Improving access to therapy for HBV patients

Miroslava Subic, Massimo Levrero & Fabien Zoulim
Hepatology Department, Hospices Civils de Lyon
INSERM U1052, Cancer Research Center of Lyon
Lyon University, France
Chronic Hepatitis B (CHB) - a global health problem

*from viral suppression to cure*

- 257 million CHB worldwide
- 1.7 million CHB treated worldwide
- Hepatocellular Carcinoma (HCC): 2nd cause of cancer death worldwide

Elimination of HBV infection and HBV-related diseases

**HBV susceptible**

- **Acute HBV**
- **Chronic HBV**
- **Cirrhosis/HCC**

**Antiviral treatment**

**Vaccine**

**Universal precautions**

*Adapted from A. Lok*
The global burden of HBV infection
Leading causes of mortality and trends, 1990–2013

Stanaway et al, Lancet 2016
### Burden of infection and disease of HBV

<table>
<thead>
<tr>
<th></th>
<th>HBV</th>
<th>HCV</th>
<th>HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic infections worldwide (WHO)</td>
<td>240m</td>
<td>188m</td>
<td>35.3m</td>
</tr>
<tr>
<td>Chronic infections in European Region (WHO)</td>
<td>13.3m</td>
<td>15m</td>
<td>2.2m</td>
</tr>
<tr>
<td>Mortality (deaths/year) worldwide</td>
<td>786,000</td>
<td>499,000</td>
<td>1.6m</td>
</tr>
<tr>
<td>Mortality (deaths/year) in WHO European Region</td>
<td>36,000</td>
<td>86,000</td>
<td>66,000</td>
</tr>
</tbody>
</table>

*Global Burden of Disease Study 2010. Lozano et al, Lancet 2012*
Map of viral hepatitis-related, age-standardised mortality rate, by GBD region

Lemoine & Thursz, J Hepatol 2016

Stanaway et al, 2016
Controlling the infection
The WHO has recommended the administration of HBV vaccine to all newborns in endemic countries within the first 24 h of birth since 2009.

The global coverage of infants with birth dose remains very low, estimated at only 38% in 2014.
Infant immunization is not sufficient to prevent MTCT in highly viremic mothers.

Barriers to treatment
Current treatments: virus suppression and sustained disease control
Why not treating more patients?

- Decreased inflammation/fibrosis
- Decreased progression
- Reversal of fibrosis
- Decreased progression
- Decreased incidence but not eliminated
- HBsAg loss rate
  Max 10% after 5 years
- Life-long therapy

## Lack of knowledge and awareness

<table>
<thead>
<tr>
<th>Lack of knowledge and awareness</th>
<th>Low-to middle-income countries with high prevalence</th>
<th>Middle-to high-income countries with low prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Education of the public</td>
<td>• Support studies to increase evidence-based knowledge to create an appreciation of the impact of the disease</td>
<td></td>
</tr>
<tr>
<td>• Education of stakeholders</td>
<td>• Increase awareness among physicians who treat with immunosuppressive drugs</td>
<td></td>
</tr>
<tr>
<td>• Improve communication to reach high risk groups</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Foreign-born individuals comprise majority of growing HDV positive population in North America and Western Europe...

Germany: Wedemeyer et al., Hepatology 2007
Heidrich et al., J Viral Hepatitis 2009
France: Le Gal et al., Hepatology 2007
Italy: Stroffolini et al., J Med Virol 2009
Piccolo et al., Eur J Publ Health 2010
Screening and linkage to care
Acceptability and feasibility of a screen-and-treat program for hepatitis B virus infection in The Gambia: the Prevention of Liver Fibrosis and Cancer in Africa (PROLIFICA) study

From screening to linkage to care – The PROLIFICA experience in Gambia

Community screening

8170 eligible for screening in 54 enumeration areas (Dec 7, 2011, to Jan 24, 2014)

2190 not screened
   714 absent because of work or travel
   567 perceived no benefit
   356 had other reasons
   553 lost to follow-up

5980 (68.9%) screened for HBsAg

495 (8.8%) tested positive for HBsAg

402 (81.3%) linked to care

18 (4.4%) eligible for antiviral therapy

Blood bank screening

6832 eligible for screening at blood bank (Jan 1, 2013, to Dec 31, 2013)

5559 (81.4%) screened for HBsAg

721 (13.0%) tested positive for HBsAg

300 (41.6%) linked to care

29 (9.7%) eligible for antiviral therapy

## Screening and linkage to care

<table>
<thead>
<tr>
<th>Limited screening and linkage to care</th>
<th>Low-to middle-income countries with high prevalence</th>
<th>Middle-to high-income countries with low prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Implementation of national policies on HBV screening</td>
<td>• International policy on appropriate HBV screening</td>
<td></td>
</tr>
<tr>
<td>• Point of care screening</td>
<td>• Screening of risk groups (according to guidelines) including vulnerable populations</td>
<td></td>
</tr>
<tr>
<td>• Diagnostic assays which are more readily available at lower costs</td>
<td>• Screening of immigrants from high prevalence regions</td>
<td></td>
</tr>
<tr>
<td>• Virological assessment and liver disease staging with POC tests</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Limited access to treatment
Main hurdles for expanding treatment access

• Life-long suppressive therapy
• Not all HBV carriers are eligible to therapy according to clinical practice guidelines (some societies are widening treatment indications)
• Management of chronic HBV infection differs across countries worldwide (cf the different local practice guidelines)
• Cost and availability of existing antivirals (generics ?)
• Cost and availability of monitoring treatment efficacy

Adult community-based screening and treatment for HBV in the Gambia is likely to be a cost-effective intervention. Higher cost-effectiveness might be achievable with targeted facility-based screening, price reductions of drugs and diagnostics, and integration of HBV screening with other public health interventions.

# Improve access to treatment

<table>
<thead>
<tr>
<th>Limited treatment</th>
<th>Low-to middle-income countries with high prevalence</th>
<th>Middle-to high-income countries with low prevalence</th>
</tr>
</thead>
</table>
|                   | • Lower cost constraints by developing insurance systems supported by local governments  
|                   | • Increase accessibility of drugs by innovative cost models | • Increase awareness among patients  
|                   | | • Better training of physicians to optimally treat according to guidelines  
|                   | | • Simplify and ensure reimbursements for treatment |
Funding limitations

• HBV has attracted far fewer resources for clinical management and research than other chronic infectious diseases such as HIV, HCV or malaria.
• In the UK, HBV receives 0.7% of total expenditures compared to 3.0% for HCV, 13.9% for malaria, and 17.5% for HIV.
• Mortality from HBV > malaria but the latter receives nearly 5 times more funding.
• HDV which co-infects 20 million HBV carriers and results in more aggressive liver disease, receives nearly no resources.
• Fight against social stigma and discrimination through education of the public, physicians, and stakeholders

Global HBV burden
257 million

Undiagnosed HBV infection 91%
Diagnosed HBV infection 9%

Linked to care ?

Awareness
Cost of testing
Lack of infrastructures

Engaged To care ?

On treatment (if eligible) ?

Availability of drugs
Cost of drugs
Cost of monitoring

Adequately treated (virologically suppressed) 1%

Duration of therapy

Awareness
Public and health professionals information
Reimbursement
Lack of defined policies for screening

low prevalence middle-high income

high prevalence low-middle income

Subic et al, Liver Int 2018 in press
HBV cure: An attainable goal within the next decade!

- Collaboration between Academia, Industry and Stakeholders
- National health programs
- International HBV cure programs