatment Uptake

http://polarisobservatory.com/polaris/datasheet.htm downloaded 9/18/2016

HCV micro-elimination in high-risk patients



Prevalence: 4.3-6.7%
Screening in 36-70%:
- 46% HCV RNA+
- 3.9-46% treated

Remy A-J.
Presse Médicale 2005 & BEH 2017

Prevalence: >3-fold higher than the general population

Limited screening

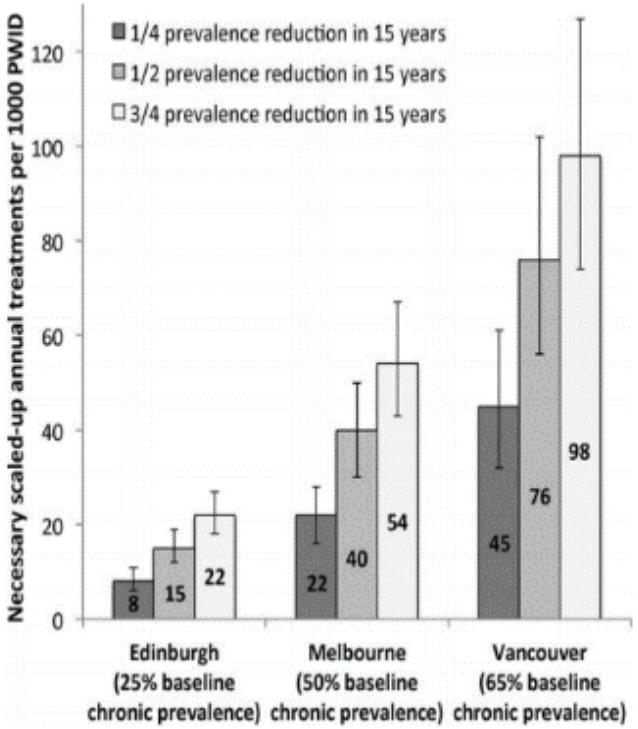
High-risk patients are also HCV high transmitters

Key GROUPS

Prisoners
MSM
PWID
Sex workers
Migrants

Treatment reluctants

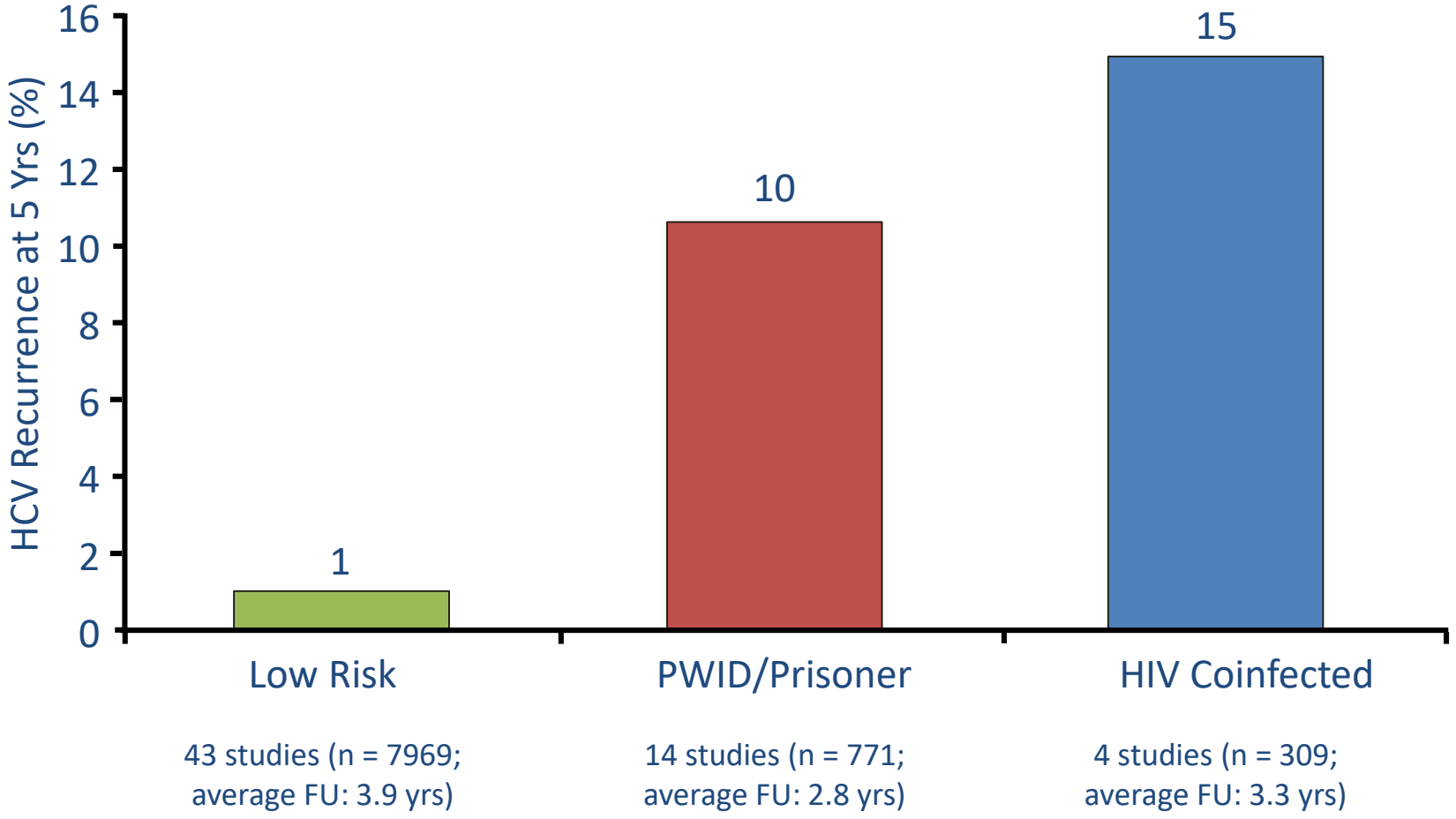
Dedicated screening programs
Counseling
Link to care



Modest rates of HCV treatment among active injecting drug users could effectively reduce transmission

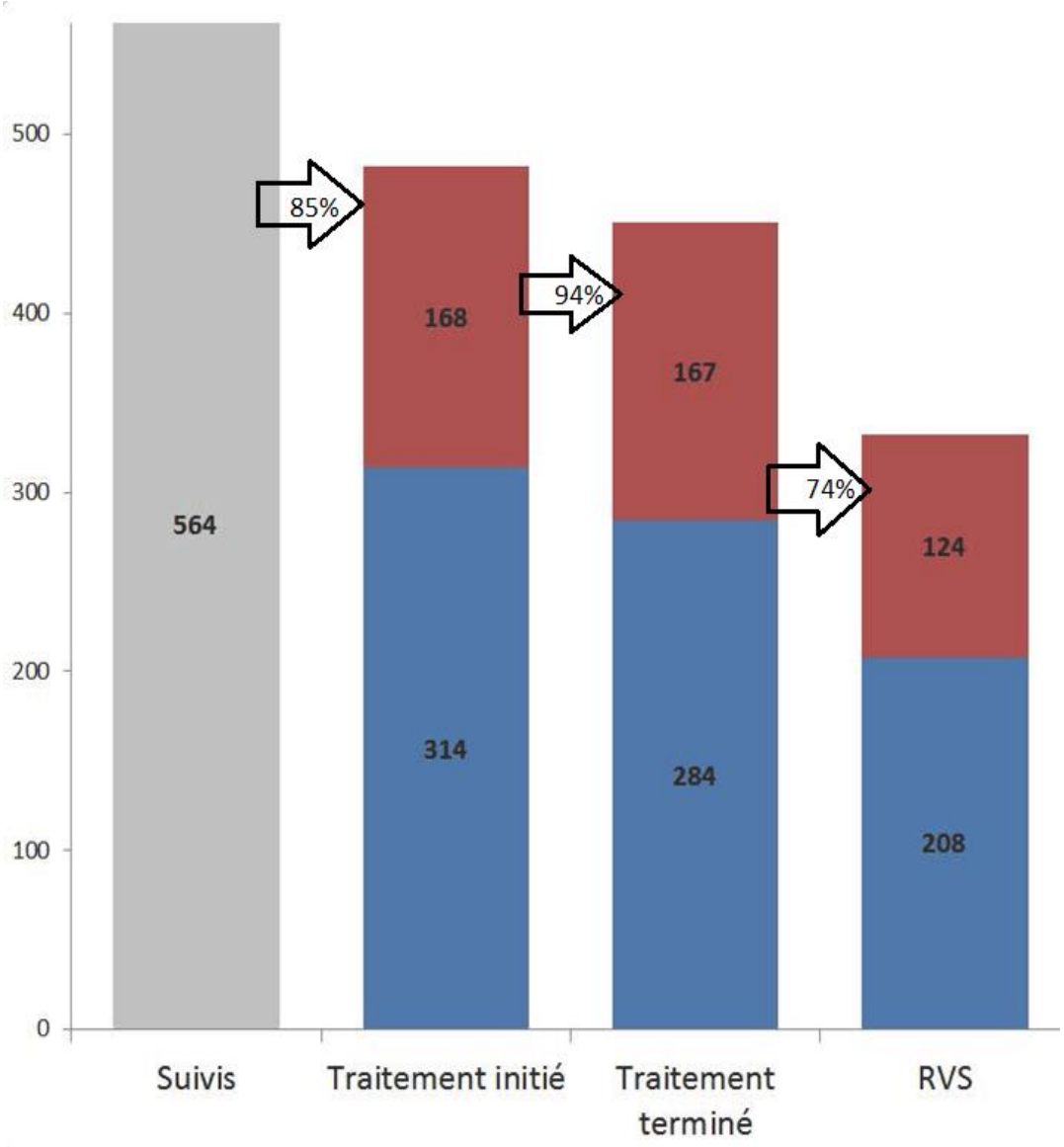
Martin NK, Hepatology 2013; 58:1598-1609

HCV reinfection over 5 years



Simmons B, et al. Clin Infect Dis. 2016:62:683-694.

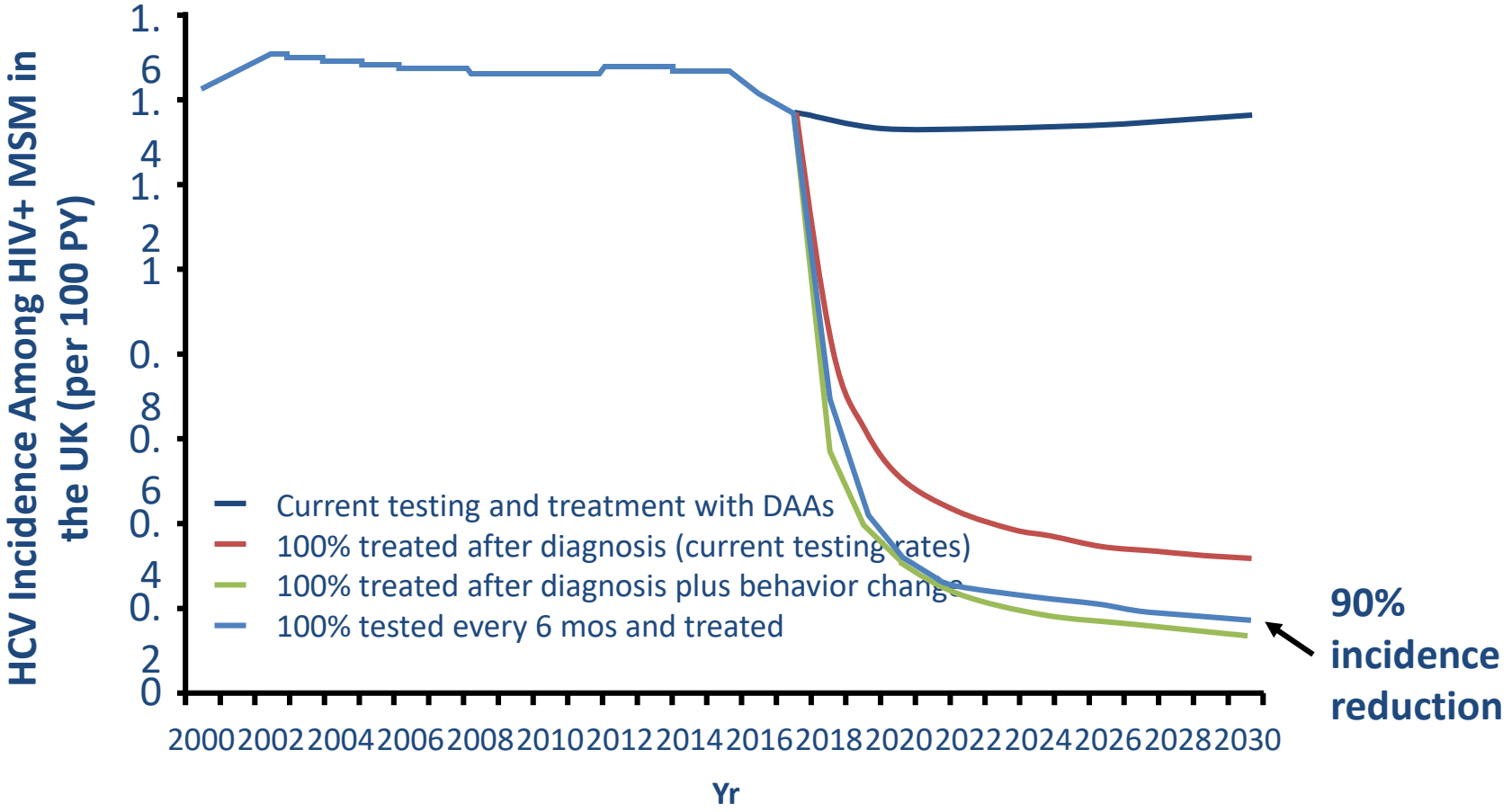
HCV elimination in the HEPAVIH ANRS cohort



In summary, proof of SVR in 59% of patients in this highly motivated cohort in Dec. 2017

Salmon D. Foie et VIH, Marseille 2017

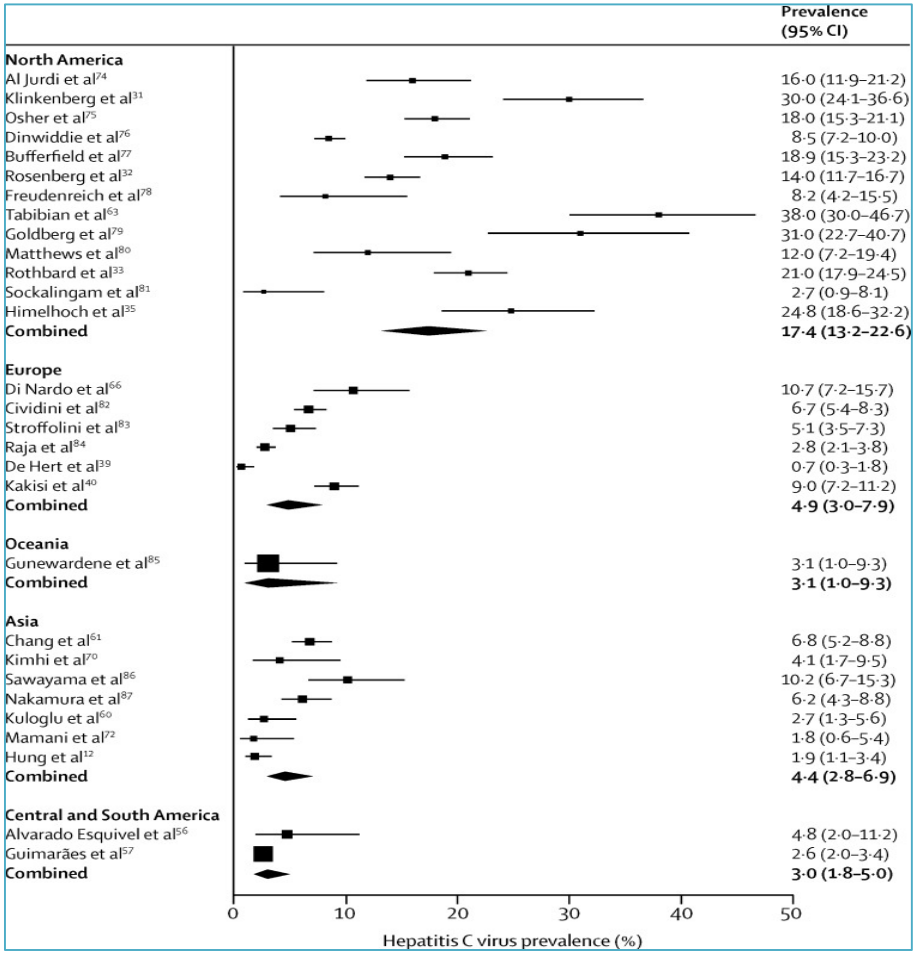
HIV+ MSM in UK Model: Elimination will require high treatment + more testing and harm reduction



Martin NK, et al. Clin Infect Dis. 2016;62:1072-1080; Salazar-Vizcaya L, et al. Hepatology. 2016;64:1856-1869.

Micro-elimination in psychiatric patients

HCV	Studies (N)	Prevalence (95% CI)
North America	13	**17.4%** (13.2 – 22.6)
Europe	6	**4.9%** (3.0 – 7.9)
Oceania	1	**3.1%** (1.0 – 9.3)
Africa	0	- -
Asia	7	**4.4%** (2.8 – 6.9)
Central and South America	2	**3.0%** (1.8 – 5.0)

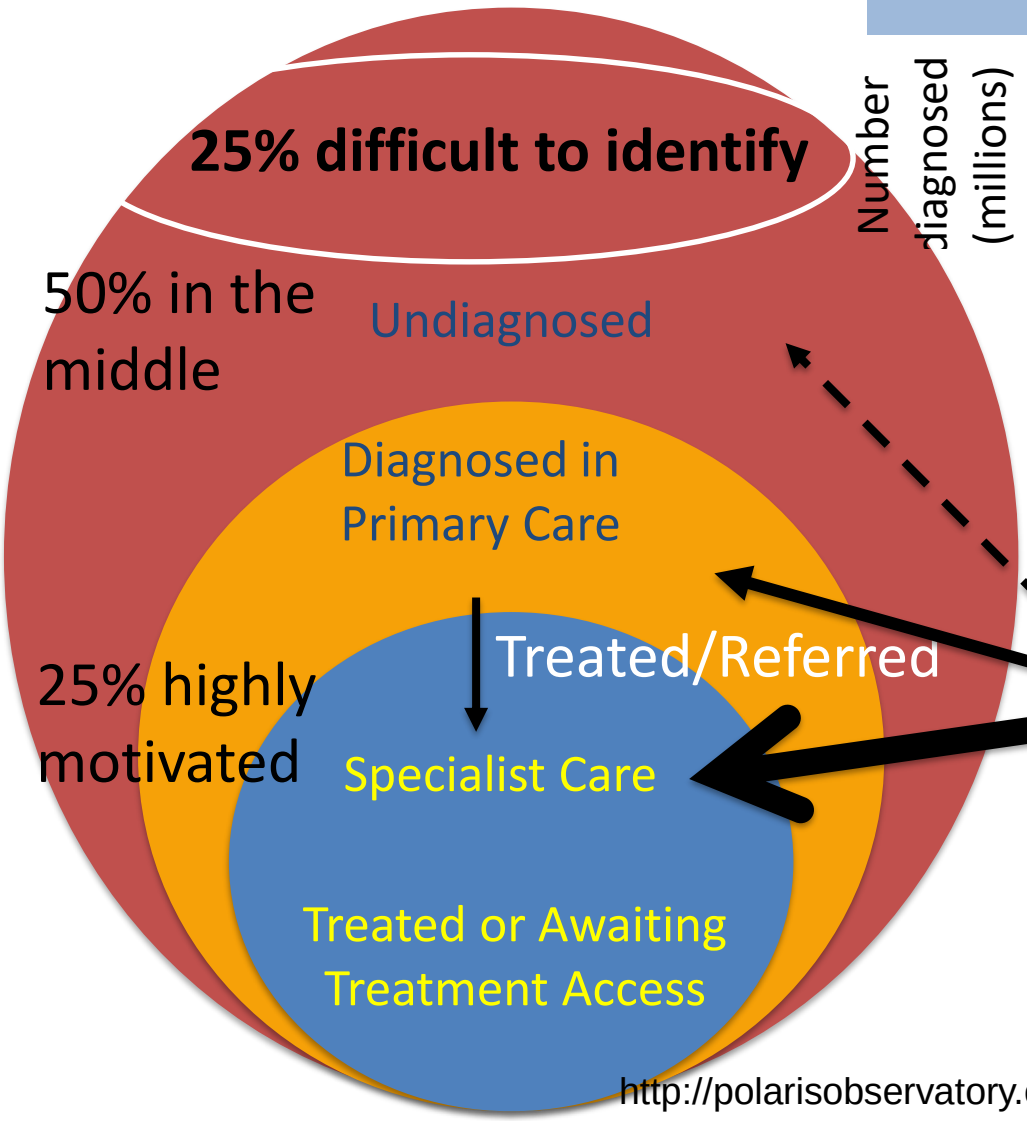


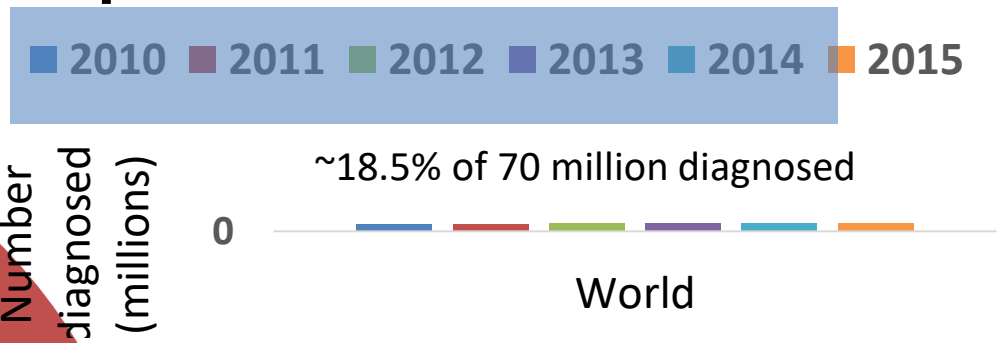
Very low rate of treatment despite a 10-fold increased prevalence

Bauer-Staeb C, et al.Lancet Psychiatry 2017; 4 : 685-693.

Hughes E, et al..Lancet Psychiatry 2016; 3 : 40-48.

Micro-elimination in “difficult to identify” patients



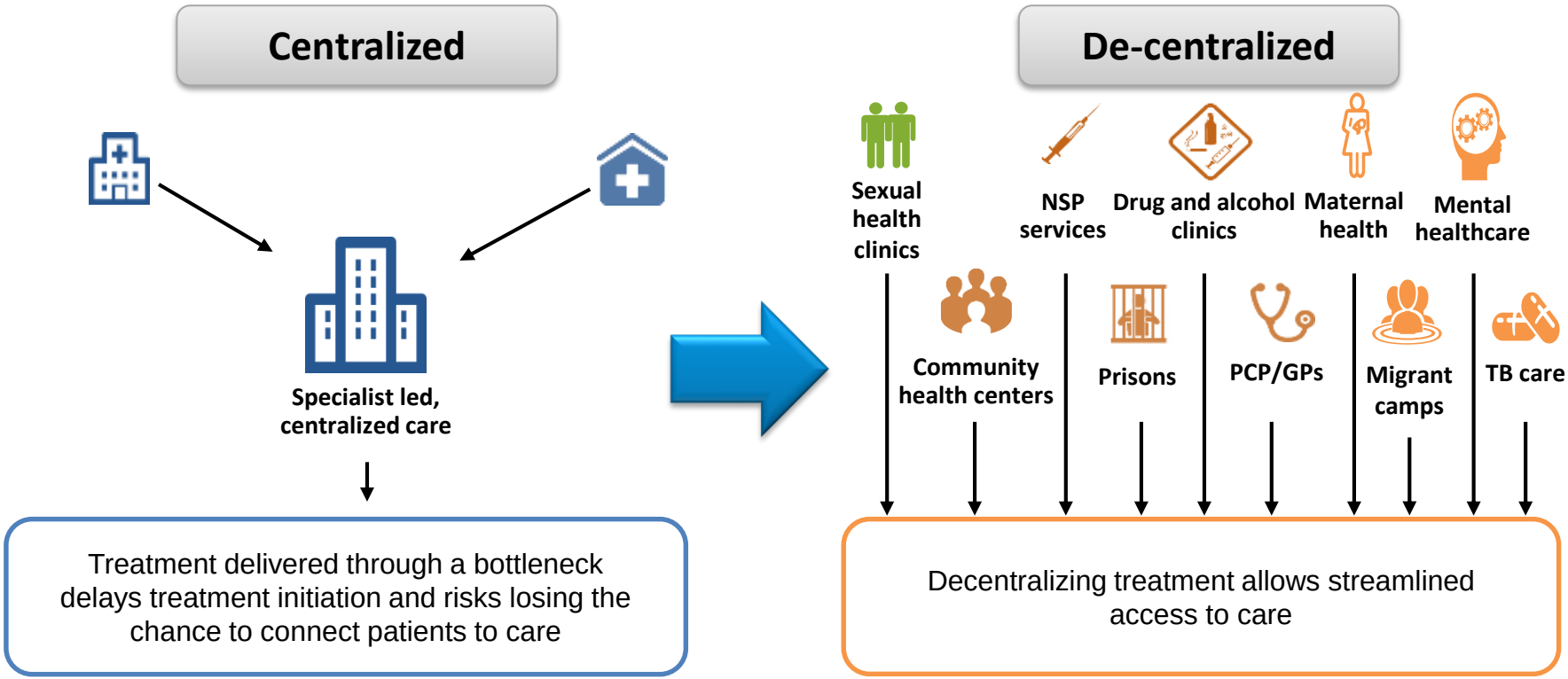


Increased Treatment Uptake

http://polarisobservatory.com/polaris/datasheet.htm downloaded 9/18/2016

“De-centralize” screening and care in communities

Patients may face difficulties in accessing testing and treatment facilities. Different populations have differing needs and require specific settings and measures in place to access treatment



GP, general practitioner; NSP, needle and syringe program; PCP, primary care practitioner; TB, tuberculosis.

1.EMCDDA Hepatitis C Among Drug Users in Europe. Available at: http://www.emcdda.europa.eu/system/files/publications/2740/att_212353_EN_EMCDDA_POD_2013_Hep%20C%20treatment.pdf (accessed December 2018).

2. WHO Implementing Comprehensive HIV and HCV Programmes with People Who Inject Drugs. Available at: http://www.who.int/hiv/pub/idu/IDUIT_2017.pdf?ua=1. (accessed December 2018)

3. WHO Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. Available at https://www.who.int/hepatitis/publications/hepatitis-c-guidelines-2018/en/ (accessed December 2018) .

“De-centralize” screening and care in communities

- HCV Elimination is feasible since tools are available

- Micro-elimination, a public health challenge, needs education of patients and health care providers, including doctors (issues about the place of screening and access to care)

Barriers to antiviral therapies concern patients and doctors

The majority of physicians considers testing and treatment of PWID as important, but there is a need for education related to HCV Treatment

Figure 1. Percentage of Physicians Rating HCV Testing and Treatment Among PWID as Important

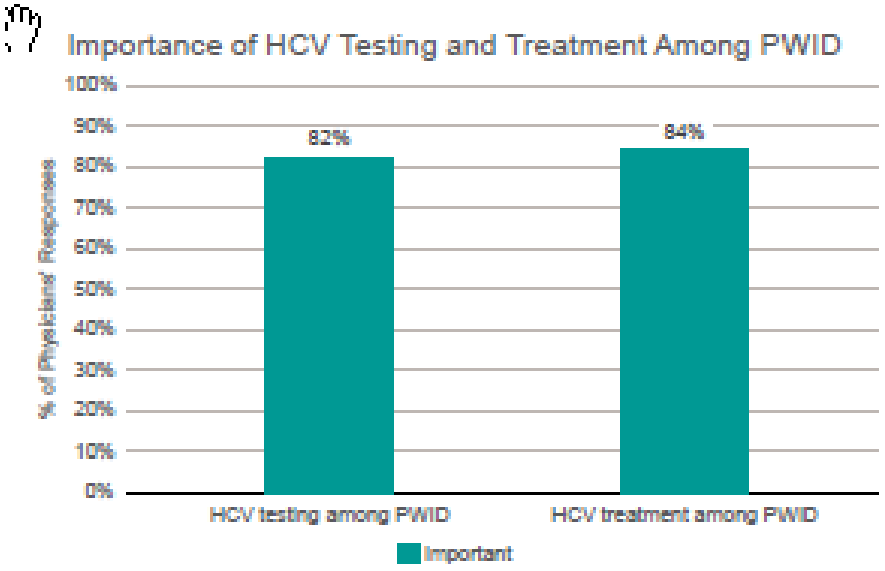
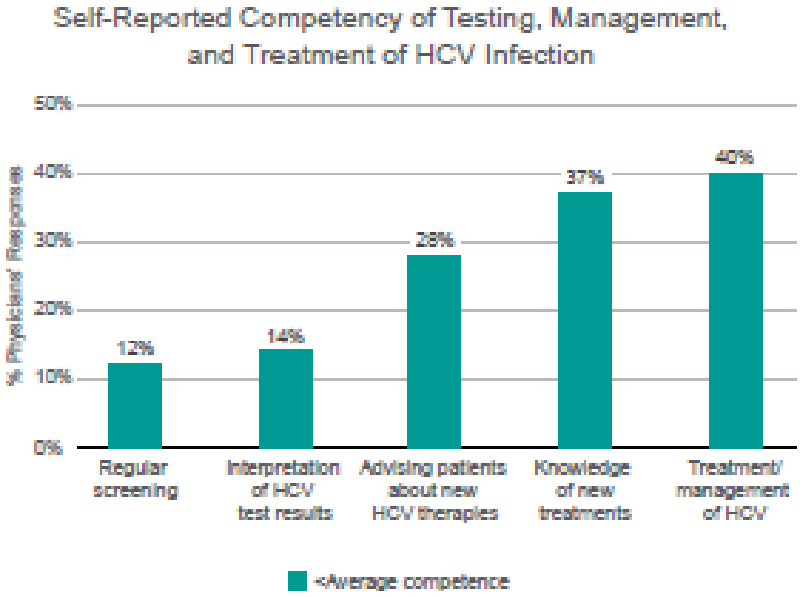


Figure 2. Physicians' Self-Reported Competence Levels Related to Testing, Management, and Treatment of HCV Infection



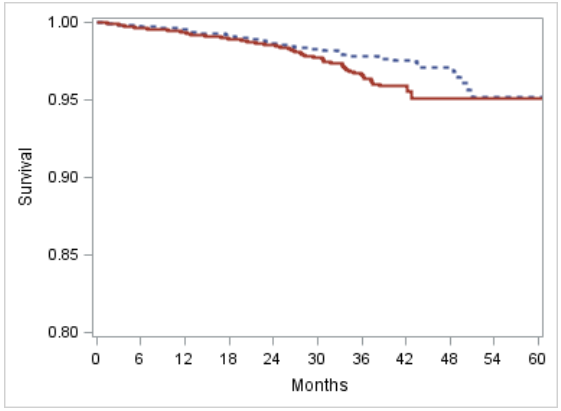
Litwin AH et al. J Viral Hepatitis 2019

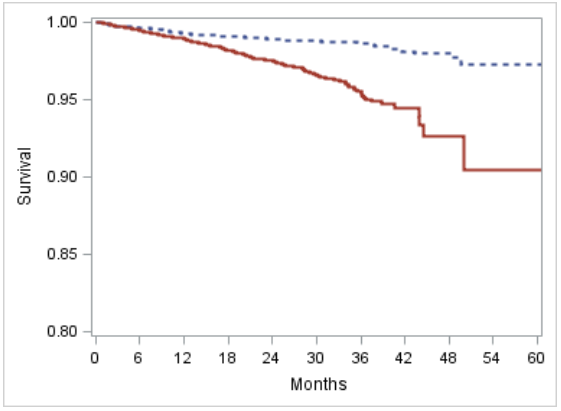
France REcherche Nord & sud Sida-hiv Hépatites
Agence autonome de l'Inserm
CO22
HEPATHER

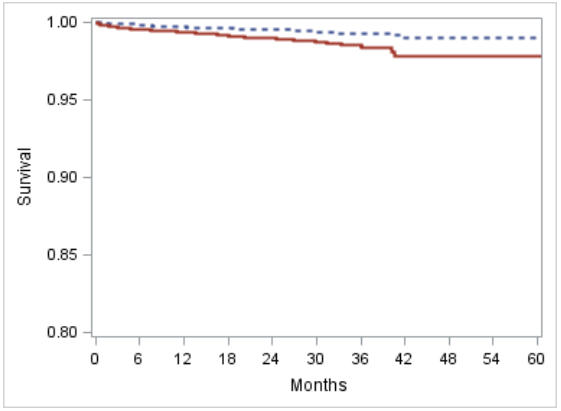
Barriers to antiviral therapies concern patients and doctors

All-cause mortality | Hepatocellular carcinoma | Decompensated cirrhosis

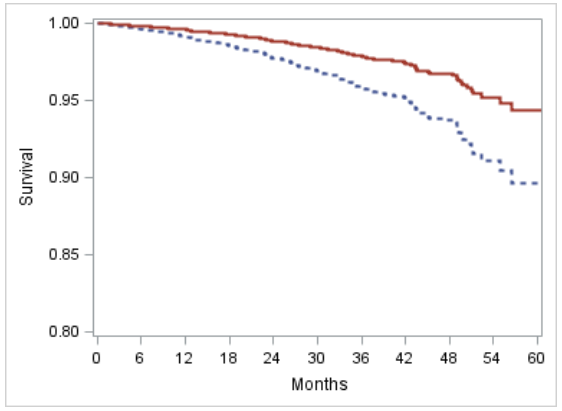
Unadjusted survival curves

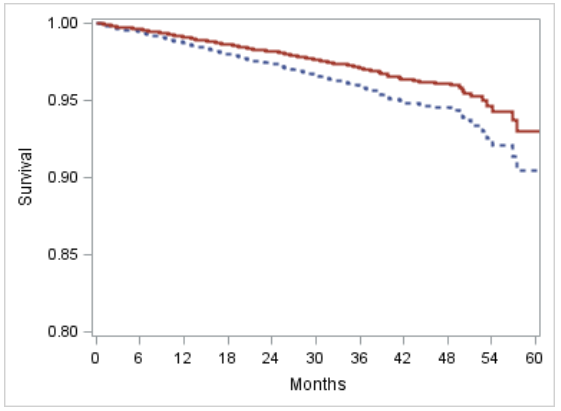


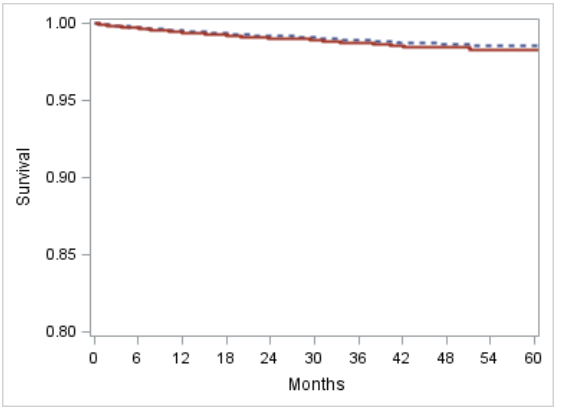




Multivariate-adjusted survival curves







	Months	0	12	24	36	48	60
N at risk	DAA+	7344	5448	3469	1012	59	6
	DAA-	9895	4774	2889	1344	360	10

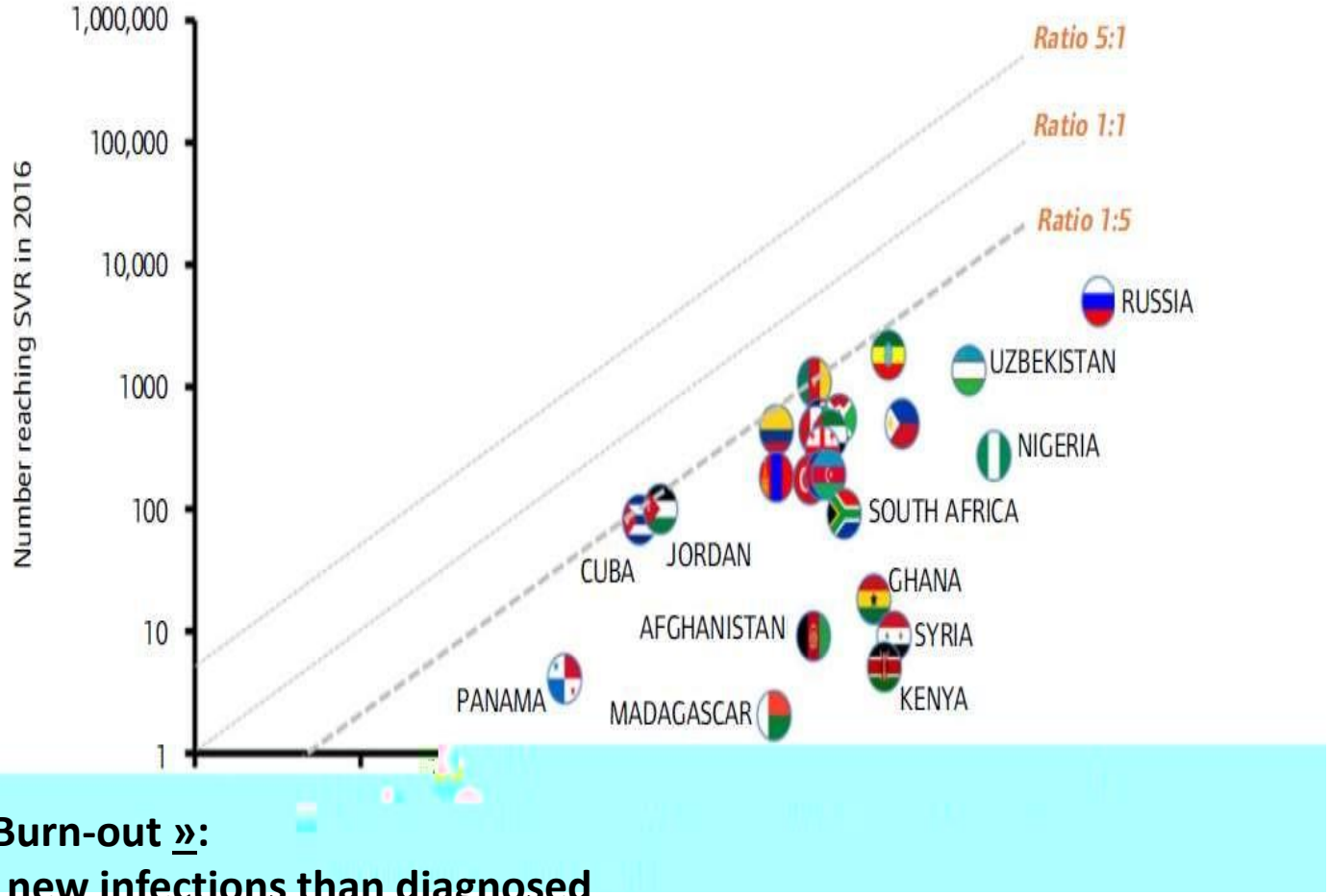
	Months	0	12	24	36	48	60
N at risk	DAA+	7308	5366	3368	977	57	6
	DAA-	9895	4751	2878	1337	355	10

	Months	0	12	24	36	48	60
N at risk	DAA+	7330	5408	3432	996	59	6
	DAA-	9895	4766	2888	1342	360	10

DAA+ DAA-

Carrat F et al. The Lancet 2019

Global HCV Elimination: Cures vs New Infections



«Diagnosis Burn-out »:
5-fold more new infections than diagnosed
5-fold less cure than new infections

Hill AM, et al. J Virus Erad 2017; **3:**117–123.

Conclusions

- HCV Elimination is feasible since tools are available
- This public health challenge needs education of patients and health care providers, including doctors (issues about the place of screening and access to care)
- One of the solutions = action by sub-populations

  Addition of micro-eliminations will help in macro-elimination
- To prefer « individualization » than simplification of screening and treatment policies