The continuum of Care and late presentation: Implementing the consensus definition in hepatitis

HepHIV 2017 Malta Conference, February 2nd 2017, Malta

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Conflict of Interest

Jürgen Rockstroh has received:

- Honoraria for lectures and/or consultancies from Abbott, AbbVie, Bionor, BMS, Cipla, Gilead, Janssen, Merck and ViiV.
- Research grants from Dt. Leberstiftung, DZIF, NEAT ID.

Natural History of HCV Liver Disease

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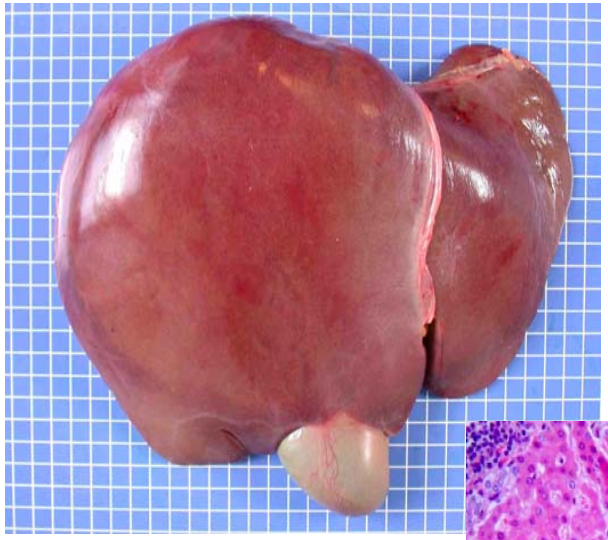
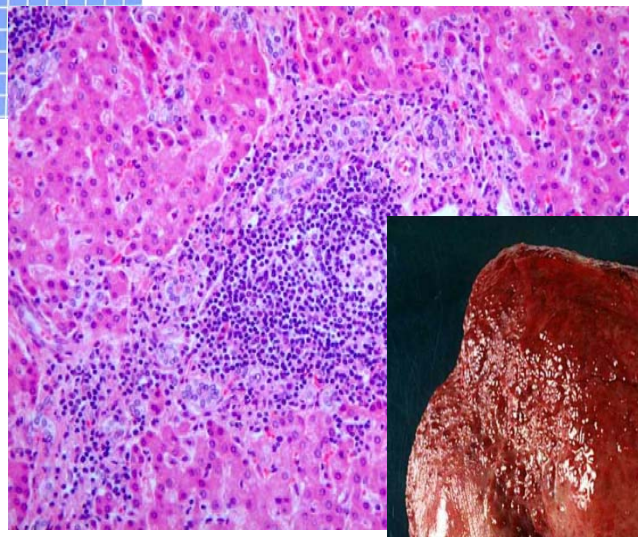
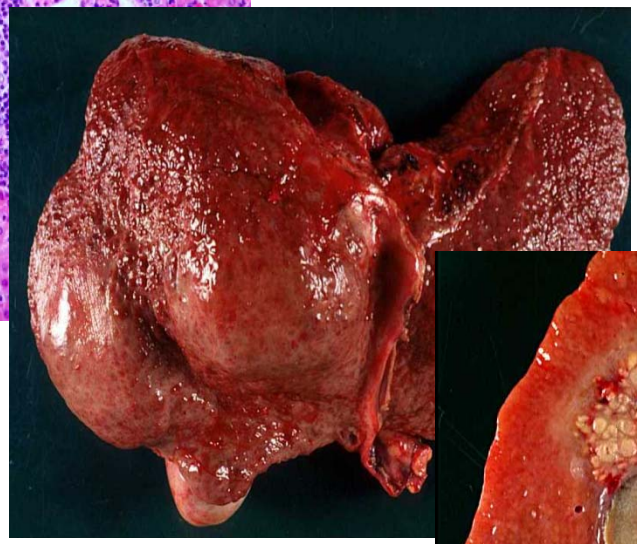


Liver failure (2 – 5% / yr)

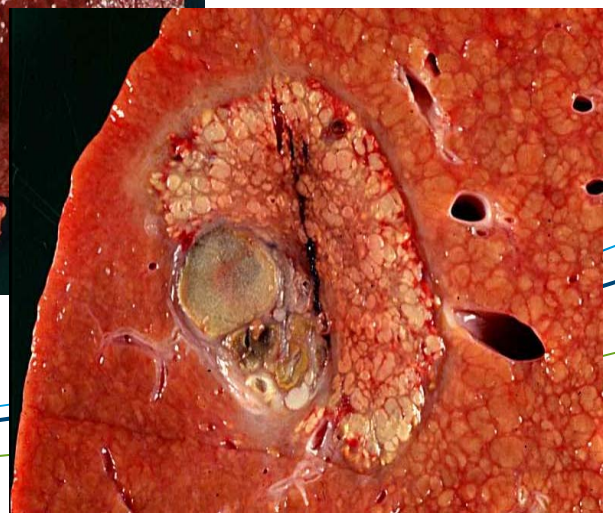


~55-85%

25-30 yrs



2 - 4% / yr



Leading causes of mortality and trends 1990 &2013

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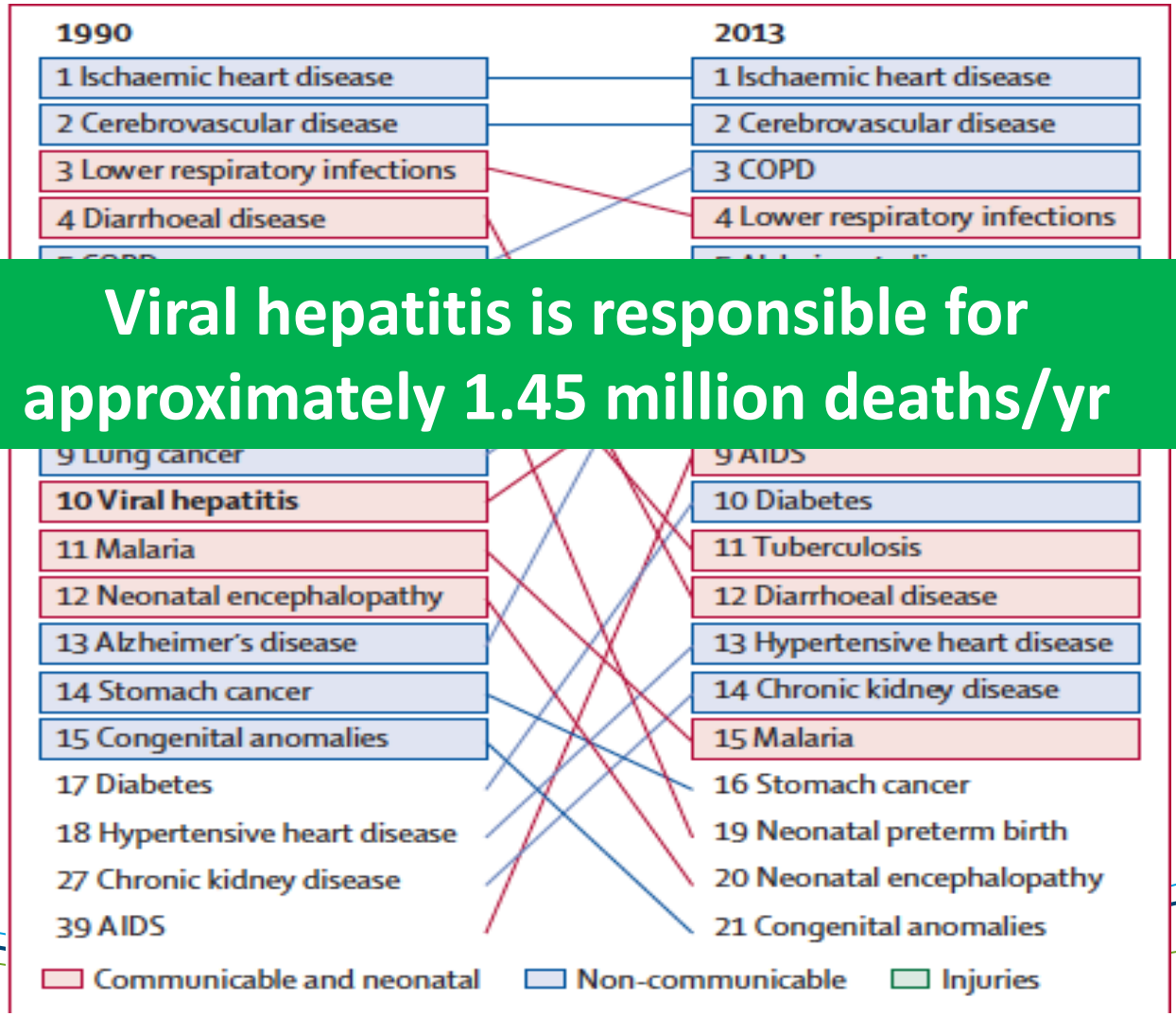
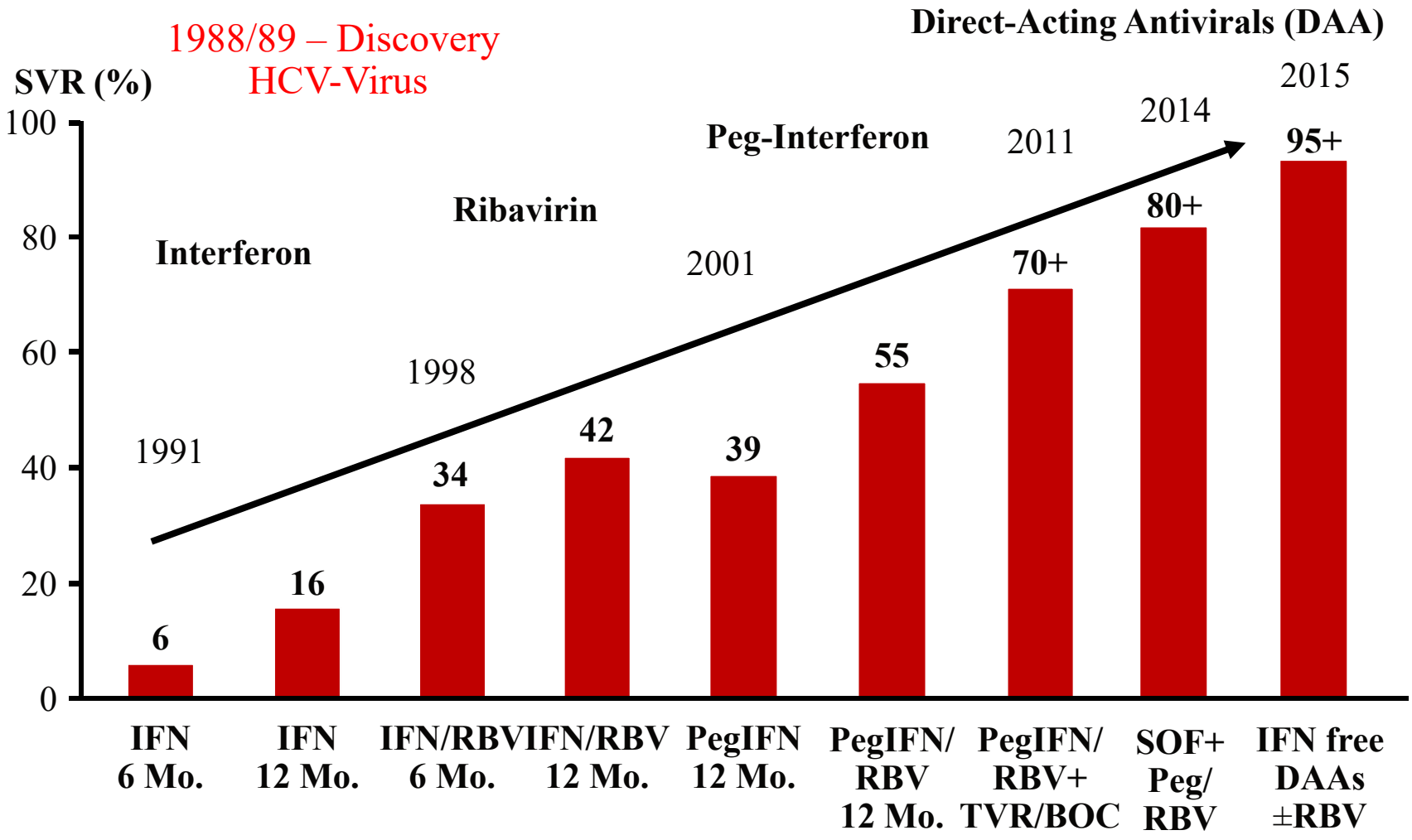


Viral hepatitis is responsible for approximately 1.45 million deaths/yr

Stanaway et al. Lancet 2016

Mile stones in the treatment of HCV Genotype 1 infection

With New Drugs most will be cured



Kronenberger B et al. *Dtsch. Med. Wochenschr*. 2013; **138**: 1796-1800.

Question

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How many people are aware of their HCV infection worldwide?

1. 75%
2. 50%
3. 25%
4. <10%

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Distribution of HCV in adults using available data and extrapolations

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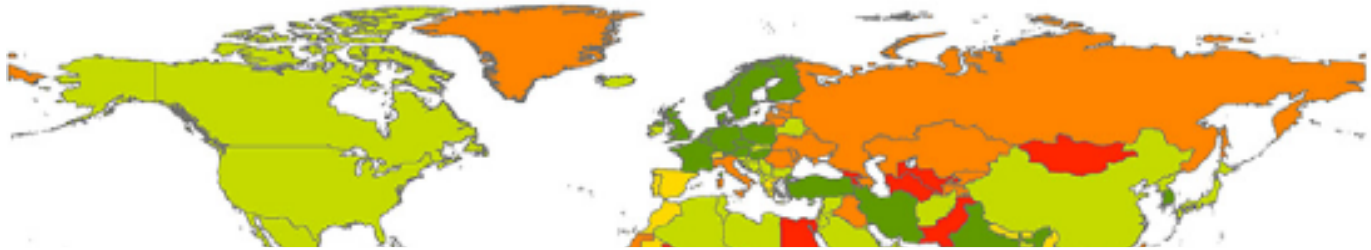

Only 5% of the 170 million HCV-infected people are aware of their infection !

Thomas DL, Lancet 2010;376:1441-1442

Thomas DL, AVT 2012

1.0% - <1.5%

1.5% - <2.0%

2.0% - <5.0%

≥5.0%

Gower J Hepatol 2014

Consensus definition

- **With the >95% cure rates achievable with modern DAA combination HCV therapy, increased interest has been generated to create a HCV treatment cascade which can provide a framework for evaluating the delivery of HCV care over time and also can be useful in monitoring the impact of new screening efforts**
- **Most cascade of care analysis so far however, show that less than 10% of HCV patients have been successfully treated so far which underlines the slow uptake of treatment mostly because of the high cost burden associated with HCV therapy and the various treatment restrictions in place.**
- **Introducing a consensus definition of late presentation with viral hepatitis is important to create a homogenous, easy to use reference for public health authorities in Europe and elsewhere to better assess the clinical situation on a population basis.**

Consensus definition

Press release

New consensus definition of late presentation for viral hepatitis

The number of people living with viral hepatitis in increasing – a better understanding of the testing policies and strategies is needed.

Thursday 22 October 2015, Barcelona: Today, EASL and HIV in Europe announce a consensus definition of late presentation for viral hepatitis. The announcement coincides with the European AIDS Conference in Barcelona and aims to encourage policy makers, health professionals, public health institutions and civil society organisations to implement this definition to improve the European surveillance of and response to the viral hepatitis epidemic.

Over 13 million adults are living with hepatitis B and 15 million with hepatitis C in the WHO European Region and most of the people remain undiagnosed. Effective treatments for both HBV and HCV are available with great impact on the possibility to treat people if they are diagnosed timely. However, it remains unknown whether current testing policies and strategies are successful in reaching the undiagnosed population at the right time. Further, linkage to the health care system and their ability to provide comprehensive care is also unknown.

As a consequence, a large proportion of the chronically infected population enters care only after they have developed clinical symptoms and others after the initiation of treatment would have provided them with an optimal treatment response.

A consensus definition on late presentation for viral hepatitis is essential in order for public health authorities in Europe and elsewhere to be able to understand and respond to the issues around late presentation of viral hepatitis. The consensus definition will contribute in both improving surveillance of viral hepatitis as well as testing policies and strategies.

In early 2015 a group of viral hepatitis experts within the HIV Europe Initiative formed a working group to develop a consensus definition for viral hepatitis. After discussions, meetings and several reviews the final two agreed upon definitions were approved by the EASL GB in early October 2015:

Definition 1:

Advanced HBV, HCV or HDV associated liver disease is clinically defined by presence of hepatocellular carcinoma or decompensated cirrhosis (jaundice, hepatic encephalopathy, clinically detectable ascites, variceal bleeding).

Definition 2:

Late presentation of HBV or HCV associated liver disease is defined as a patient with chronic hepatitis B or C and significant fibrosis (≥F3 assessed by APRI score >1.5, FIB-4 >3.25, Fibrotest > 0.59 or alternatively a FibroScan >9.5 kPa) with no previous antiviral treatment.

Stefan Mauss, HIV in Europe Steering Committee Member, says: 'this is an important milestone for the public health response to viral hepatitis. A key step will be to convince policy makers, health authorities and researchers to implement the definition to contribute to understanding the magnitude of the proportion of late presenters and monitor and evaluate changes in these numbers.'

In 2011 a consensus definition for late presentation for HIV was presented and has since then been widely implemented in Europe. It has contributed to shed light on the number of people diagnosed late for HIV and has been used to evaluate current testing policies and strategies.

Jürgen Rockstroh, co-chair of the HIV in Europe Steering Committee, continues: 'the HIV late presentation definition has been a valuable tool in assessing current HIV testing strategies and dealing more effectively with HIV testing. I am excited to see improvements in viral hepatitis surveillance and testing as a result of this new definition and hope that it will be well received and widely implemented in Europe and elsewhere as we have seen with the HIV definition.'

Consensus definition

- **Presentation with advanced liver disease due to chronic viral hepatitis for medical care is defined as a patient with chronic hepatitis B, C or D and significant fibrosis (≥F3 assessed by APRI score >1.5, FIB-4 >3.25, Fibrotest > 0.59 or alternatively a transient elastography (FibroScan) >9.5 kPa) with no previous antiviral treatment.**
- **Late stage liver disease due to chronic viral hepatitis is clinically defined by presence of decompensated cirrhosis (jaundice, hepatic encephalopathy, clinically detectable ascites, variceal bleeding) and/or hepatocellular carcinoma.**

Submitted 2016

Has increased rollout of DAA therapy decreased the burden of late presentation and advanced liver disease in patients starting HCV therapy in Germany?

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- **The GECCO cohort is a multicenter cohort from 9 German sites.**
- **All treatment-naïve HCV mono- (n=822) and coinfected (n=197) patients (n=1019) initiating DAA-based treatment since 2014 were analysed.**
- **Advanced liver disease was considered a liver stiffness >9.5 kPa in transient elastography (n=718) or APRI score >1.5 (n=301).**
- **Fisher's exact, chi-square and Mann-Whitney U test were used for statistical analysis.**

Results: GECCO cohort

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Baseline characteristics

	n=1019
Median age [years] (IQR)	50 (41-57)
Sex male [%] (n)	64 (651)
Median CD4-cells [/µl] (IQR)	585 (398-768)
Median HCV-RNA [IU/ml] (IQR)	1.000.000 (288.327-2.933.105)
IL28B C/C GT [%]	31 (129/416)
Median baseline ALT [U/l] (IQR)	69 (43-121)
Liver cirrhosis [%] (n)	22 (219/1019)
OST [%]	25 (254/1019)

Distribution of DAA-treated HCV patients with/without advanced liver disease over time

year	% no/minimal fibrosis (n)	% advanced fibrosis (n)
2014 (n=264)	56 (149)	44 (115)
2015 (n=586)	75 (439)	25 (147)
2016 (n=169)	70 (119)	30 (50)

Question

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How many patients with chronic HCV present late in your country?

1. >50%
2. 25-50%
3. 10-25%
4. <10%

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Regional Differences across Europe in Advanced Fibrosis and Cirrhosis among HIV/HCV Co-infected Persons between 2010-2015

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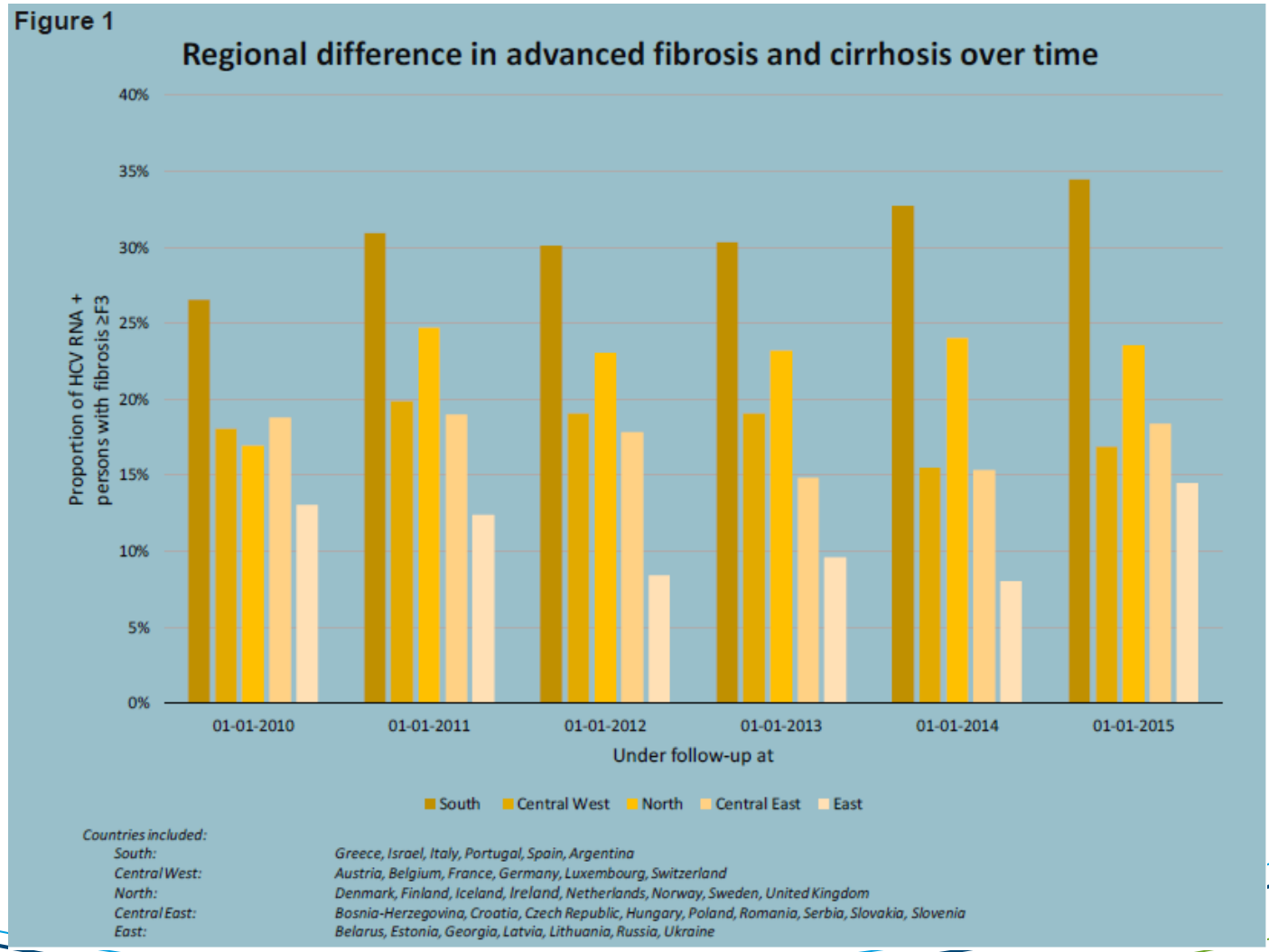
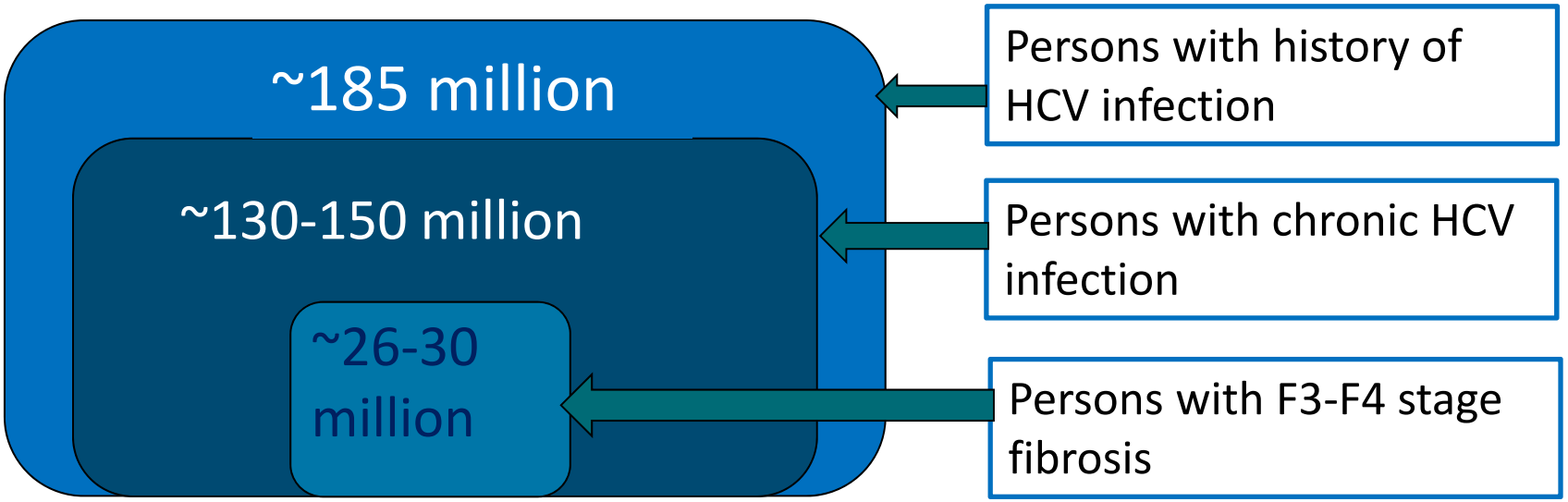
Figure 1

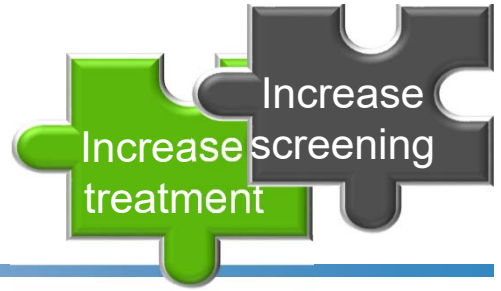


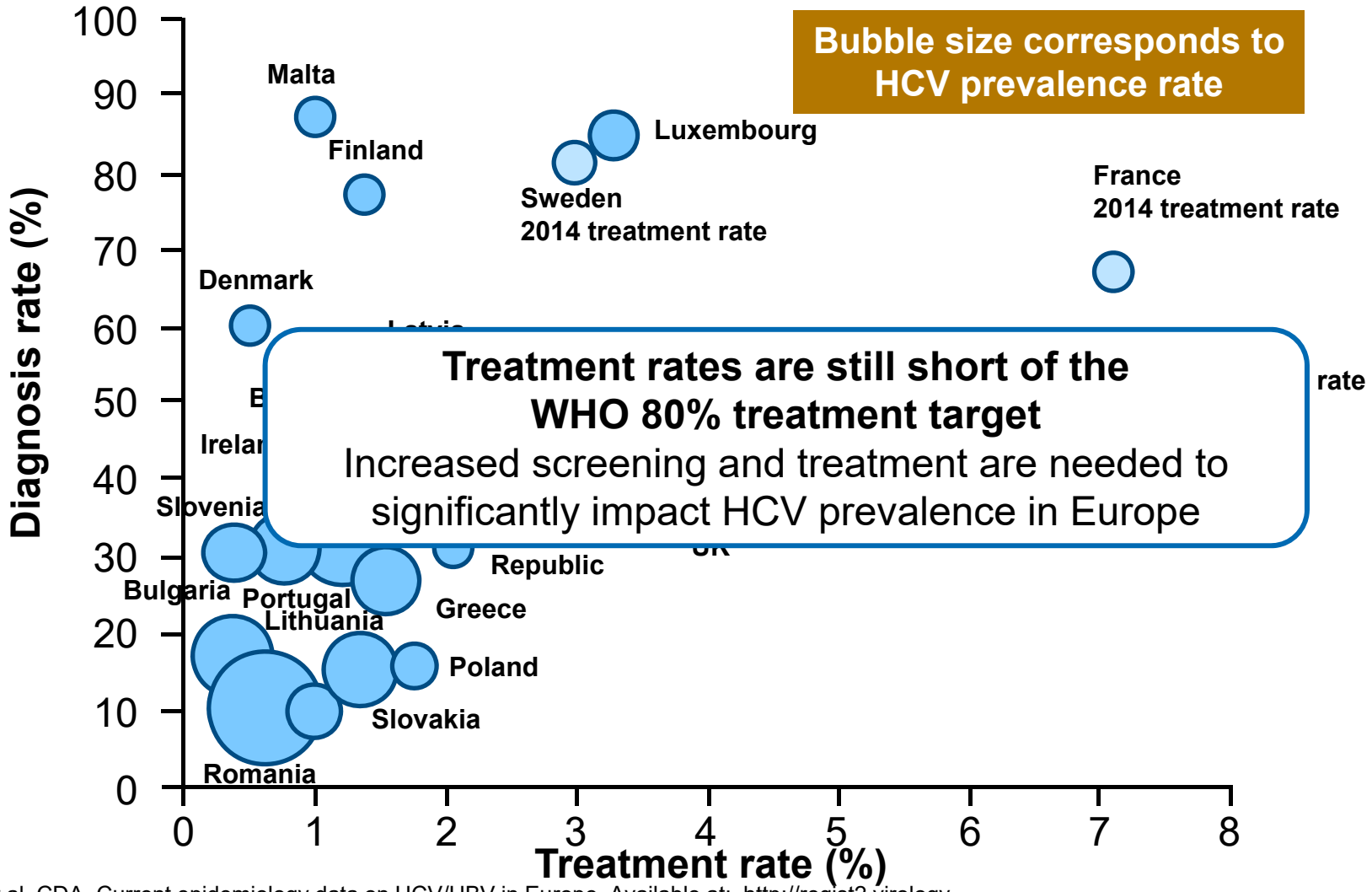
Amale S et al. HepHIV 2017 Malta Conference 2017

How many people need HCV treatment?
Everyone with HCV !!



Diagnosis and treatment rates vary around the world and across regions



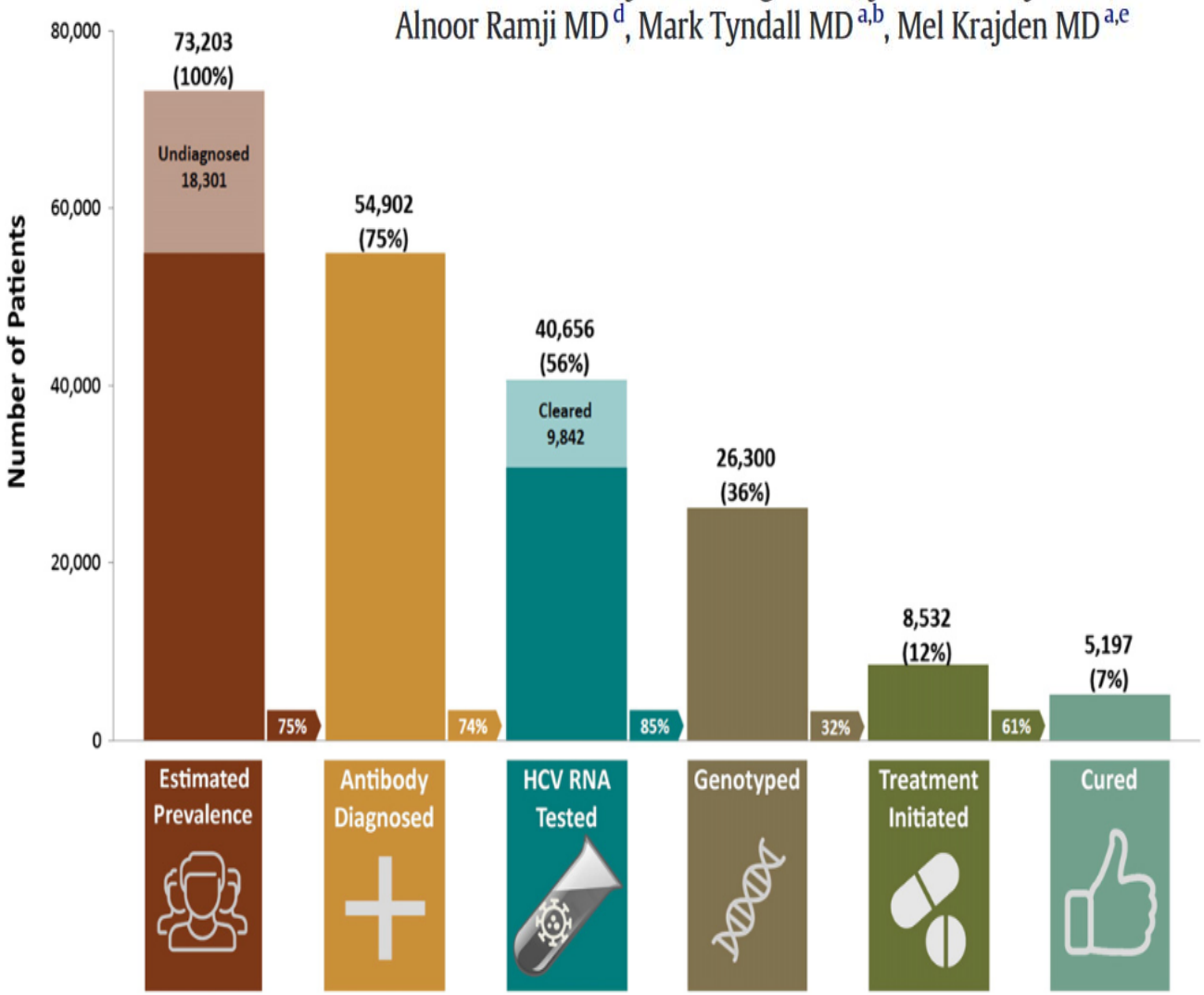


Razavi H, et al. CDA. Current epidemiology data on HCV/HBV in Europe. Available at: http://regist2.virology-education.com/2015/1euhep/03_Razavi.pdf (accessed October 2016)

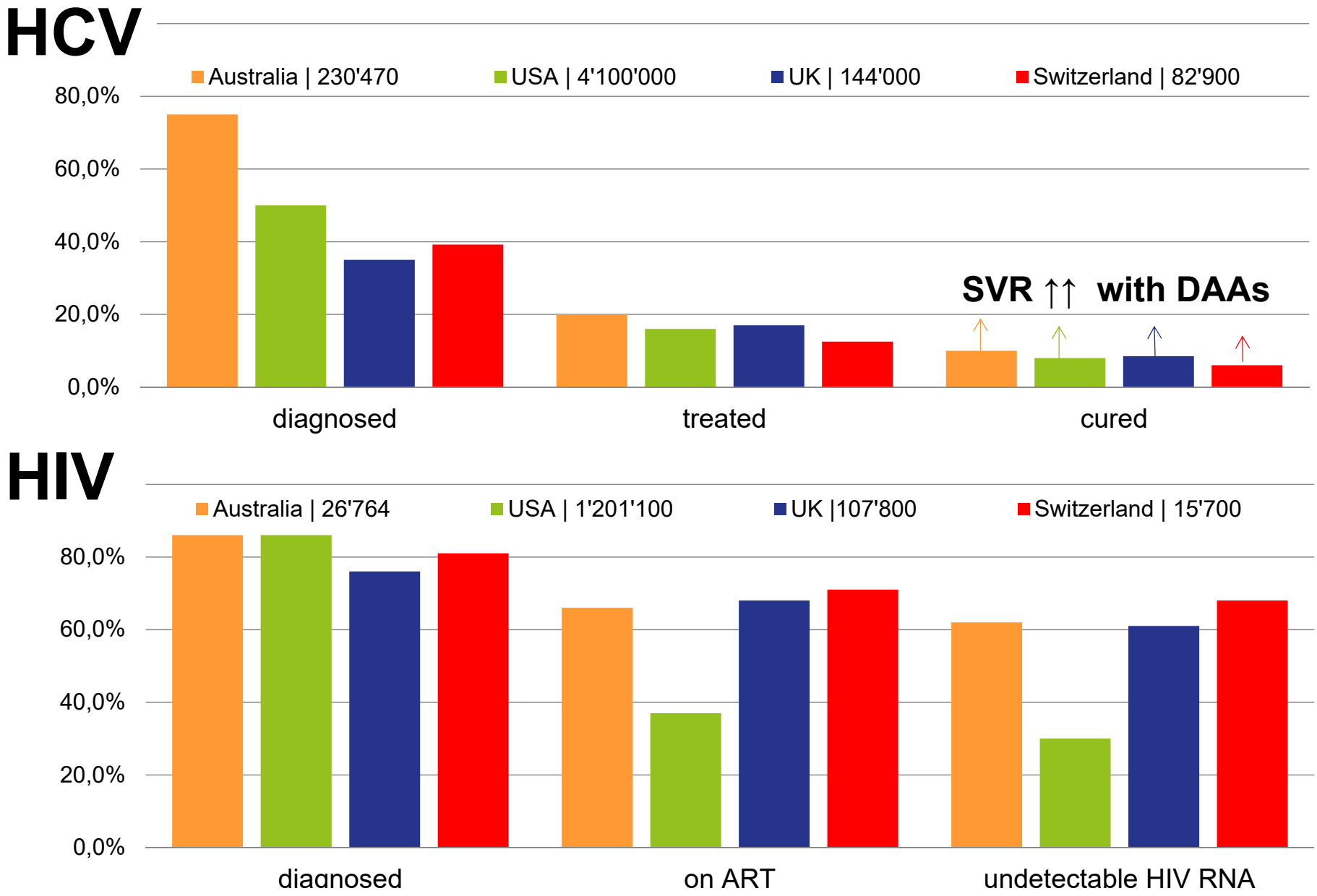
WHO: World Health Organisation

The Population Level Cascade of Care for Hepatitis C in British Columbia, Canada: The BC Hepatitis Testers Cohort (BC-HTC)

Naveed Z. Janjua DrPH [a,b,*], Margot Kuo MPH [a], Amanda Yu MSc [a], Maria Alvarez MSc [a], Stanley Wong MSc Darrel Cook MSc [a], Jason Wong MD [a,b], Jason Grebely PhD [c], Zahid A. Butt PhD [a,b], Hasina Samji PhD [a,b], Alnoor Ramji MD [d], Mark Tyndall MD [a,b], Mel Krajden MD [a,e]



The cascade of care: comparing HCV with HIV



Hajarizadeh B, et al. J Gastroenterol Hepatol 2016 | Harris et al, Journal of Hepatology, 2014 61:530-537 | Yehia et al, Plos one 2014 Bruggmann P et al. Praxis 2016; 105 (15): 885–889 ; Levi et al, IAS 2015 Vancouver

Summary

- In line with recommendations from clinical guidelines first real life data confirm that initially DAA therapy was prioritized to HCV patients with advanced liver disease.
- As a consequence the proportion of patients initiating
- disease will contribute to both improving the epidemiological understanding of viral hepatitis and other liver diseases as well as testing policies and linkage to care.

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