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WHO guidelines on Hepatitis C testing and treatment

3-rd webinar of the Virtual Medical Concilium, December 4, 2020

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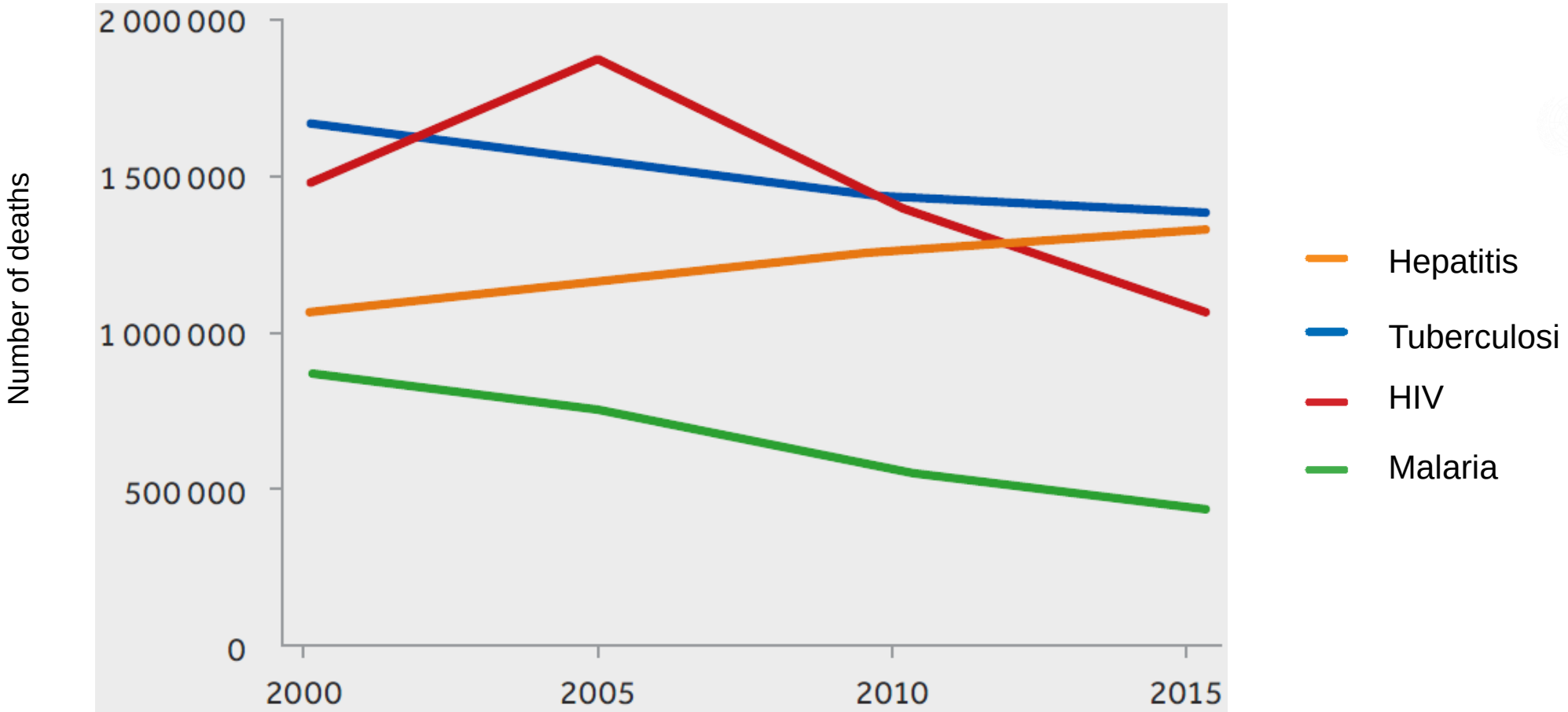
Increase in mortality

. Estimated global number of deaths due to the viral hepatitis, HIV, malaria and TB, 2000-2015



Elimination of viral hepatitis by 2030

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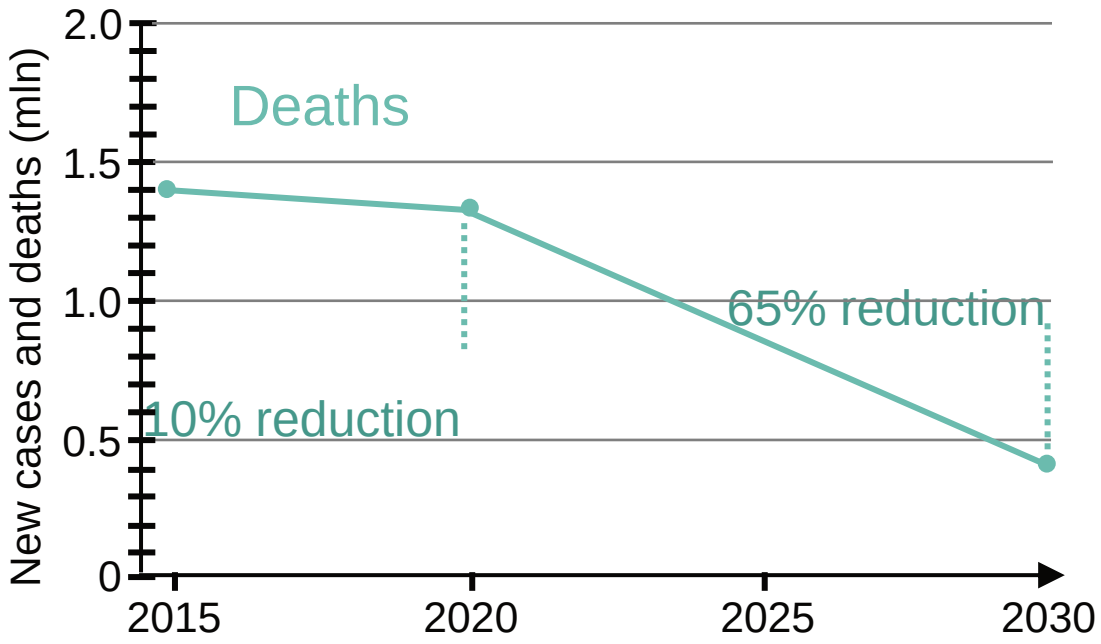
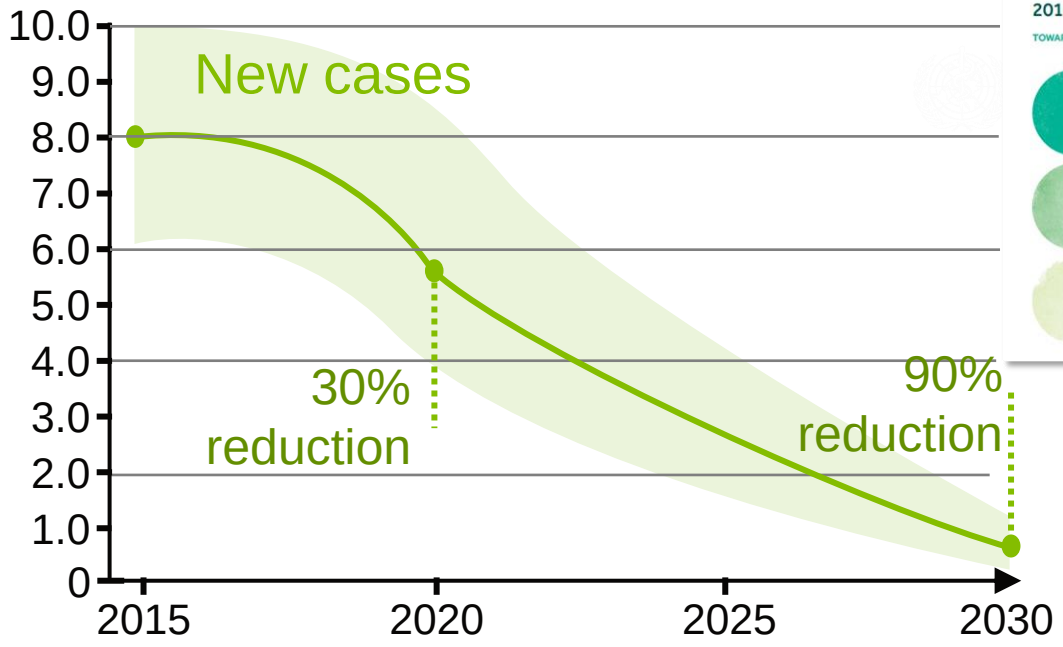
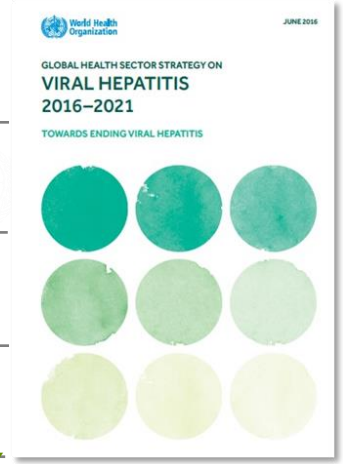
65% reduction in deaths due to HBV and HCV



From 1.4 million deaths in 2015 to less than 500,000 deaths in 2030.

90% reduction in new cases of chronic HBV and HCV





From 6–10 millions in 2015 to 900 000 in 2030
Decrease in HBV by 95%
Decrease in HCV by 80%

Source: Global Health Sector Strategy for Viral Hepatitis, 2016

Hepatitis strategy, 2016: elimination by 2030

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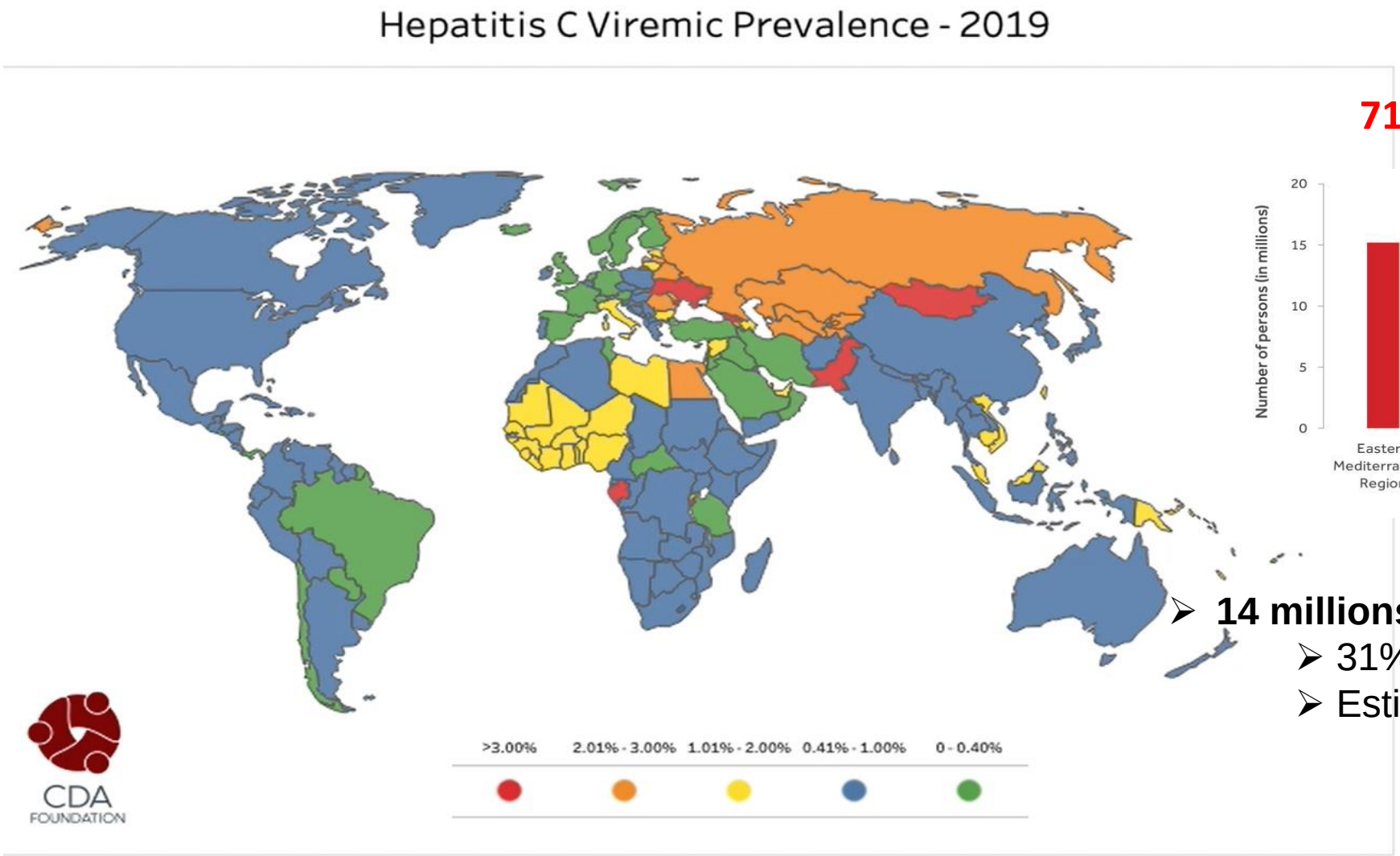
	Interventions	2030 Targets
1. Service coverage	1. Three doses of HBV vaccine	90%
	2. HBV PMTCT	90%
	3. Blood and injections safety	100 % of blood donations tested
		100% of Safe injections
	4. Harm reduction	300 kits for injections/ PWID/ year
	5. Testing and treatment	90% diagnosed
		80% on treatment/ cured
2. Results	A. Reduction of incidence	90%
	B. Reduction of mortality	65%

Global prevalence of chronic hepatitis C



HCV prevalence:

71 million of infected individuals

- **14 millions in the WHO European region**
  - 31% diagnosed (2015)
  - Estimated **mortality**: **112 500/year**

Source: POLARIS obsevatory

WHO guidelines on hepatitis B and C testing (2017)

The main recommendations specify:

- who to test for chronic hepatitis B and C infection
- how to test serologically for chronic hepatitis B and C infection (rapid tests or laboratory diagnosis/ one or two tests)
- how to confirm chronic HCV infection
- interventions to promote uptake of testing and linkage to care

https://www.who.int/hepatitis/publications/guidelines-hepatitis-c-b-testing/ru/

Who to test for chronic hepatitis B and C infection?

Testing approach	Recommendation
Focused testing in most affected populations	Irrespective of the general epidemiology, it is recommended to offer HBsAg testing and/or anti-HCV to adults and adolescents • from populations most affected by HBV and HCV infection (i.e. who are either part of a population with high seroprevalence or who have a history of exposure and/or high-risk behaviours); • with a clinical suspicion of chronic viral hepatitis (i.e. symptoms, laboratory markers); • HBV: sexual partners, children and other family members, and close household contacts of those with HBV infection; • Health care workers: in all cases followed by the hepatitis B vaccination

Who to test for chronic hepatitis B and C infection?

Testing approach	Recommendation
General population testing ***(total screening)***	• In settings with a >2% (moderate) or >5% (high) prevalence in the general population, it is recommended that all adults to be offered testing with linkage to prevention, care and treatment services. • General population testing approaches should make use of existing community- or health facility-based testing opportunities (such as at antenatal clinics, HIV or TB clinics).
Testing in specific age groups (HCV)	• Consider a feasibility of identifying cohorts at high risk of HCV infection
Routine prenatal screening (HBV)	• In settings with >2% (moderate) / >5% (high) HBsAg seroprevalence, it is recommended that HBsAg serological testing be routinely offered to all pregnant women with linkage to prevention, care and treatment services

What tests to use for serological testing?

- **HBV:** For the diagnosis of HBV infection in adults, adolescents and children (>12 months of age), a serological assay (in either RDT or laboratory-based immunoassay format) that meets minimum performance standards is recommended
  - In settings where existing laboratory testing is already available and accessible, **laboratory-based immunoassays** (for instance, EIA) are recommended
  - In settings where there is limited access to laboratory testing and/or in populations where access to rapid testing would facilitate linkage to care and treatment, use of **RDTs** is recommended
- **HCV:** To test for serological evidence of past or present infection in adults and children (>18 months of age), an HCV serological assay (antibody or antibody/antigen) using either RDT or laboratory-based immunoassay formats that meets minimum performance standards is recommended
  - In settings where there is limited access to laboratory infrastructure and testing, and/or in populations where access to rapid testing would facilitate linkage to care and treatment, **RDTs** are recommended.

Confirming viraemic infection and monitoring for HCV treatment response

- Following a reactive anti-HCV antibody serological test result, a **nucleic acid test (NAT- quantitative or qualitative nucleic acid RNA)** is recommended as a preferred testing strategy to diagnose HCV infection
- Detection of core HCV antigen, where the assay has comparable clinical sensitivity to NAT technologies, may be considered as an alternative.

- Use of **qualitative or quantitative HCV RNA** as a **test of cure** at 12 weeks or 24 weeks after completion of antiviral treatment (i.e. presence of a stable virologic response – **SVR12 or SVR24**) is recommended

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What has changed since the publication of the updated 2016 WHO guidelines on HCV?

- Reduced cost and expanded access to generics
- Registration of new pangenotypic DAA - based regimens:
  - Sofosbuvir / Velpatasvir
  - Glecaprevir / Pinbretasvir
- Accumulated data on the safety and effectiveness of DAAs in practice (e.g. Sofosbuvir/Daclatasvir)

https://www.euro.who.int/en/health-topics/communicable-diseases/hepatitis/publications/2019/guidelines-for-the-care-and-treatment-of-persons-diagnosed-with-chronic-hepatitis-c-virus-infection-2018

Who to treat and when to start treatment?

- Updated WHO guidelines review the recommendation **to treat all HCV-infected people** over 12 years of age (except pregnant women)

  - The use of DAAs leads to high cure associated with a decrease in HCC mortality and incidence (*according to the studies using IFN*)
  - SVR is associated with the improved course of comorbidities such as diabetes, depression, and chronic kidney disease
  - Treatment of HCV infection in adolescents is effective and well tolerated

“Treat all”: pros and cons

Pro arguments:

- Significant reduction in liver complications and mortality
- Prevention of concomitant diseases
- Some decrease in the number of new infections
- Feasibility of public health approach

Possible risks:

- Possibility of more frequent side effects with the increased use of DAAs (need for enhanced pharmacovigilance)
- Risk of HBV reactivation in the presence of co-infection

How to treat ?

WHO considers it appropriate to use pangenotypic direct acting antivirals (DAAs) for treatment of people with chronic hepatitis C aged 18 years and older

- Available pangenotypic DAA regimens:
  1. Sofosbuvir / Velpatasvir (12 weeks)
  2. Glecaprevir / Pinbretasvir (8 (12) weeks)
  3. Sofosbuvir / Daclatasvir (12 (24) weeks)

Use of pangenotypic regimens: balance between advantages and disadvantages

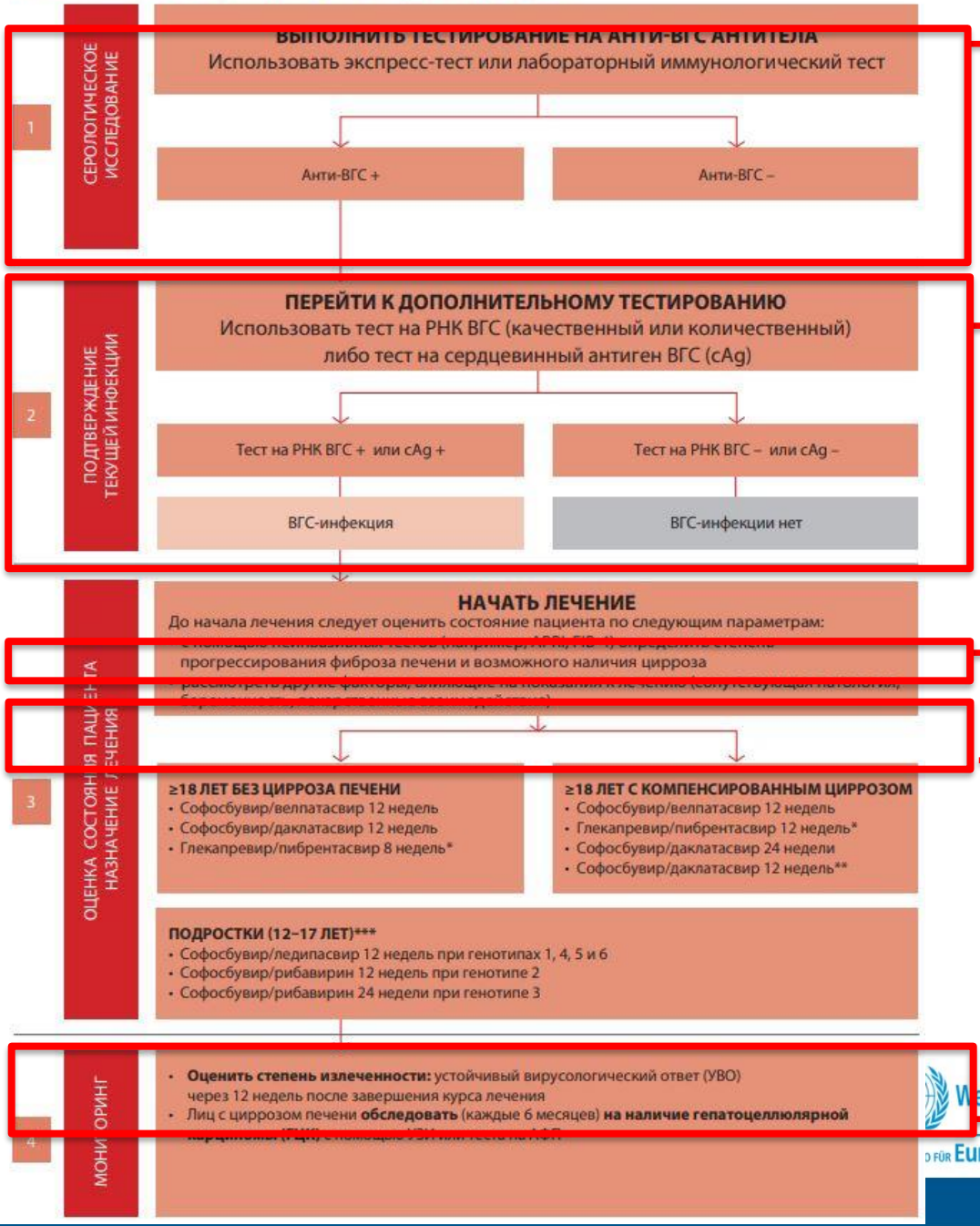
Advantages

- No need for genotyping, reduced cost and complexity of treatment;
- Pangenotypic DAA-based regimens can facilitate rapid scaling up of treatment, especially in the lower-middle-income countries where genotyping may be too expensive;
- Easier procurement and supply of medicines.

Potential disadvantages

- In some countries, the recommended pangenotypic regimens are currently less available;
- In some rare cases, HCV is almost entirely caused by a single HCV genotype allowing for effective use of non-pangenotypic therapy regimens during the transition period

Сводный алгоритм для диагностики, лечения и мониторинга
хронической ВГС-инфекции у взрослых и подростков



– Rapid test
– EIA

– Qualitative PCR
– Quantitative PCR
– HCVcAg

– APRI
– FibroScan

– HIV test
– HBsAg, HBeAg, HBV VL
– Genotyping (?)
– Pregnancy test
– Liver/ kidney function tests

– – Qualitative PCR
– Quantitative PCR

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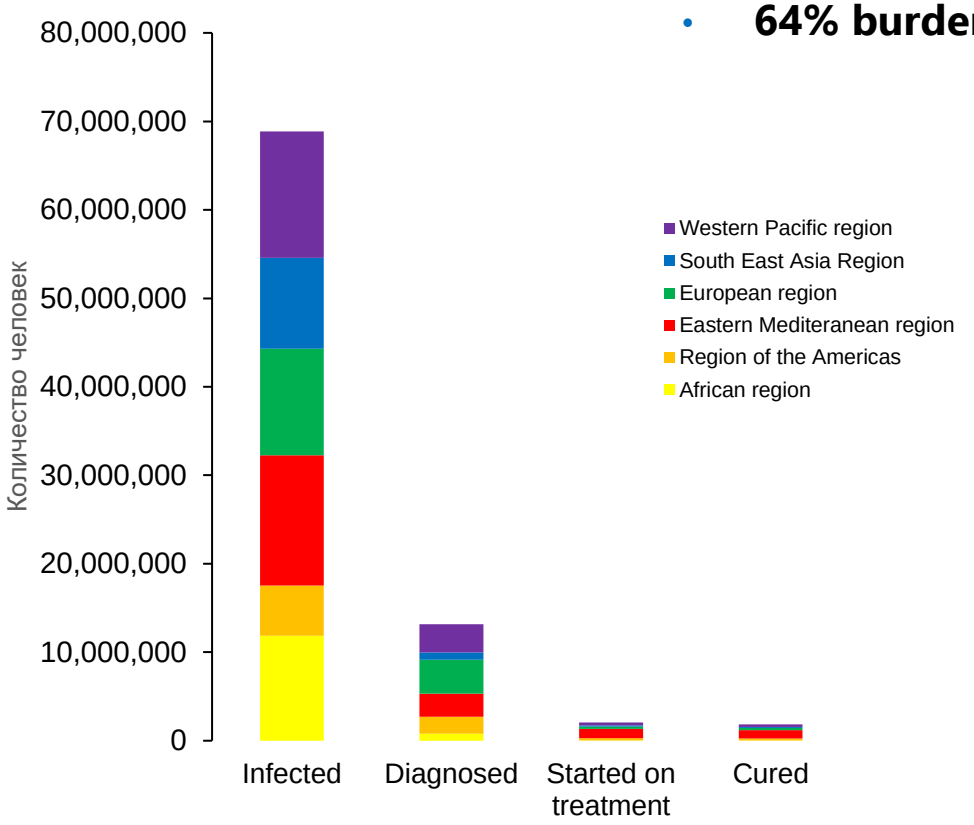
Hepatitis C treatment cascade by the WHO regions, 2017



- **HCV: 71 million infections in adults in 2015.**
- **64% burden – in 14 countries**

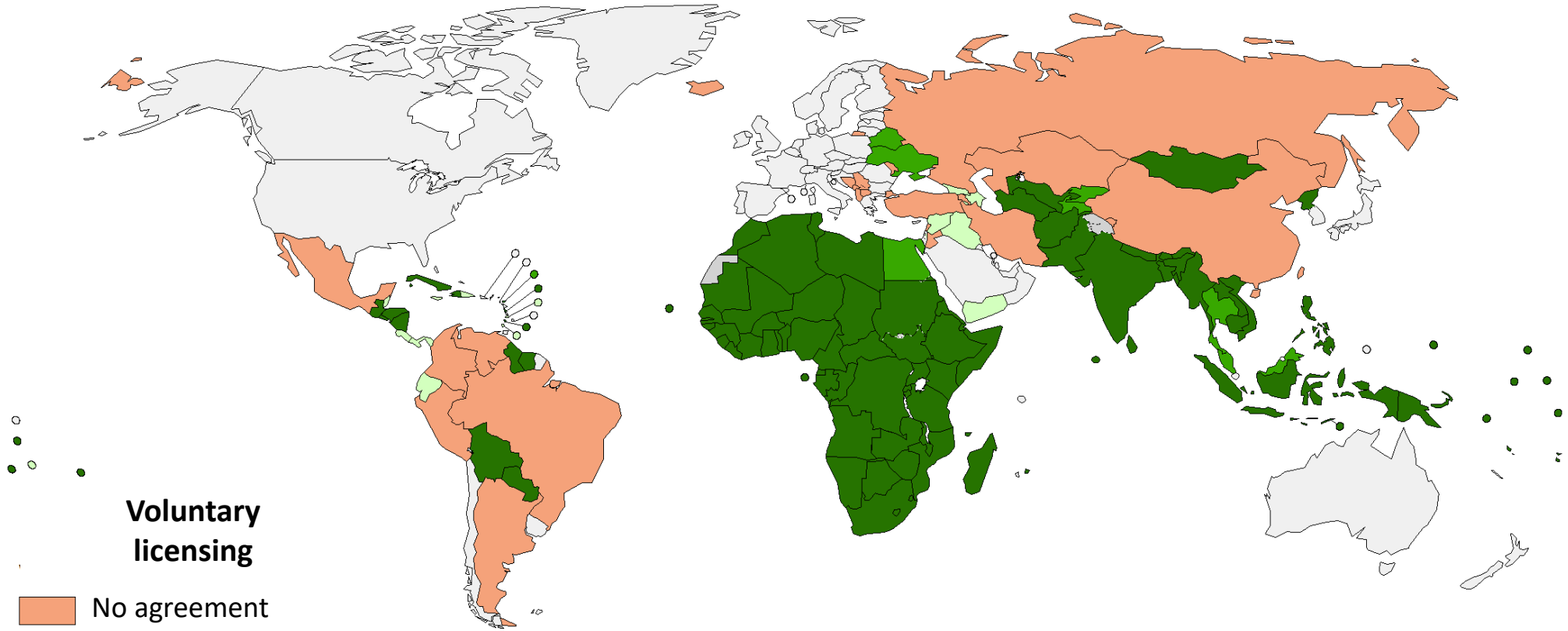
- 2014: < 200 000
- 2015: 1.1 million
- 2016: 1.7 million
- 2017: 2.1 million

- **In total: ~5 mln treated with DAAs**

The majority of treated patients are in the "champion countries": Australia, Brazil, Egypt, Georgia, India, Spain, Mongolia, and Rwanda

Source: Center for Disease Analysis/Polaris

62% of hepatitis C patients live in the countries that can procure generic DAAs



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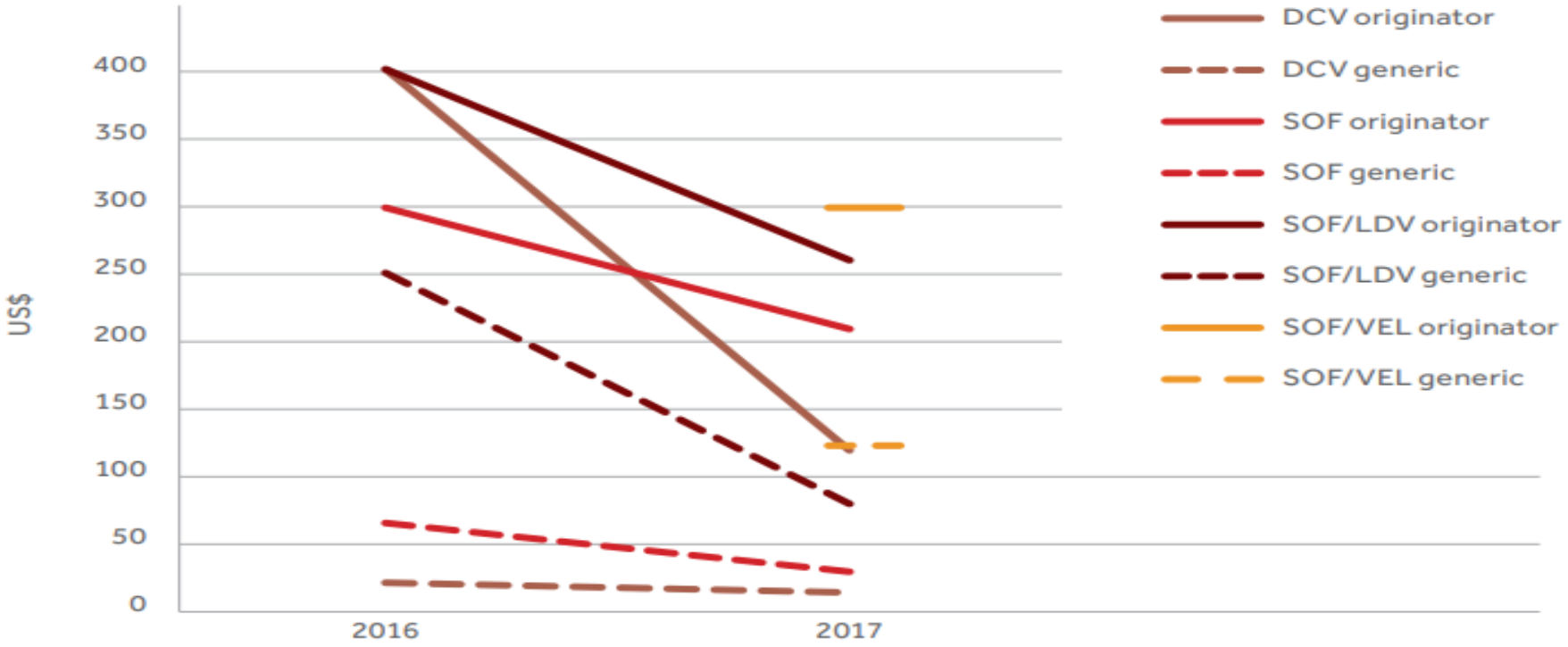
Отчет ВОЗ по доступности лечения гепатита С, март 2018 г

Monitoring of DAAs price reduction

Increased competition drives price reduction (> $ 100 per course)

Fig. 3.3. Trends in the lowest reported prices for direct-acting antivirals per 28-day supply, 2016–2017



Note: Prices as reported by DAA producers and countries in the WHO 2016 and 2017 surveys

WHO Report on Access to Hepatitis C Treatment, March 2018

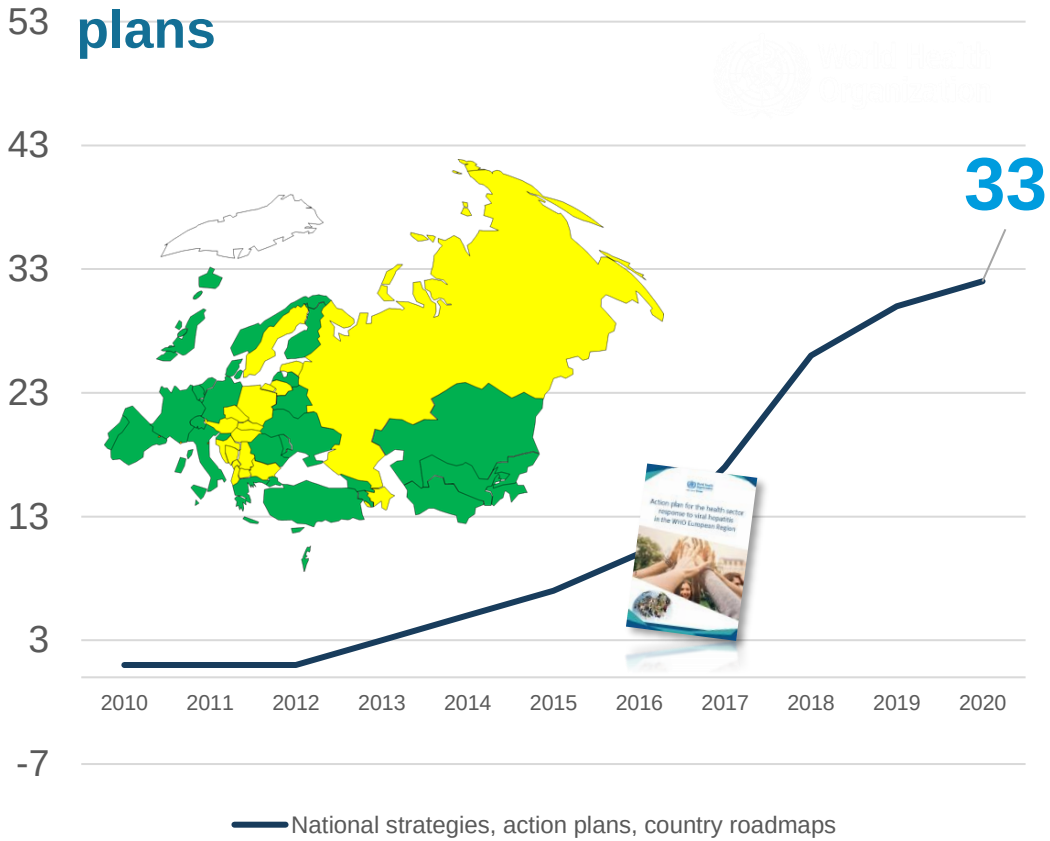
What is needed to achieve elimination?

- Uptake of the effective measures for prevention of transmission
- Expanded access to testing and treatment
- Simplified treatment and monitoring
- Development, implementation and evaluation of the elimination programs

In the WHO European region

- **14 million** people live with HCV infection
- 31% diagnosed (2015)
- **At least 230 thousand courses of DAA treatment per year** (2017-2020)*
  - Based on data provided to WHO and ECDC or published in the manuscripts
  - **Eleven** member states have access to the generic DAAs

More countries in the WHO European Region have developed **National viral hepatitis action plans**



European Centre for Disease Prevention and Control. Monitoring the responses to hepatitis B and C epidemics in EU/EEA Member States, 2019. Stockholm: ECDC; 2020; CDA Foundation's Polaris Observatory; 2020; AIDS Foundation East-West (AFEW-Ukraine); (2018); UNDP; 2020; MSF; 2018; Flisiak R, et al (2019); Idilman R, et al (2020); Meijerink H, et al (2017);

Conclusion

- **Simplified** diagnostic and treatment **algorithms** adapted for primary health care can greatly facilitate scaling up of the elimination programs;
- Transition to the **use of DAAs to "treat all"** (except for pregnant women and children under 12 years of age);
- Genotyping is still a difficulty, which is why WHO **recommends DAA-based pan-genotypic regimens;**
- A pricing scenario for DAA regimens is highly dynamic; registration of drugs in some countries is still a barrier and should be a high priority;
- **Equitable** access to DAA treatment is a key guiding principle.

Thank you for your attention!

Acknowledgement to:

Member States, partners, donors, affected communities, WHO headquarters, country offices and the JTH team at WHO / Europe

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