Patients and TB: Improving treatment outcomes through a patient centred approach and access to new treatments

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Hepatitis C and Tuberculosis

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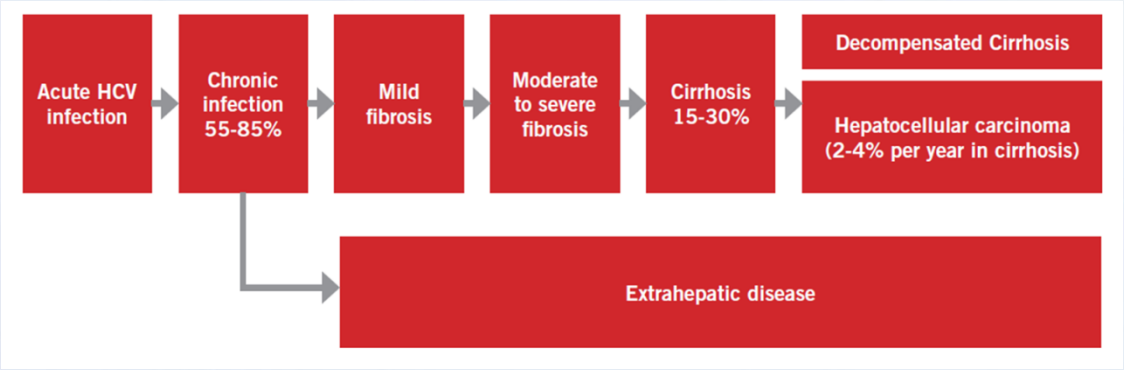
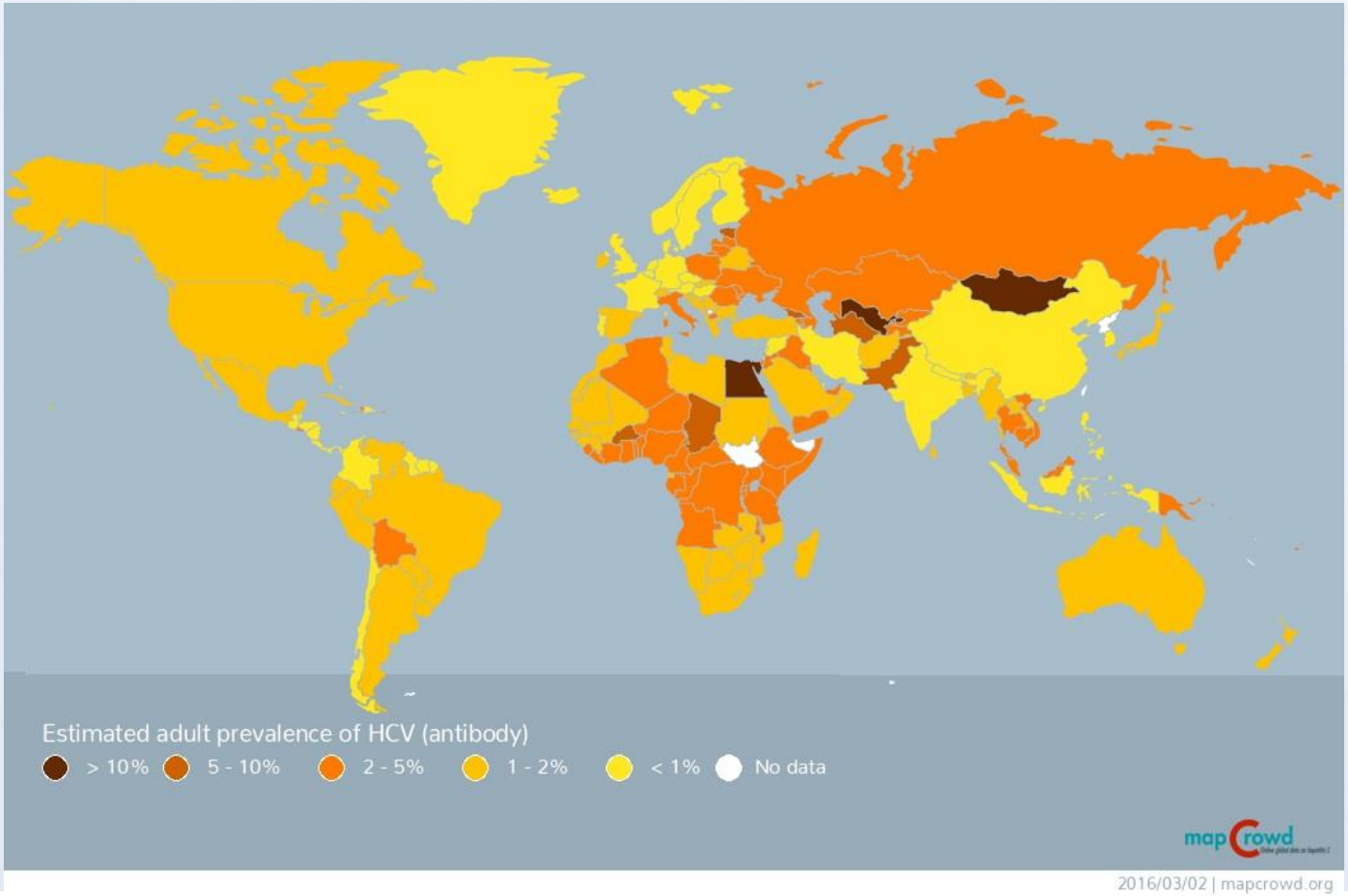
Chronic hepatitis C

- Around 185-200 million people worldwide are chronically infected with HCV.
- This is around 3% of world's population but in some countries it is more than 10%, mainly due to unsafe needle procedures in the past.
- Disease kills about 350,000- 500,000 people each year.
- Actual figures are unknown as around 60 % of world's population has no access to HCV diagnostics and even less to treatment.
- Majority of cases live in resource-poor settings and were infected in hospitals or other health care settings.



- Most of people are unaware of infection.
- Vast majority of acute HCV infection will become chronic and in around 30% will lead to liver cirrhosis.

Estimated worldwide adult prevalence of HCV (antibodies)

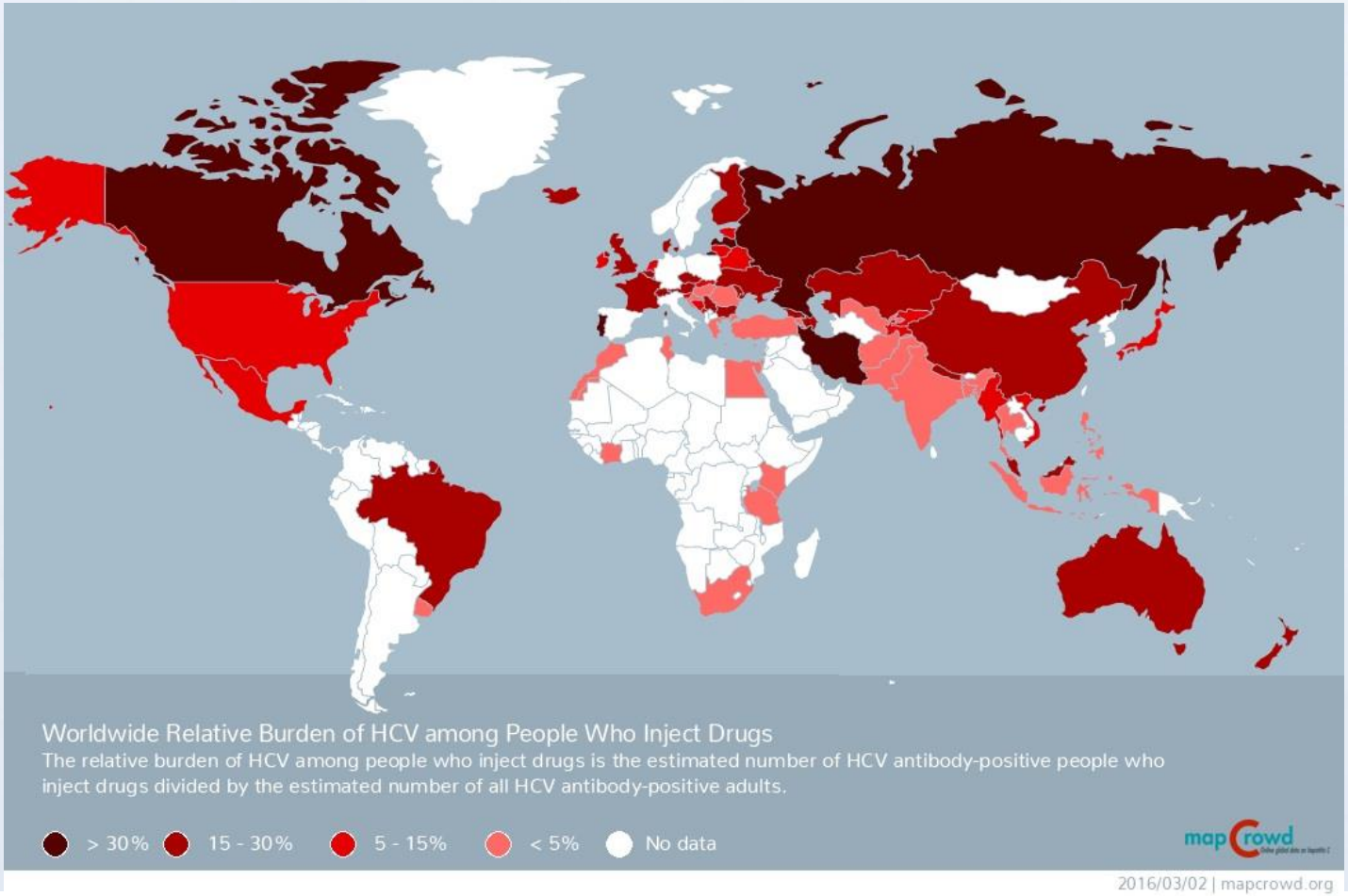


Chronic hepatitis C and TB

- There are limited data on the prevalence of chronic hepatitis C in people with TB.
- TB, hepatitis C virus and HIV are often more prevalent in different groups like people who inject drugs.
- HIV and HCV share the same route of transmission and are often associated with intra-venous drug use, especially in the post-soviet countries.
- TB is one of the opportunistic infection of HIV.
- TB and hepatitis C have been noted to be more frequent in homeless[1] or otherwise neglected social groups.

[1]Beiter et al. Lancet Inf Dis vol 12 Nov 2012

Worldwide relative burden of HCV among people who inject drugs



Hepatotoxicity of TB drugs

- Hepatotoxicity is a major adverse effect of three first line TB drugs- Isoniazid, Rifampicin and Pyrazinamide.
- Some second line TB drugs like Ethionamide/ Prothionamide and PAS are known to be hepatotoxic.
- Bedaquiline, one the novel TB drugs is known to be significantly harmful to the liver.
- Chronic liver disease raises a risk of hepatotoxicity during TB treatment up to five times[2]

[2] "Ungo et al. "Antituberculosis Drug–induced Hepatotoxicity", American Journal of Respiratory and Critical Care Medicine, Vol. 157, No. 6 (1998),

Drug induced hepatotoxicity

- The study conducted in Egypt[3] (country with world highest HCV prevalence) showed different drug induced hepatotoxicity during DS TB treatment:
  - 40% in HCV positive** patients
  - 3.8% in HCV negative** patients

* DIH defined as increase AST/ALT above 120 IU/L

** HCV positive- HCV PCR detectable, HCV negative- HCV PCR non-detectable

[3]Agha et al. "Prevalence of hepatitis C virus in patients with tuberculosis and its impact in the incidence of anti-tuberculosis drugs induced hepatotoxicity"- Egyptian Journal of Chest Diseases and Tuberculosis (2015)

HCV Treatment

- Currently available treatment with oral directly acting antivirals (DAAs) has shown extremely high effectiveness and simplicity.
- The treatment's duration has been reduced to 8-24 weeks, depending on the virus genotype, with the effectiveness up to 100% of the HCV eradication[4]
- Similar results have been demonstrated for HIV positive and negative patients.
- The earlier antiviral therapy is started in the individual, before development of advanced liver fibrosis, the better results could be achieved.
- It is nowadays possible to design combinations of two DAAs (e.g. Sofosbuvir + Daclatasvir) well tolerated, with minimum drug-to-drug interactions including ARVs.
- Such combination can be pan-genotypic (with action against all HCV genotypes), which significantly reduces the cost of necessary diagnostics.

4 Everson G, Tran T, Towner W et al. Safety and efficacy of treatment with interferon-free, ribavirin-free combination of sofosbuvir + GS-5816 in treatment-naive patients with genotypes 1-6 HCV infection. Oral abstract 111. 49th Annual Meeting of the European Association for the Study of the Liver, London, 9–13 April 2014

HCV treatment in TB patients

- Patients with XDR-TB have very limited therapeutic options remaining, they already exhausted most of TB drugs and it is often not possible to design the proper regimen without drugs to be known hepatotoxic (like Bedaquiline).
- Failure of such regimen means that patient has no more chances in the fight with TB.
- Unfortunately the new, most potent anti-HCV drug- Sofosbuvir should not be co-administered with Rifampicin, so its role in DST TB is limited

- Question:
  Should the anti-HCV treatment be provided to all patients with resistant TB prior anti-tuberculosis therapy?

Hepatitis C prevalence in MSF OCA project in Chechnya, the Russian Federation

- 89 patients admitted to MSF project in Chechnya until end 2015
- 14 patients (16 %) had anti Hepatitis C antibodies present
- 5 patients had suspected advanced liver fibrosis calculated by APRI score and underwent further assessment
- 3 of them had HCV present and are considered for anti-HCV treatment

No.	Drug/ Regimen	AST	PLT	APRI	HIV	Result			
						HCV RNA qualitative	HCV RNA viral load	Genotype	Fibroscan
1	Bdq	33	265	0.31	Neg				
2	Bdq	12	297	0.10	Neg				
3	Bdq	18	300	0.15	Neg				
4	Dlm	61	267	0.57	Neg	Detected	4.1*10^4	3	10.8 Kpa
5	Bdq	38	251	0.38	Neg				
6	Bdq	131	81	4.04	Pos	Neg	Neg	Neg	12.0 Kpa
7	Bdq	28	397	0.18	Neg				
8	Bdq	21	297	0.18	Neg				
9	Bdq	30	125	0.60	Neg	Detected	1.7*10^6	3	6.4 Kpa
10	Bdq	176	332	1.33	Neg	Detected	2.7*100	Not typed	13.1 Kpa
11	Cat 4	63	211	0.75	Neg	Neg	Neg	Neg	not done
12	Cat 1	39	353	0.28	Neg				
13	Dlm	24	283	0.34	Neg				
14		27	260	0.28					

Thanks for your attention