Taking Stock:
Where are we now on the priorities set in Durban?

Monique Andersson
University of Oxford NHS Foundation Trust, UK and University of Stellenbosch, South Africa
Priorities

1. Universal implementation of birth dose vaccination for HBV without further delay
2. Sustainable access to antiviral therapy for HBV mono-infected individuals
3. Increased diagnosis and treatment of viral hepatitis, particularly HCV amongst PWID
4. End of stigmatization of people living with HIV and/or viral hepatitis
Priority # 1.

Universal implementation of birth dose vaccination for HBV without further delay.
Recommendations

Existing recommendations in infants and neonates

- All infants should receive their first dose of hepatitis B vaccine as soon as possible after birth, preferably within 24 hours\(^a\), followed by two or three doses.


\(^a\) In countries where there is high disease endemicity and where HBV is mainly spread from mother to infant at birth or from child to child during early childhood, providing the first dose at birth is particularly important, but even in countries where there is intermediate or low endemicity, a substantial proportion of chronic infections are acquired through early transmission.
HBV Vaccination Coverage

- 2015 Global coverage of 3\textsuperscript{rd} HB vaccine dose was 84\%
- GHSS target 2020 90\%
- 2015 185 of 194 WHO member states (95\%) had included HB vaccine in the EPI
Three dose vaccine coverage by WHO region, 1990-2015

Source: Joint UNICEF–WHO reporting form
Birth Dose Vaccine

- WHO recommendations in 2004 and 2009 coverage BD vaccine
- Effectiveness reduces with the passage of time\(^1\)

- Globally BDV coverage only 39%

- 2015 BDV >70% Americas and WPacific
  2015 BDV African Region 10%

Countries with Hepatitis B Birth dose (HepB-BD) vaccine in the national immunization programme

Data source: WHO/V&B Database as at 05 September 2016 and ECDC published data at http://vaccine-schedule.ecdc.europa.eu/Pages/Scheduler.aspx

Map production: Immunization: Vaccines and Biologicals (IVB), World Health Organization

Date of slide: 05 September 2016

HepB-BD introduced to date
(97 countries or 49%)

HepB-BD only for infants born to HBsAG-positive mothers
(22 countries or 11%)

HepB in schedule but no HepB-BD
(71 countries or 37%)

HepB given only for risk groups or adolescents
(4 countries or 2%)

Not available
Not applicable
**Cumulated incidence of chronic HBV infection in children <5 years 2015**

<table>
<thead>
<tr>
<th>WHO region</th>
<th>Map key</th>
<th>Prevalence of HBsAg (%)</th>
<th>Uncertainty intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Best</td>
<td>Lower</td>
</tr>
<tr>
<td>African Region</td>
<td></td>
<td>3.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Region of the Americas</td>
<td></td>
<td>0.2</td>
<td>0.1</td>
</tr>
<tr>
<td>Eastern Mediterranean Region</td>
<td></td>
<td>1.6</td>
<td>1.2</td>
</tr>
<tr>
<td>European Region</td>
<td></td>
<td>0.4</td>
<td>0.2</td>
</tr>
<tr>
<td>South-East Asia Region</td>
<td></td>
<td>0.7</td>
<td>0.5</td>
</tr>
<tr>
<td>Western Pacific Region</td>
<td></td>
<td>0.9</td>
<td>0.6</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>1.3</strong></td>
<td><strong>0.9</strong></td>
</tr>
</tbody>
</table>

*Source: WHO, work conducted by the London School of Hygiene & Tropical Medicine (LSHTM). See Annex 2.*
BDV Africa

- 10/47 countries have implemented BDV
- Cameroon 2017, Sierra Leone 2018, Niger 2019

- 2015 Coverage
  <80% Angola (19%), Mauritania (51%), Nigeria (43%)

80-95% Botswana and Namibia 87%, CapVert 93%, Sao Tome 91%
>95% Algeria, The Gambia
Barriers to BDV Implementation

• Most frequent factor associated with low coverage was being born at home\textsuperscript{1,2}
• Quality of health worker training\textsuperscript{1,3,4}
• Parent awareness\textsuperscript{2}
• Cost to patient\textsuperscript{1}
• Vaccine supply

1. Patel et al. Vaccine 2014;32(39);5140-44
Global BD Vaccine

Aim: Analysis of global and regional data to assess correlations between HepB BD coverage, IDR, SBA and other co-variates

Findings: Significant correlations BD and SBA (rho=0.24, p=0.03), IDR (rho=0.42, p<0.001), adult literacy rate (rho=0.37, p=0.003), total health expenditure per capita (rho=0.24, p=0.03)

Conclusion: Increasing IDR and SBA rates, training and supervising staff, increased community awareness, using BD outside cold chain would increase coverage

Allison RD et al. Vaccine 2017;35(33):4094-98
Other approaches
What is Uniject?

An injection system that is:

- Single-dose
- Prefilled
- Easy to use
- Not reusable
- Small in size
Improving hepatitis B birth dose coverage through village health volunteer training and pregnant women education

Xi Li a,1, James Heffelfinger a, Eric Wiesen b, Sergey Diorditsa a, Jayaprakash Valiakolleri c, Agnes Bauro Nikuata e, Ezekial Nukuro e, Beia Tabwaia d, Joseph Woodring a,*

• Republic Kiribati Coverage BDV 66% 2014
• i) Improve linkage between village health volunteers and health workers
  ii) educate pregnant women
• Improved BDV Outer islands 57% to 83% (108/189 to 72/88)
  Tarawa 89% to 95% (505/570 to 292/306)

1. Li et al. Vaccine 2017; epub 5th July 2017
Other approaches

• Use of mobile technology to improve communication\(^1\)
• Engagement of private sector\(^2\)

1. Xeuatvongsa et al. Vaccine 2016;34(47):5777-84
Priority # 2.

ii. Sustainable access to antiviral therapy for HBV mono-infected individuals.
Access to Treatment

- Of those diagnosed 9%, (22 million) 8% (1.7 million) were on treatment

Of 22 million diagnosed not known what proportion are eligible for treatment
Cascade of care for HBV infection, by WHO region 2015

Cascade of care

Source: WHO estimates, conducted by the Center for Disease Analysis. See Annex 2.

*a As the proportion of persons eligible for treatment among those diagnosed is unknown, the treatment gap cannot be calculated.
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Access to Treatment

• Of those diagnosed 9%, 22million)
  8% (1.7 million) were on treatment

Of 22 million diagnosed not known what proportion are eligible for treatment

• Who should be treated?
Feasibility of screen and treat - 27 rural and 27 urban communities
- 2011-2014 community screening, referral for care
- 5980/8170 HBsAg positive
- Almost none of the participants had been tested HBV
- No term to define cirrhosis in Mandinka, local Gambian language
- HBsAg prevalence 8.8% (7.9-9.7)
- 81.3% (402/495 attended clinic)
- Male sex strongly associated with treatment eligibility OR 4.35, 1.50-12.58; p=0.007
- 81% good adherence 12 months, similar ARVs for HIV
- 91.5% achieved virological response, in line European cohort data

Mills et al. JAMA 2006:296;
HBV Treatment

• 2015 WHO guideline recommends antinucleos(t)ides with a high barrier to resistance as first line therapy
• Two medicines are available: entecavir and tenofovir
• Entecavir is off-patent
• Tenofovir off-patent in many LMIC
### 6.4.4.1 Medicines for hepatitis B

#### 6.4.4.1.1 Nucleoside/Nucleotide reverse transcriptase inhibitors

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Oral liquid: 0.05 mg/ mL</th>
<th>Tablet: 0.5 mg; 1 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>entecavir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>tenofovir disoproxil fumarate (TDF)</td>
<td>Tablet: 300 mg (tenofovir disoproxil fumarate – equivalent to 245 mg tenofovir disoproxil).</td>
<td></td>
</tr>
</tbody>
</table>
Tenofovir

- Protected by a patent until 2018 in most upper-middle/HICs
- Cost ranges from USD40D-USD1500/year*
- L/MIC generic tenofovir is available
- Some MICs barriers to access
- GPRM cost/year quality assured treatment USD48*
- Fear of re-importation an obstacle to such distribution?

* Feb 2017
Uganda

‘Screening programmes have been established in the areas of highest prevalence, but those who test HBsAg positive do not get referral and there is no ‘free’ access to tenofovir or entecavir. There are no clear guidelines on further testing to determine treatment candidacy. This has certainly been frustrating to the infected population.’

Academic, Makerere University
## Access to Screening and Treatment

<table>
<thead>
<tr>
<th>Country</th>
<th>Clinical Guidelines</th>
<th>Referral Pathway</th>
<th>Screening</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bangladesh</td>
<td>No</td>
<td>No</td>
<td>Patient</td>
<td>Patient</td>
</tr>
<tr>
<td>China</td>
<td>Yes</td>
<td>Yes</td>
<td>Insurance/Patient</td>
<td>Limited access Patient/Insurance pay</td>
</tr>
<tr>
<td>Indonesia</td>
<td>Yes</td>
<td>Yes</td>
<td>Patient</td>
<td>Civil Servants – Govt Others - Patient</td>
</tr>
<tr>
<td>Malaysia</td>
<td>No</td>
<td>No</td>
<td>Patient</td>
<td>Patient/Government (50%)</td>
</tr>
<tr>
<td>Myanmar</td>
<td>Yes</td>
<td>No</td>
<td>Patient</td>
<td>Patient</td>
</tr>
<tr>
<td>Vietnam</td>
<td>Yes</td>
<td>No</td>
<td>Patient</td>
<td>Patient</td>
</tr>
</tbody>
</table>

1. Meyers et al. Viral Hepatitis Policy in Asia 2016 Survey, June 2017
Entecavir

- Off-patent

For treatment of hepatitis B, entecavir is given daily for life. In South Africa, a month of entecavir costs between ZAR 2,755 (US$ 195) and ZAR 5,510 (US$ 390), depending upon the dosage required. With the removal of patent barriers globally – allowing for greater economies of scale in production – entecavir could be available for as little as ZAR 41 (US$ 3) per month.
Entecavir
Priority # 3.

Increased diagnosis and treatment of viral hepatitis, particularly HCV amongst PWID.
HCV Incidence

• 1.75 million new infections in 2015 (global incidence rate: 23.7 per 100,000)\(^1\)

• New infections 1.75 million (2015)
  > 399,000 died + 843,000 cured

Need to upscale responses to eliminate HCV

1. WHO Global Hepatitis Report 2017
## Incidence of HCV infection, 2015

<table>
<thead>
<tr>
<th>WHO region</th>
<th>Map key</th>
<th>Incidence rate (per 100,000)</th>
<th>Best estimate</th>
<th>Uncertainty interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>African Region</td>
<td></td>
<td>31.0</td>
<td>22.5–54.4</td>
<td></td>
</tr>
<tr>
<td>Region of the Americas</td>
<td></td>
<td>6.4</td>
<td>5.9–7.0</td>
<td></td>
</tr>
<tr>
<td>Eastern Mediterranean Region</td>
<td></td>
<td>62.5</td>
<td>55.6–65.2</td>
<td></td>
</tr>
<tr>
<td>European Region</td>
<td></td>
<td>61.8</td>
<td>50.3–66.0</td>
<td></td>
</tr>
<tr>
<td>South-East Asia Region</td>
<td></td>
<td>14.8</td>
<td>12.5–26.9</td>
<td></td>
</tr>
<tr>
<td>Western Pacific Region</td>
<td></td>
<td>6.0</td>
<td>5.6–6.6</td>
<td></td>
</tr>
<tr>
<td><strong>Global</strong></td>
<td></td>
<td><strong>23.7</strong></td>
<td><strong>21.3–28.7</strong></td>
<td></td>
</tr>
</tbody>
</table>

*Source: WHO, work conducted by the Center for Disease Analysis. See Annex 2.*
PWIDs and HCV

- New Infections: 23% of new HCV infections in PWID
- Chronic Infections: Around 8% of current PWID are HCV infected
- 2.3 million (IQR 1.3-4.4) of 36.7 million living with HIV globally have serological evidence of HCV
- Of these 1.36 million currently inject drugs
Cascade of care for HCV infection, 2015

Source: WHO estimates, conducted by the Center for Disease Analysis. See Annex 2.
First WHO prequalified HCV POCT
SD Bioline HCV RDT

- One study evaluating performance
- Compared to RIBA (MP Biomedical)
- Sensitivity 78.8% (95% CI 71.2-86.8)
- Specificity 100% (95% CI 97.1-100)
- Concordance with RIBA 0.831 (95% CI 0.74-0.91)

Dried blood Spots

• Avoids venepuncture
• Easy transportation
• Simple storage
• Centralised laboratories
• Cost effective
Dried Blood Spots

Lower sensitivity 50uL vs 500ul (m2000) and 650uL (CAP/CTM)
12/24 weeks post therapy HCV RNA levels are high if treatment failure thus if neg can be trusted as indicative of SVR
Core antigen detected (low sens 64.1%)
Genotyping not possible with low HCV VL subtype may remain undetermined eg 1a vs 1b

1. Soulier A et al. JID 2016;213:1087-95
DOT-C: A cluster randomised feasibility trial evaluating directly observed HCV therapy in a population receiving OST from community pharmacy

- Feasibility study - Cluster randomised controlled trial with mixed methods evaluation compare in conventional service pathway versus a pharmacist lead pathway in population receiving OST

- PC 58/244 (24%)  PL 94/262 (36%) (p<0.002)
- Total pathway cost C:  GBP 933
  PL: GBP 238

Pipeline for Viral Load POCT

- **Alere Q Analyzer** (Alere Inc. Waltham, MA, USA) ¹
- **SAMBA** (DRW, Sunnyvale CA USA) ²
- Field testing for HIV performed well, Could they be adapted to HBV?

- **Truenat** (Molbio Diagnostics, Goa, India)
- **EOSCAPE-HIV** (Wave80 Biosciences, San Francisco, CA)
- **Genedrive** (Epistem, Manchester, UK)

¹ J Clin Microbiol 2014;52(9);3377-3383
² J Acquir Im Defic Syndr 2014;67(1):e1-14
PWID treatment with DAAs

- 174 PWIDs (1 year) (63% cirrhosis, 37% previous treatment) 95% completed therapy and 93% SVR

- SIMPLIFY study* Genotype 1-6 SOF+VEL 12 weeks 103 participants (58% OST, 74% IDU last 30 days) 99/103 completed treatment and all had ETR. ITT analysis 96% ETR; 94% SVR (96/102) with no virological failures and 1 relapse/reinfection

1. Boglione L et al. J of Viral Hepatitis 2017 Epub
Primary health care setting

• Observational cohort study
• 72 individuals commencing
• DAAs and durations decided individually
• ITT population 69/72 (96%) completed planned treatment
• ITT SVR12 population 59/72 (82%)

• Non-SVR group no association with freq of injecting, last drug injected or planned treatment duration

Harm reduction

NEEDLE EXCHANGE SAVES LIVES
OST and NSP

- Combined OST and high coverage NSP can reduce HCV incidence by >80%\(^1\)
- <1% prisons globally provide NSP making it a priority for prevention activities\(^2\)
- Modelling studies suggest HCV treatment for PWID can lead to substantial reductions in HCV prevalence and reduce transmission\(^3\)

1. Hagan H JID 2011;204:74-83
3. Martin N CID 2013;579(S2):539-545
NSP

- On average globally only 27/person/year
- 2030 target of 300 syringes/person/year
- Only 26% of countries have data to allow them to monitor this
- Need to scale up harm reduction and implement policies that address stigma and discrimination

Size of the population of PWID and harm reduction indicators

<table>
<thead>
<tr>
<th>WHO region</th>
<th>Size of the population injecting drugs</th>
<th>Proportion of countries with needle and syringe programmes (%)</th>
<th>Needle and syringe distribution(^c) (93)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number(^a) (millions)</td>
<td>Prevalence (%) in the population 15–64 years</td>
<td>% of countries with data(^d)</td>
</tr>
<tr>
<td>African Region</td>
<td>0.52</td>
<td>0.1</td>
<td>30</td>
</tr>
<tr>
<td>Region of the Americas</td>
<td>2.75</td>
<td>0.42</td>
<td>34</td>
</tr>
<tr>
<td>Eastern Mediterranean Region</td>
<td>0.92</td>
<td>0.23</td>
<td>43</td>
</tr>
<tr>
<td>European Region</td>
<td>3.97</td>
<td>0.66</td>
<td>92</td>
</tr>
<tr>
<td>South-East Asia Region</td>
<td>0.56</td>
<td>0.04</td>
<td>82</td>
</tr>
<tr>
<td>Western Pacific Region</td>
<td>3.03</td>
<td>0.23</td>
<td>33</td>
</tr>
<tr>
<td>World</td>
<td>11.75(^f)</td>
<td>0.25</td>
<td>53</td>
</tr>
</tbody>
</table>

WHO Global Hepatitis Report, 2017 WHO
Restrictions on access to direct-acting antivirals for people who inject drugs: The European Hep-CORE study and the role of patient groups in monitoring national HCV responses

J.V. Lazarus, K. Safreed-Harmon, S.R. Stumo, M. Jauffret-Roustide, M. Maticic, T. Reich, E. Schatz, J. Tallada, M. Harris, on behalf of the Hep-CORE Study Group

Widespread treatment restrictions affected PWID in European countries.

Involving civil society stakeholders is essential for implementing HCV treatment strategies

PWID and HCV Elimination

• HCV elimination is dependent on addressing IDU broad policy of prevention of initiation of drug use, prevention of stigma and discrimination, treatment and provision of harm reduction¹

• Mathematical models high service coverage essential to eliminate HCV

Priority # 4.

End of stigmatization of people living with HIV and/or viral hepatitis
Postponement or Rejection of Treatment, Care and Support

Stigma and Discrimination Disproportionately Affect Women and Girls

Reduced and Delayed Disclosure

Magnified Effects among Socially Vulnerable Groups

Lower Uptake of HIV Preventive Services and Testing and Counselling
Impact of Stigma

- Reduced access to opportunities diagnostic screening\(^1\)
- Reduced uptake of clinical care\(^2\)
- Anxiety about spread to family members is common\(^3\)
- Sense of bringing shame upon the family\(^4\)
- Difficulties in establishing/maintaining intimate relationships\(^5\)

2. Liu K et al. Liv Int 2016;36:1582-84
• <1% Gambians had heard of HBV despite prevalence being >8%
• Lack recognition of HBV in Burkina Faso, Cote d’Ivoire, Madagascar
• Some languages no word for viral hepatitis
• Need to improve communication about viral hepatitis in Africa

Shimakawa Y et al. Lancet 2017;17:688-9
“Health care workers are ignorant and don’t know how to handle or manage a situation when an individual discloses they are Hepatitis B positive but HIV negative. This confusion creates a situation where the health care workers are discriminating and stigmatising HBV patients due to lack of information.”

“Hepatitis B is associated with HIV/AIDS, which means having a diagnosis comes with stigma and discrimination. This starts a trend of finger pointing, and slowly results in isolation. Although there has been a lot of work done to educate people about HIV, there has not been enough work to educate people about Hep B.”

“In our culture what happens to one person becomes the concern of the all family and the community. Having a Hep B diagnosis will bring shame to one’s family. This can cost family members jobs and school places.”
Mr X refused testing for fear of losing his job if he was diagnosed with HBV.

Mr M refused testing until it was explained that HBV was not HIV and he was not secretly being tested for HIV.

Mr A refused to believe he was HBV infected. He believed that his result was positive because he had had too much to drink the previous night.
HCW, viral hepatitis and discrimination

• Study recruited 500 people 65% reported negative experiences and health care discrimination \(^1\)

• Reports of refusal or withdrawal of health care were common and contributed to a reluctance to disclose to health professionals\(^2\)

2. Harris NZ Sociol 2005;20:4-19
Stigma and Discrimination

GUIDANCE NOTE | 2012

KEY PROGRAMMES TO REDUCE STIGMA AND DISCRIMINATION AND INCREASE ACCESS TO JUSTICE IN NATIONAL HIV RESPONSES

www.iasociety.org
HCP

• Can we address stigma in hospitals and clinics by improving understanding of viral hepatitis?

• Can we engage social media to address issues around stigma amongst HCW?

• Can we work with sociologists and anthropologists to better understand and address viral hepatitis related stigma?
Priorities

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2. Sustainable access to antiviral therapy for HBV mono-infected individuals
3. Increased diagnosis and treatment of viral hepatitis, particularly HCV amongst PWID
4. End of stigmatization of people living with HIV and/or viral hepatitis
‘That is the paradox of the epidemic that in order to create one contagious movement, you have to create many small movements first’

Malcolm Gladwell
Acknowledgments

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Mashiko Setshedhi

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Posiano Ocama

University of Hong Kong
Tammy Meyers

University Stellebosch
Wolfgang Preiser
Tongai Maponga
Nafiisah Chotun
Cynthia Tamandjou
I AM SPEAKING OUT

Take action today. Eliminate hepatitis.

World Hepatitis Day
28 July

#ShowYourFace #NOhep

28th July World Hepatitis Day