3\textsuperscript{rd} International Meeting on Elimination of Viral Hepatitis

Elimination by 2030 – what will it take?

A focus on Hepatitis B and C

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Disclosure speaker interests

Disclosure of speaker interest

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Overview

- **Viral hepatitis – the global burden**
- First-ever global elimination strategy and targets
- Strategic directions - areas of focus
  - Making the case and strengthening the evidence
  - Delivering for impact
  - Delivering for equity
  - Financing for sustainability
  - Embracing innovation

- WHO’s role in a partnership approach
Viral hepatitis: the global epidemic

7th leading cause of death globally (2013)

95% of the burden from hepatitis B and C
HIV deaths declining – Hepatitis deaths increasing (1.4 million deaths)

Sources – Hepatitis: GBD; HIV, TB and Malaria: WHO
What have we learned from HIV?

- Advocacy and activism
- Focus on surveillance and data
- Focus on treatment access, rights and price
- R&D, and implementation science
- Public health approach – simplified yet quality services
- Major international investments paired with domestic funding
- A culture of partnership and inclusiveness

- No appetite for another large vertical programme
- HIV sometimes process-heavy and donor-driven
- Build hepatitis from a “systems starting point”
- Major international investments unlikely
70 million people with chronic hepatitis C (2015)

Prevalence (Viremic)
- 0.0%-0.6%
- 0.6%-0.8%
- 0.8%-1.3%
- 1.3%-2.9%
- 2.9%-6.7%

Courtesy: Center for Data Analysis, Homie Razavi
Countries with largest Hepatitis C burden

Courtesy: Center for Data Analysis, Homie Razavi
Persons living with HBV infection: 324 million

Global prevalence of HBV infection: 4.4%
Highest in AFR [8.6%] and WPR [7.9%]
<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>Viral hepatitis on agenda at the World Health Assembly for the first time</td>
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<td>2010</td>
<td>First World Health Assembly Resolution on viral hepatitis</td>
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<tr>
<td>2011</td>
<td>Global Hepatitis Programme established at WHO</td>
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<tr>
<td>2012</td>
<td>Civil society advocacy - World Hepatitis Alliance - official WHO relations</td>
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<td>2012</td>
<td>Prevention and Control of Viral Hepatitis: Framework for Global Action</td>
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<tr>
<td>2014</td>
<td>WHA resolution examine the feasibility of elimination of hepatitis B and C</td>
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<td>2014</td>
<td>Toronto Declaration: strategies to control and eliminate viral hepatitis</td>
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<td>2015</td>
<td>WHO PAHO Regional Action Plan on Viral Hepatitis Adopted</td>
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<td>2015</td>
<td>Glasgow Declaration from the first World Hepatitis Summit</td>
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<tr>
<td>2016</td>
<td>Adoption of first global health sector strategy on viral hepatitis “Eliminate viral hepatitis as a major public health threat by 2030”</td>
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</tbody>
</table>
Elimination in the SDG era

Elimination as a public health threat focus for:

- HIV
- Malaria
- Sexually transmitted infections
- Tuberculosis
- *Viral Hepatitis*

Focus on eradication of Polio
The first-ever global WHO Strategy on viral hepatitis, 2016-2021

Vision: “A world where viral hepatitis transmission is halted and everyone living with viral hepatitis has access to safe, affordable and effective prevention, care and treatment services”

Goal: Eliminate viral hepatitis as a major public health threat by 2030

Five strategic directions:
1. Information for focused action
2. Interventions for impact
3. Delivering for equity
4. Financing for sustainability
5. Innovation for acceleration
<table>
<thead>
<tr>
<th>Intervention</th>
<th>2030</th>
<th>2020</th>
<th>Baseline 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. HBV vaccination</td>
<td>90%</td>
<td>90%</td>
<td>82%</td>
</tr>
<tr>
<td>2. HBV MTCT; birthdose</td>
<td>90%</td>
<td>50%</td>
<td>38%</td>
</tr>
<tr>
<td>3. Safe injection</td>
<td>90%</td>
<td>50% coverage</td>
<td>5%</td>
</tr>
<tr>
<td>4. Harm reduction</td>
<td>300 (75% coverage)</td>
<td>200 (50% coverage)</td>
<td>20</td>
</tr>
<tr>
<td>5. HBV Treatment</td>
<td>80%</td>
<td>8 million treated (5m HBV, 3m HCV)</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>6. HCV Treatment</td>
<td>80%</td>
<td>8 million treated (5m HBV, 3m HCV)</td>
<td>&lt;1%</td>
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</table>
Elimination targets for Hepatitis B and C

6-10 million infections (in 2015) to
900,000 infections (by 2030)

1.4 million deaths (in 2015) to under
500,000 deaths (by 2030)
Striving for elimination *as a public health threat* will prevent 7.1 million hepatitis deaths by 2030.
Accountability through the World Health Assembly (WHA)

Progress on the implementation of the global strategy adopted in 2016 will be twice:
- on midterm progress in 2018
- final report on progress towards 2020 targets 2021

WHO works with countries to establish a global monitoring system
Towards stronger national plans – for an effective and coordinated response

- Global Health Sector Strategy
- Regional Action Frameworks
- National Strategies or Plans

World Health Organization
Regional Action Plans/Frameworks

✓ Regional Action Plan of Action for the Prevention and Control of Viral Hepatitis in the Americas
✓ Regional Action Plan of Action for the Prevention and Control of Viral Hepatitis in the South East Asia
✓ Prevention, Care and Treatment of viral hepatitis in the African Region: Framework for action 2016–2020
✓ Action plan for the health sector response to viral hepatitis in the WHO European Region
✓ Eastern Mediterranean Region plan and framework being developed
Countries with National Viral Hepatitis Plans – Nov 2016

39 countries have plans, 35 are developing
Country examples: striving towards elimination of hepatitis

- **Australia**: universal access to HCV treatment to all persons with chronic HCV infection; prisoners and PWID are priority populations

- **France**: universal access to HCV treatment under the national health insurance system

- **Georgia**: hepatitis C elimination programme with plan for 20,000 people treated per year

- **Morocco**: goal of Morocco without hepatitis C in 2030

- **Portugal**: universal access to treatment

- **Egypt**: National Plan of Action — largest treatment programme to date
Overview

- Viral hepatitis – the global burden and response
- First-ever global elimination strategy and targets
- **5 Strategic directions - areas of focus**
  - Making the case and strengthening the evidence
  - Delivering for impact
  - Delivering for equity
  - Financing for sustainability
  - Embracing innovation

WHO’s role in a partnership approach
Strategic Direction one: Strategic information
WHO information documents
Viral Hepatitis Surveillance

1. Detect outbreaks, monitor trends in incidence and identify risk factors for new, incident infections

2. Estimate the prevalence of chronic infections and monitor trends in sentinel groups

3. Estimate the burden of sequelae

Surveillance for acute hepatitis

Surveillance for chronic infections

Surveillance for cirrhosis and HCC

HCC: Hepatocellular carcinoma
M&E: 10 core indicators for Hepatitis B and C along the result chain

**Context & needs**
- Epidemic patterns, stigma, and population in need

**Inputs**
- Policy, laws, health system inputs and financing

**Output & outcomes**
- Prevention
  - C3. Vaccination coverage
  - C4. Needle syringe distribution
  - C5. Injection safety
- Testing
  - C6. People diagnosed
- Care and treatment
  - C7. Treatment coverage / initiation
- Cure / suppression
  - C8. Viral suppression (HBV) or cure (HCV)

**Impact**
- New infections, deaths, equity

- C9. Incidence
- C10. Mortality from HCC, cirrhosis and chronic liver diseases
Strategic Direction 2: Delivering for Impact

Prioritizing five strategic intervention areas:
1. Vaccination (particularly HBV)
2. HBV mother-to-child transmission
3. Injection, blood and surgical safety
4. Harm reduction for people who inject drugs; safe sex
5. Testing and Treatment for chronic viral hepatitis B and C
Hepatitis Prevention, Tx and Care Cascade

Linked / Retained in Hepatitis Prevention
Linked / Retained in Care and Treatment

% in Prevention or Care

Source: Modified from Frits van Griensven, 2014 Thailand
Focus on prevention

Immunisation for Hepatitis B

Prevention of sexual transmission
Promoting safer sex and intensification of condom programming

Injection safety for C:
Global initiative to make all injections safe through syringes that can only be used ONCE

Harm reduction
Harm reduction and needle syringe program
2020 target of 200 syringes/year/PWID
EUR 52.5; WPR 44.5; SEAR 24.0; EMR 22.5; AMR 11.5; AFR 3.0
Comparing WHO regions: three-dose hepatitis B vaccine coverage

Infants receiving three doses of hepatitis B vaccine, by WHO region, 1989–2014

Source: WHO/UNICEF
Comparing WHO regions: Hepatitis B birth dose coverage

2015: Global 38%

- WPR: 80%
- AMR: 70%
- EUR: 40%
- SEAR: 30%
- EMR: 20%
- AFR: 10%

Source: WHO/UNICEF
HBsAg in under 5 (proxy for cumulated incidence): 0.4%

Progress in hepatitis B vaccine coverage led to lower prevalence of HBsAg in under 5’s (only AFR exceeds 1%)

Source: London School of Hygiene and Tropical Medicine
Comparing WHO regions – unsafe health care injections 2010

Source: Pepin et al, 2010
WHO Guidelines on Hepatitis B and C Testing, Care and Treatment

- Hepatitis B Guidelines 2015
- Hepatitis C Guidelines 2016 (2nd edition)
- Hepatitis Testing Policy brief 2016
Over 1 million people treated with DAAs
WHO launched “Barriers Report” in October 2016

Brazil started with 7460 in 2015

Egypt 670 000

Georgia 19 300

India started with 42 000 in 2015

Rwanda started with 120 patients in 2015

Ukraine started with 320 patients in 2015

China 200 100

Mongolia 5600

Viet Nam 4500

Cambodia 800

Lao PDR 200

2016

Pakistan 82 000

Ukraine

2016

India

2016

Pakistan

Lao PDR

Viet Nam

Cambodia

Mongolia

China

Georgia

Brazil

Ukraine

2016

India

2016

Pakistan

Lao PDR

Viet Nam

Cambodia

Mongolia

China

Georgia

Brazil

Ukraine

2016

India

2016

Pakistan

Lao PDR

Viet Nam

Cambodia

Mongolia

China

Georgia

Brazil

Ukraine
Strategic Direction 3: Delivering for Equity

Focus on securing access to quality commodities – driving down prices

Tailoring and targeting services for different population groups

Involving people living with viral hepatitis
Making elimination affordable for all

- Radical reductions in costs for diagnostics and treatment (includes ineffective treatment and care costs in middle and high income countries)

- Shared costs with other strategies
  - Harm reduction costs, immunization and blood safety
  - Co-infection with HIV and service delivery

- Innovations and efficiencies over time
  - Simplified treatment package, non-specialist care
  - Hepatitis B cure
In Egypt the price for a 3 month Hepatitis C treatment dropped from US$900 in 2014 to less than US$200 in 2016.

Prices of Hepatitis C drugs continue to vary considerably across countries.

The steepest price decrease is observed in countries with generic competition, confirming experience with HIV treatment.

**Prices of sofosbuvir per bottle (US$)**
i innovator (red), generic (grey)

*Data from: WHO survey 2016*
... but prices still remain high in some countries

- High cost have led to treatment rationing in some countries
- For example in Romania, where Hepatitis C treatment prices are as high as US$79,900

**Prices of daclatasvir per bottle (US$)**
innovator (red), generic (grey)

*Data from:* WHO survey 2016
Overcoming patent-related barriers to access

DAA patent landscapes

Coverage of voluntary licenses

- daclatasvir 112 countries > 2/3 thirds of middle-income countries / 68.6% of disease burden LMICs (MPP)

- sofosbuvir, sofosbuvir/ledipasvir, and sofosbuvir/velpatasvir: 101 countries - 31 LICs, 2 HICs (Equatorial Guinea and Seychelles), 68 MICs

Local production

- Argentina, Bangladesh, India, Egypt, Morocco, Pakistan

Compulsory licensing

WHO Patent Landscapes

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Brand Name</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>sofosbuvir</td>
<td>Harvoni</td>
<td>Gilead Sciences</td>
</tr>
<tr>
<td>ledipasvir</td>
<td></td>
<td>Gilead Sciences</td>
</tr>
<tr>
<td>daclatasvir</td>
<td></td>
<td>BMS</td>
</tr>
<tr>
<td>dasabuvir</td>
<td>Viekira Pak with ritonavir</td>
<td>AbbVie</td>
</tr>
<tr>
<td>ombitasvir</td>
<td></td>
<td>AbbVie</td>
</tr>
<tr>
<td>paritaprevir</td>
<td></td>
<td>AbbVie</td>
</tr>
<tr>
<td>simeprevir</td>
<td></td>
<td>Janssen</td>
</tr>
</tbody>
</table>

Updated in June 2016: www.who.int/phi/implementation/ip_trade/ip_patent_landscapes/en/
Targeting populations most affected

- Responses must be based on the epidemiological and social context.
- In many countries, much transmission of hepatitis B virus and hepatitis C occurs in health care settings.
- Populations exposed through sexual transmission may include young people and adolescents, men who have sex with men, sex workers, transgender people and prisoners.
- People who inject drugs are at high risk of hepatitis C and hepatitis B infection because of the shared use of contaminated injecting equipment.
Promoting an enabling environment and reaching all populations: civil society a critical partner
Example: Egypt's HCV programme success

- Prevalence of HCV 7% among 18–59 y
- National Plan of Action 2014 – 2018 and treatment guidelines with DAAs
- From US$ 900 to less than US$200 for a 3 month DAA treatment
- Rapid treatment uptake:
  - Political commitment
  - Mass information
  - National Committee
  - National network of treatment centres
  - Local production
  - Know your epidemic: 90% genotype 4
  - Online patient registration for treatment
  - Treatment cost covered by MoH for large majority
Strategic Direction 4: Financing for Sustainability

First ever global strategy - an advocacy tool to drive investment

Develop robust investment case at country level

Ensure viral hepatitis is covered in the national health financing system
Financing Hepatitis

• Some strategic, catalytic and regional support is likely to emerge
• Unlikely there will ever be a “Global Fund for Hepatitis B and C”
• Critical to focus on optimal domestic financing
  – Health insurance, revenue raising, pooling of funds across the health system
• Price reduction and access
• Efficiencies
• Move to public health population-level approaches
Scenario: Chinese patients currently pay out of pocket

Cost for one patient in one year

<table>
<thead>
<tr>
<th>No care</th>
<th>CP</th>
<th>SP - current price</th>
<th>SP - ideal price</th>
</tr>
</thead>
<tbody>
<tr>
<td>RMB</td>
<td>22464</td>
<td>19295</td>
<td>3378</td>
</tr>
</tbody>
</table>

2014 Urban income = 28,844 RMB

2014 Disposable per capita income = 20,167 RMB

2014 Rural income = 10,489 RMB

Catastrophic threshold = 8,066 RMB
Findings of Chinese cost analysis

• Current hep B treatment practice is **unaffordable** for patients

• Treatment averts medical costs; it is **cheaper** to treat than not to treat

• Standardized package **rationalizes** cost
  – More people can receive treatment

• Health insurance can save **1.7 times more ¥** by investing in treatment
Strategic Direction 5: Innovation for Acceleration

Optimizing testing and diagnostics

Optimizing medicines and Tx regimens

Investment in the cure agenda for Hepatitis B

Rethinking service delivery
WHO’s action and focus in hepatitis

✓ Global health sector strategy; regional action plans; monitoring progress
✓ Global advocacy and leadership. eg. First global Hepatitis summit (2015)
✓ Normative and policy work:
  ✓ Hep B and C guidelines; surveillance guidelines; testing guidelines
  ✓ Safe injection policy; service delivery approaches
✓ Country support for policy uptake and implementation – national hepatitis plans
✓ Supporting access to affordable medicines (B and C) – price reporting, pre-qualification; patent landscape; access approaches for countries; innovation
✓ Surveillance support and global reporting: first global Report early 2017
Moving the hepatitis response towards elimination

- Partnerships - governments, civil society, private sector, academia – move beyond “clinical world”
- Country champions emerging
- Concrete and tailored action in countries
- Prices need to come down further
- A combined approach – prevention, testing, and treatment (B and C!)
- Innovation is key (diagnostics, medicines, services)
- Momentum is building up – ready to take off.....
- WHO has a critical role to support global and country action – together we can do it!!!!!
THANK YOU
Additional slides
Reaching global targets - programmatic assumptions

- Immunization scale-up; and approaches to eliminate mother to child transmission, e.g. innovations in delivery of birth dose
- Universal access to blood and injection safety in and beyond health settings and to Harm Reduction
- Scale up and innovations in treatment: innovations in diagnostics, including point of care testing, new case finding, radical reductions in treatment costs, and innovations in curative HBV treatment
- Strong linkages of hepatitis interventions to HIV, TB, MCH, NCDs and health system simplifications
- Significant investment in surveillance
- Large regional variations in baselines
# 2030 Elimination Targets

## Global Health Sector Strategy

<table>
<thead>
<tr>
<th>Targets</th>
<th>Interventions</th>
<th>2030 target</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Service coverage</td>
<td>1. Three dose hepatitis B vaccine</td>
<td>90%</td>
</tr>
<tr>
<td></td>
<td>2. HBV PMTCT</td>
<td>90%</td>
</tr>
<tr>
<td></td>
<td>3. Blood and injection safety</td>
<td>100% screened donations</td>
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<td></td>
<td>4. Harm reduction</td>
<td>300 injection sets / PWID</td>
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<tr>
<td></td>
<td>5. Treatment</td>
<td>90% diagnosed</td>
</tr>
<tr>
<td>2. Impact</td>
<td>A. Incidence</td>
<td>-90%</td>
</tr>
<tr>
<td></td>
<td>B. Mortality</td>
<td>-65%</td>
</tr>
</tbody>
</table>

PMTCT: Prevention of mother to child transmission  
PWID: Person who injects drugs
## Accelerating DAA registration status

- In many countries: new DAAs are still not registered and consequently not available
- India: waiver for the requirement of local trials
- Importance of the registration of the originator company products – FDCs and single component
- WHO pre-qualification speeds up registration process and introduction of generics
- Strong role of advocacy

| February 2016: Alert to Falsified hepatitis C products in South-East Asia |
| WHO surveillance and monitoring system |
| - improve the quantity and quality of data on substandard, spurious, falsely labelled, falsified and counterfeit (SSFFC) medical products |
| - As of March 2016, over 1050 products reported to the WHO database. |
China case study
Exploring expanded access to TDF

Who pays?

1. Patients pay 100% (out-of-pocket)
2. Government pays 100%
3. Both insurance and patients pay
Overview

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WHO’s role in a partnership approach
### How do WHO guidelines differ from other guidelines?

<table>
<thead>
<tr>
<th>Feature</th>
<th>WHO Guideline</th>
<th>Other Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TARGET AUDIENCE</strong></td>
<td>National programme managers</td>
<td>Prescribing clinicians</td>
</tr>
<tr>
<td><strong>SETTINGS</strong></td>
<td>• Low and middle income countries</td>
<td>High income countries</td>
</tr>
<tr>
<td></td>
<td>• Variable access to laboratory testing (e.g. viral load, genotyping,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>transient elastography)</td>
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</tr>
<tr>
<td><strong>EVIDENCE-BASED GRADE APPROACH</strong></td>
<td>• Strength and quality of evidence</td>
<td>Variable use of evidence-based framework</td>
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<td></td>
<td>• Feasibility, equity, resource use considered</td>
<td></td>
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<tr>
<td><strong>APPROACH</strong></td>
<td>The “Public health approach”</td>
<td>Individualised treatment</td>
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