Session Objectives

Review and share
1. Review progress and recent developments in HBV prevention and HCV treatment interventions for adolescents and children
2. Share clinical experience with treating children for HCV infection

Listen and discuss
1. To discuss key challenges and next steps
2. To hear from most affected countries how to advance agenda of promoting access to:
   - Testing and treatment for adolescents and children
   - Birth dose HBV vaccination
Hepatitis B and C prevention, care and treatment in adolescents and children

Philippa Easterbrook

World Health Organization
First WHO Global hepatitis strategy and targets

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

- Identifies priorities and sets global targets towards "Elimination"
  - Impact targets for HBV and HCV—reduction by 90% in incidence and 65% in mortality by 2030
  - Supported by Coverage targets for scaling up six key interventions:
    - HBV vaccination (including birth-dose)
    - Safe injection practices + safe blood
    - Harm reduction in PWIDs and safer sex
    - Hepatitis B and C diagnosis
    - Hepatitis B and C treatment

- Five Strategic directions to guide country response
A global hepatitis elimination strategy must include children and adolescents.

Definitions
Adolescent: 10-19 yr
Children: <10 yr

1.9 billion children (<15yrs)-27% of world's population

Leaving no one behind in hepatitis response

HIV & AIDS: Leaving no child behind

“Every child and young person deserves to live in a world free from HIV and AIDS. We are all that you have. We are your future.”

Nur Syakirin Husnal “Az” Hari, 16
- Launch of the Unite for Children, Unite Against AIDS campaign in Malaysia, 2005

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- Prevent mother-to-child transmission
- Provide paediatric treatment
- Prevent infection among adolescents and young people
- Protect and support children affected by viral hepatitis
Burden, Epidemiology and Natural History of Hepatitis B in Children

HBsAg estimates in <5 yrs (2015): Global average: 1.3%

Transmission:
- MTCT or early childhood are main routes of transmission
- 50% horizontal or intrafamilial
- In non-endemic settings, most CHB children are migrants

Natural history
- 70-90% of children exposed in childhood will become chronically infected
- HBV morbidity is low in childhood as in immune tolerant phase.
- Entecavir recommended <12 years

Source: WHO, HBsAg estimates, modelling conducted by the London School of Hygiene and Tropical Medicine. Disclaimer: The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2016. All rights reserved.
Hepatitis B vaccination

Global coverage (%) of hepatitis B vaccines in newborns (2000 – 2015)

In 2016 nearly half of all unvaccinated infants for DTP3 were in Sub-Saharan Africa

At least 3 doses of the hepatitis B vaccine (including the birth-dose)
Preventing mother-to-child transmission

- Most countries screening pregnant women
- Poor uptake of Hepatitis B birth-dose; particular challenge in Africa
- Poor linkage-to-care
- Triple elimination an opportunity: HIV, hepatitis B and syphilis

A comprehensive package

- Antiviral treatment
- HBIG
- Testing, linkage-to-care, follow-up of infants
- Birth-dose to reduce mother-to-child transmission
- At least 3 doses of hepatitis B vaccine to reduce incidence

Indicator: Hep-BD coverage

| Targets: 50% (2020), 90% (2030) | Baseline (2015): 39% |
Burden, Epidemiology and Natural History of Hepatitis C in Children

Transmission:
- MTCT main route of transmission: risk is 10% in HIV-HCV co-infected mothers and 6% among HIV-negative
- Iatrogenic transmission through unsafe injections
- Horizontal transmission in adolescents

Natural history:
- spontaneous clearance: 20%
- Histological course of chronic hepatitis C is unpredictable
- Chronic active hepatitis: 30%
- Risk of cirrhosis: 1-2%
- Few children with HCC

Countries Accounting for 80% of all Pediatric HCV Infections
- Globally, estimated 3.5 (3.1-3.9) million children 1-15 years are HCV Ab +ve
- Viraemic prevalence: 0.3% in HIC and 0.6% in LIC


## Why treat Hepatitis C infection in adolescents and children?

- **Important burden of infection in some settings**
- **Reduce development of chronic liver disease (cirrhosis and hepatocellular carcinoma)**
- **Reduce horizontal transmission within families and school and among adolescents**
- **Give child the opportunity to grow up free of potential stigma and psychological consequences**
- **Reduce economic burden of managing chronic liver disease in adults and costs are lower in children**
- **Absence of comorbidities, better compliance, better tolerance, higher SVR rates**
Treatment of Chronic Hepatitis C in Adolescents and Children Up To June 2017

- PEG IFN α-2a or α-2b + ribavirin
- FDA and EMA approved for children 3-18 years
- 24 weeks of treatment for genotype 2 and 3
- 48 weeks of treatment for genotype 1,4,5 and 6
FDA Approves HCV Drugs for Ages 12-17

— First pediatric approval for direct-acting agents

Sofosbuvir_{NS5B} / Ledipasvir_{NS5A} (FDC)

12-17 years, GT1, treatment-naïve and experienced

12 weeks

<table>
<thead>
<tr>
<th></th>
<th>SVR 12, %</th>
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<tbody>
<tr>
<td>overall*</td>
<td>98/100</td>
</tr>
<tr>
<td>treatment naïve ± cirrhosis*</td>
<td>78/80</td>
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<tr>
<td>treatment experienced no cirrhosis</td>
<td>20/20</td>
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</table>

Sofosbuvir_{NS5B} + Ribavirin

12-17 years, GT2 and 3 treatment-naïve and experienced

GT2: 12 weeks; GT3 24 weeks

<table>
<thead>
<tr>
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<th>SVR 12, %</th>
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<tbody>
<tr>
<td>overall*</td>
<td>51/52</td>
</tr>
<tr>
<td>GT2</td>
<td>13/13</td>
</tr>
<tr>
<td>GT3*</td>
<td>38/39</td>
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</table>
### Ongoing Studies with DAAs in Children (3-12yrs) and Adolescents (12-18yrs) with Chronic Hepatitis C

<table>
<thead>
<tr>
<th>Combined regimens</th>
<th>Genotype</th>
<th>ClinicalTrials.gov Identifier</th>
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</thead>
<tbody>
<tr>
<td>Sofosbuvir/ledipasvir ± ribavirin</td>
<td>1,3,4,5,6</td>
<td><strong>NCT 02249182</strong></td>
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<tr>
<td>Sofosbuvir + ribavirin</td>
<td>2,3</td>
<td><strong>NCT 02175758</strong></td>
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<tr>
<td>Ombitasvir, paritaprevir, ritonavir ± dasabuvir ± ribavirin</td>
<td>1,4</td>
<td><strong>NCT 02486406</strong></td>
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<tr>
<td>Sofosbuvir/ledipasvir</td>
<td>1,4</td>
<td><strong>NCT 02868242</strong></td>
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<tr>
<td>Glecaprevir/Pibrentasvir</td>
<td>1-6</td>
<td><strong>NCT 03067129</strong></td>
</tr>
<tr>
<td>SOF/Velpatasvir</td>
<td>1-6</td>
<td><strong>NCT 03022981</strong></td>
</tr>
</tbody>
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**ClinicalTrials.gov**
## EMA and FDA-Approved DAA Adult Regimens + Potential regimens for children

<table>
<thead>
<tr>
<th>individual oral regimen</th>
<th>GT</th>
<th>weeks</th>
<th>dosing (mg)</th>
<th>posology</th>
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</thead>
<tbody>
<tr>
<td><strong>SOF + R</strong></td>
<td>2,3</td>
<td>12-24</td>
<td>400/as per bw</td>
<td>1 tab QD</td>
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<tr>
<td><strong>SOF/LDP (_{(FDC)})</strong></td>
<td>1,4-6</td>
<td>12</td>
<td>400/90</td>
<td>1 tab QD</td>
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<tr>
<td><strong>SOF/VEL (_{(FDC)})</strong></td>
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<td>12</td>
<td>400/100</td>
<td>1 tab QD</td>
</tr>
<tr>
<td><strong>PAR/OMB/RTV (3D) (_{(FDC)}) + R</strong></td>
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<td>12</td>
<td>75/12.5/50</td>
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<td><strong>3D + DAS (±R)</strong></td>
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<td>12</td>
<td>3D + 250</td>
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<tr>
<td><strong>GZR/EBR (_{(FDC)})</strong></td>
<td>1,4-6</td>
<td>12</td>
<td>100/50</td>
<td>1 tab QD</td>
</tr>
<tr>
<td><strong>SOF + DAC</strong></td>
<td>1-4</td>
<td>12-24</td>
<td>400/30-60</td>
<td>2 tab QD</td>
</tr>
<tr>
<td><strong>SOF + SIM (±R)</strong></td>
<td>1,4</td>
<td>12</td>
<td>400/150</td>
<td>2 tab QD</td>
</tr>
<tr>
<td><strong>SOF/VEL/VOX</strong></td>
<td>1-6</td>
<td>8</td>
<td>400/100/100</td>
<td>1 tab QD</td>
</tr>
<tr>
<td><strong>GLE/PIB</strong></td>
<td>1-6</td>
<td>8</td>
<td>300/120</td>
<td>3 tabs QD</td>
</tr>
</tbody>
</table>

bw, body weight; QD, 1 time per day; TD, two times per day
Increase viral hepatitis testing in children and adolescents

- Significant gaps and missed opportunities for diagnosis and documenting HBV and HCV status of children of HBV-positive parents or HCV-positive mothers.

- Prioritise testing children of all HBV or HCV positive mothers (especially if mother HIV coinfectected)

- Offer testing to all children and adolescents with signs and symptoms suggestive of viral hepatitis

- Consider offering testing to all adolescents attending HIV services, STI clinics and TB clinics

- Target HCV testing to children who have had medical interventions or received blood products in countries where screening not optimal or where infection control practices suboptimal.
Two groups of adolescents need consideration
1. Adolescents infected vertically
2. Adolescents acquiring HBV or HCV horizontally, through sexual transmission or IDU

• **Age of consent**
  – Legal, policy and ethical barriers limit access for adolescents especially 10-14 year olds

• **Disclosure**
  – Adolescents may need particular support and involve family members and teachers

• **Access:**
  – How to access adolescents – most are either at home or in schools – environments often not easy to access

• **Cultural and social barriers**
  – Sexual issues sometimes considered taboo and socially inappropriate to discuss with adolescents
Next steps

- Children must not be left behind with Global hepatitis response
- Need **champion countries** with higher burden to promote testing and treatment in children: Egypt, China, Pakistan, Mongolia, India, Nigeria
- Track number of adolescents and children treated with DAAs
- Addressing **barriers to hepatitis B birth dose vaccination**
- Accelerate studies on DAAs in children 3-12 years, development of age-specific formulation
- **Addressing Research gaps:**
  - Define indications for treatment in children;
  - Identify predictive factors to select children who could be treated for shorter duration;
  - Role of DAAs in pregnancy to prevent vertical transmission

The Global Accelerator for Paediatric Formulations (GAP-f)
Ensuring children have accelerated access to optimal drug formulations