Global Efforts on Viral Hepatitis Elimination
CALDA 2019
Cairo, Egypt

John W Ward, MD
Task Force for Global Health
US Centers for Disease control and Prevention
Agenda

• Burden of disease

• Why elimination

• Key interventions

• Progress and challenges

• Working together to accelerate progress toward elimination
Hepatitis B Virus and Hepatitis C Virus
Cause > 96% of Deaths from Viral Hepatitis - 2017

Parenteral transmission
Acute and chronic disease

Fecal-oral transmission
Acute disease

HBV and HCV Burden of Disease

- **HBV**
  - Global 257 M persons with chronic HBV
    - AFRO: 60 M
    - EMRO: 21M
  - Major risks: Perinatal and horizontal contact < 5 yrs of age

- **HCV**
  - 71 million persons with current HCV
    - AFRO: 11 M
    - EMRO: 15M
  - Major risk: health care associated transmission
  - Highest prevalence: Persons who inject drugs (50%)

Sources – WHO (LSHTM); Lancet 2016; 388: 1459–544
Over Two of Three Liver Cancer Deaths Attributable to HBV and HCV

HBV 40%

HCV 29%

Source: https://www.globalhep.org/
Increases in HBV and HCV Deaths 2005-2017

Global Burden of Disease
Why HBV and HCV Elimination

- **Biologic feasibility**
  - Human required for replication; No intermediate hosts, environmental propagation

- **Technical feasibility**
  - Prevent transmission-
    - Hepatitis B vaccine >95% efficacy
    - Avoid parenteral blood exposures, sexual contact
  - Prevent mortality – HBV and HCV treatment
    - HBV treatment- long term viral suppressive therapy
      - Reduced risk of liver cancer (50%), mortality (40%)
    - HCV treatment and cure
      - Reduced risk of liver cancer (80%), mortality (75%)
  - Reliable tests- high sensitivity and specificity

- **Call to Action**
  - Create sense of urgency
  - Bring stakeholder together

- **Achieve Health equity**

Ward J, Gastroenterology 2019
## Scale up and Monitor Implementation of WHO Recommended Interventions

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<tbody>
<tr>
<td>Population (million)</td>
<td>989</td>
<td>994</td>
<td>914</td>
<td>1945</td>
<td>1867</td>
<td>7369</td>
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<tr>
<td>Prevalence chronic HBV (%)</td>
<td>6.1%</td>
<td>0.7%</td>
<td>2.3%</td>
<td>1.6%</td>
<td>2%</td>
<td>0.2%</td>
<td>3.5%</td>
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<tr>
<td>Prevalence chronic HCV (%)</td>
<td>1%</td>
<td>0.7%</td>
<td>2.3%</td>
<td>1.5%</td>
<td>0.5%</td>
<td>0.7%</td>
<td>1%</td>
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<td><strong>Indicators</strong></td>
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<tr>
<td>Timely birth dose vaccine (%)</td>
<td>10%</td>
<td>7%</td>
<td>7.3%</td>
<td>30%</td>
<td>34%</td>
<td>84%</td>
<td>39%</td>
<td>50%</td>
<td>90%</td>
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<tr>
<td>Third dose HBV vaccine (%)</td>
<td>78%</td>
<td>89%</td>
<td>80%</td>
<td>81%</td>
<td>87%</td>
<td>90%</td>
<td>84%</td>
<td>90%</td>
<td>90%</td>
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<tr>
<td>Blood donations screened (%)</td>
<td>80%</td>
<td>98%</td>
<td>81%</td>
<td>99.9</td>
<td>85%</td>
<td>98%</td>
<td>97%</td>
<td>95%</td>
<td>100%</td>
</tr>
<tr>
<td>Needle/syringe distribution (/1000 IPV year)</td>
<td>6</td>
<td>22</td>
<td>25</td>
<td>59</td>
<td>29</td>
<td>57</td>
<td>27</td>
<td>200</td>
<td>300</td>
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<tr>
<td>Injection safety (% reused needles)</td>
<td>3.7%</td>
<td>3.4%</td>
<td>14%</td>
<td>4.6%</td>
<td>5.2%</td>
<td>3.2%</td>
<td>3%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Proportion of chronic HBV diagnosed (%)</td>
<td>0.3%</td>
<td>9.1%</td>
<td>1.8%</td>
<td>14%</td>
<td>2.6%</td>
<td>2%</td>
<td>9%</td>
<td>30%</td>
<td>90%</td>
</tr>
<tr>
<td>Proportion of chronic HCV diagnosed (%)</td>
<td>5.7%</td>
<td>36.3%</td>
<td>17.7%</td>
<td>31.2%</td>
<td>8.7%</td>
<td>21.5%</td>
<td>70%</td>
<td>30%</td>
<td>90%</td>
</tr>
<tr>
<td>Treatment coverage HBV (%)</td>
<td>&lt;1%*</td>
<td>13%*</td>
<td>23%*</td>
<td>7%*</td>
<td>&lt;1%*</td>
<td>10%*</td>
<td>5%*</td>
<td>5 million</td>
<td>80%</td>
</tr>
<tr>
<td>Treatment coverage HCV (%)</td>
<td>2.2%</td>
<td>11.1%</td>
<td>12.1%</td>
<td>4.9%</td>
<td>7.1%</td>
<td>4.8%</td>
<td>7.4%</td>
<td>3 million</td>
<td>80%</td>
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<tr>
<td><strong>Incidence estimates</strong></td>
<td></td>
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</tr>
<tr>
<td>Cumulative incidence of HBV in under 5% (%)</td>
<td>3%</td>
<td>0.2%</td>
<td>1.6%</td>
<td>0.4%</td>
<td>0.7%</td>
<td>0.9%</td>
<td>1.3%</td>
<td>130%</td>
<td>190%</td>
</tr>
<tr>
<td>Incidence HCV (/100 000)</td>
<td>30.9</td>
<td>6.4</td>
<td>6.25</td>
<td>6.18</td>
<td>14.8</td>
<td>6</td>
<td>23.7</td>
<td>130%</td>
<td>190%</td>
</tr>
</tbody>
</table>

- Routine reporting from countries
- Estimates meeting standards defined by GATHER (gather.statement.org)
- Other estimates (including modelling)
- Extrapolation and inferences
Hepatitis B Vaccination to Eliminate New Cases of Chronic HBV Infection

- Tenofovir for HBV+ women with high viral loads (99% efficacy)
- HB Ig + vaccine (92% efficacy)
- HBsAG Testing for women, linkage to care, and follow-up of infants
- Timely birth dose to reduce mother to child transmission (72% efficacy) 43% coverage
- At least 3 doses hepatitis B vaccine to reduce incidence (95% efficacy) 84% coverage

HepB vaccination cited as best buy for cancer prevention by United Nations
Hepatitis B Vaccine is the Cornerstone for HBV Elimination

Western Pacific Region achieved goal of <1% of children with HBV by 2017

EMRO has adopted HBV goal certification
HepB3 Coverage for the African Region is Similar to Other Vaccines, Birth Dose Coverage is Low

<table>
<thead>
<tr>
<th>No. (%) countries with vaccine in schedule</th>
<th>Number of countries with vaccine in schedule</th>
<th>% Coverage 2018,* by region</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Global (all regions)</td>
<td>African</td>
</tr>
<tr>
<td>HepB BD</td>
<td>84 (43)</td>
<td>4</td>
</tr>
<tr>
<td>HepB3</td>
<td>185 (95)</td>
<td>76</td>
</tr>
<tr>
<td>DTP3</td>
<td>194 (100)</td>
<td>76</td>
</tr>
</tbody>
</table>

Improving Newborn Hepatitis B Vaccination - Africa

• Need - Newborns with HBV at greatest risk for liver cancer

• Opportunities
  • Good infant immunization systems- HepB coverage 76%
  • New Gavi support for birth dose administration (2021)
  • Implementation strategies from other countries
    • Birth attendant training; reliable supply/ storage; evaluation data

• Challenges
  • Cost of vaccine ( < $.40 per dose)
  • Serologic surveys to assess cost/effectiveness
  • Strategies for high proportion of births at home- ~40%
  • Require large changes in maternal and child care
  • Collaboration and technical assistance needs

WHO global hepatitis report
Large Reductions in Blood borne Transmission in Health Care Settings

- Improvements in injection safety and infection control
  - 88% decrease in the proportion of injections administered with non-sterile equipment
  - 91% reduction in HBV transmission
  - 83% reduction in HCV transmission
  - 5% injections continue to be given with reused equipment
  - Accounts for 1.2 M new HCV infections/year

A Challenge to Elimination of HCV Transmission Prevention Services for Persons Who Inject Drugs

- Drug treatment+ safe injection equipment reduces transmission risk by 71%
- Only 93 of 176 countries have prevention programs
- Models indicate HCV cure as prevention (CAP) strategies reduce risk by > 90%

Larney S, Lancet Glob Health. 2017
HBV and HCV are Under-diagnosed and Under-treated Infections

**HBV 257 million**
Global: Diagnosed 10%; On treatment 2%

**HCV 71 million**
Global: Diagnosed: 13%; Treated 5 million

Progress report on HIV, viral hepatitis and sexually transmitted infections 2019
http://www.who.int/hepatitis/publications/
Viral Hepatitis Elimination is Highly Cost Effective/Saving with Affordable Diagnostics and Treatments

- Elimination by 2030 will cost **$66.8 B**
- 1.5% increase in WHO SDG projected resource needs ($3,944 B)
- Highly cost-effective or cost-saving in most countries
- **Elimination will require investments in screening and treatment**
  - HBV screen 5.5 B people; treat 32.2 M
  - HCV screen 6.1 B for HCV; treat 61.6 M
- Avert 4.5 million premature deaths and decrease global mortality by 5% and 10% increase in healthy life-years

To move from planning to implementation, financing solutions must be tailored to the context-- more support is needed for LICs

<table>
<thead>
<tr>
<th>High-income countries</th>
<th>Middle-income countries</th>
<th>Low-income countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hepatitis testing and treatment must continue to be integrated into UHC schemes and covered by public and private payers, with removal of all restrictions to care</td>
<td>• Revenue growth in many countries could finance hepatitis screening and treatment within UHC schemes</td>
<td>• Testing and treatment programs will have to be built from the ground up-- which will require a greater proportion of new resources</td>
</tr>
<tr>
<td>• HCV treatment is likely to be cost-saving given high costs of managing sequelae</td>
<td>• Strong economic argument for governments to invest in elimination given downstream healthcare costs associated with sequelae</td>
<td>• Access to care for liver disease is often limited, so cost offsets not as high</td>
</tr>
<tr>
<td></td>
<td>• Donor support might be needed to help catalyze these programs given generally more limited economic growth and nascent UHC schemes</td>
<td></td>
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### Australia: Example of strong foundation for elimination

<table>
<thead>
<tr>
<th>Elimination component</th>
<th>Details</th>
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<tbody>
<tr>
<td>Low DAA prices</td>
<td>• Government negotiated low DAA prices</td>
</tr>
<tr>
<td>Unrestricted access to DAAs</td>
<td>• Since introduced in 2016, &gt; 70,000 individuals treated</td>
</tr>
<tr>
<td>Government commitment</td>
<td>• Government has not capped treatment budget and annual treatment numbers</td>
</tr>
<tr>
<td>Removal of prescriber restrictions</td>
<td>• General practitioners and other non-specialists can prescribe treatment</td>
</tr>
</tbody>
</table>
| Diverse range of models of care     | • As treatment uptake stalls overall, uptake among priority populations such as PWID and gay, bisexual, and HIV+ men and other MSM  
|                                     | • Australia has been a trailblazer in piloting models of care for PWID   |
| High coverage of harm reduction     | • Evidence suggests access to syringe exchange and OST has led to a decline in prevalence among PWID |

Japan is on the Path to Elimination Through a Series of Policy Reforms to Expand HCV Testing and Treatment

1986: Maternal HBV screening
1989: Blood bank HCV screening
2002: HCV screening > 40 yrs
2007: HCV treatment centers
2008: HCV medical coverage
2009:
  • HCV testing for all ages
  • Hepatitis health system law- regional treatment network

Burden of disease

Declines in HCV Prevalence - United States

2.4 million HCV infected persons

Contributors to declines
- Change in methodology
- Mortality
- Cure of HCV infection
  - Decrease % of HCV exposed with HCV RNA
  - One company reported ~675,000 treatments with DAA
- Decline in HCV RNA + a marker of impact of cure on prevalence

Hofmeister M, Hepatology 2018
Strategies that Expand Access to HCV Testing, Care and Cure - United States

- Provider education
- Clinical decision tools
- Reflex RNA testing (figure)
- Performance indicators/incentives
- Case management
- Co-localization of HCV and primary care
- Accessible HCV therapies

<table>
<thead>
<tr>
<th>Study</th>
<th>Strategy</th>
<th>Increase in testing</th>
<th>Total tested</th>
</tr>
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<tbody>
<tr>
<td>Primary care</td>
<td>BPA- Best practice alert</td>
<td>Two fold increase</td>
<td>71%</td>
</tr>
<tr>
<td>Primary care</td>
<td>BPA</td>
<td>15 fold increase</td>
<td>11%</td>
</tr>
<tr>
<td>Health system</td>
<td>BPA and clinical support</td>
<td>Two fold increase</td>
<td>50% coverage with 5 years of testing</td>
</tr>
</tbody>
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Low number of persons in the birth cohort report testing - ~ 11-13% (2013-2015)

HCV Treatment scale-up in France: 2014-Today

- **2014-16**: Restricted access to DAAs & complicated algorithm
  - Used primarily in clinical trials and in compassionate use programs
  - Treatment restrictions for: a) stage F3, F4 or “severe F2” liver fibrosis, or b) comorbidities
  - Treatment initiation required multidisciplinary team at reference center hospital
- **2016**: Universal access to DAAs, no more treatment restrictions
- **2019**: Removed provider prescriptions– not only specialists can prescribe DAAs

Source: Brouard et al. BMC Infectious Diseases (2017) 17:784
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5738822
“As Native People and as Cherokee Nation Citizens, We Must Keep Striving to Eliminate Hepatitis C.”

- American Indians have highest HCV incidence and mortality
- Cherokee Nation launched elimination program in 2015
  - Universal HCV testing for patients 20-69 yrs.
  - Training and electronic tools to prompt testing
  - Care managed by mid-level providers (e.g., pharmacists)
  - Health system strategies to pay for testing and treatment
  - Contact tracing to identify new HCV infections
  - Partnerships with CDC, state/local health dept., UOK, NGOs, Gilead Foundation

*preliminary data

Mera J, personal communication
Changes In HCV Testing and Treatment- United States

- CDC supporting state and local hepatitis elimination planning
- States and cities adopting HCV elimination goals- San Diego, San Francisco, Washington State, Louisiana, New York
- States negotiating lower treatment costs; pharma to pay for HCV testing in some states
- Expanded HCV testing- increases in younger persons (largely driven by increased injection drug use)

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<tbody>
<tr>
<td><strong>Age groups</strong></td>
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</tr>
<tr>
<td>• Persons high-risk of for infection</td>
<td>• All adults ages 18-79 years</td>
</tr>
<tr>
<td>• Adults born between 1945 and 1965</td>
<td>• Pregnant women</td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td></td>
</tr>
<tr>
<td>• Periodic screening for persons at high-risk</td>
<td>• Most adults need only one time screening</td>
</tr>
<tr>
<td>• One-time screening for adults born 1945-1965</td>
<td>• Persons with continued risk for HCV infection (e.g., PWID) should be screened periodically</td>
</tr>
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</table>

Potential impact: Would identify 256,000 additional HCV cases, 280,000 additional cures and 4,400 fewer cases of hepatocellular carcinoma in same time period as current recommendation (1)

Comment period: Ends September 23, 2019 at 8:00 PM EST

Malaysia: Expanding testing and committed to national scale-up

Lower prices-
- **2016:** Government began negotiations to reduce DAA prices

Expand treatment-
- **2018:** Government announced that it would provide 2,000 courses of free HCV treatment at 18 hospitals, with plans to continue to scale (23,000 individuals on wait list for treatment)

Expand screening-
- **2019:** National screening campaign launched

Partnerships with FIND and DNDI have supported expansion of screening & treatment

India’s National Action Plan released in 2019

37 M (3%) adults are HBsAg +
12-18M (1%) adults are HCV+

The National Viral Hepatitis Control Program launched on WHD in 2018, committing to elimination by 2030.

Action Plan includes these key components:

1. **Prevention**: Awareness, immunization (BD, high risk groups, HCWs), Blood safety, injection safety
2. **Diagnosis and treatment**: Free screening, diagnosis, and treatment for HBV and HCV at all levels (in phased manner)
3. **Monitoring and evaluation**: operational research and strong surveillance system strengthened
4. **Training and capacity building**: Cascade training model, e-learning, e-courses
5. Subnational HCV elimination - Punjab

HCV Elimination in Rwanda: Bold Leadership for Elimination, Example of Building on HIV Program

Rwanda launches a 5-year national hepatitis C elimination plan: A landmark in sub-Saharan Africa

Grace Umutesi1, Fabienne Shumbusho1, Fredrick Kateera1, Janvier Serumondo2, Jules Kabahizi3, Emmanuel Musabeyezu1, Alida Ngwije2, Neil Gupta1, Sabin Nsanzimana2
1Research Department, Partners in Health/Inshuti Mu Buzima, Kigali, Rwanda; 2Division of HIV/AIDS, STI and Viral Hepatitis, Rwanda Biomedical Center, Kigali, Rwanda; 3Rwanda Military Hospital, Kigali, Rwanda; 4King Faisal Hospital, Kigali, Rwanda; 5Clinton Health Access Initiative (CHAI), Kigali, Rwanda; 6Division of Global Health Equity, Brigham & Women’s Hospital, Boston, USA

Path to Elimination Plan:
→ Systematic HCV screening for donated blood since 1999
→ Training of safe injection practices among health-care workers
→ A national hepatitis control unit established in 2011; in 2013 the first guidelines for viral hepatitis developed and disseminated
→ HCV diagnostic capacities based on HIV testing systems.
   → Lower costs $2 HBV/HCV screening; $8 HCV PCR
→ As of May 2018, a total of 110 prescribing physicians from district hospitals have been trained in HCV management, DAA initiation at $ 80 per course
→ Now moving to train nurses in HCV care and treatment
→ Developing multiple partnerships

The plan projects to screen over 4 million individuals and treat approximately 112,000 adults

Plan includes targets & costs

- Expected number of individuals screened: 4,064,919
- Expected number of individuals for confirmatory testing: 232,069
- Expected number of individuals treated: 112,000
- Expected number of individuals achieving SVR12: 110,880 (cumulative)
- Estimated number of new infections averted: 10,638
- Estimated number of premature deaths averted: 35,000
- Total estimated cost of elimination plan: $13 million USD

Pakistan Launches Hepatitis Elimination Initiative
Creating local coalitions and public-private partnerships

5 M (4%) of adults are HBsAg+
8 M (6%) of adults have current HCV infection

Government commitment to planning
Safe injections
Birth dose vaccination
HCV treatment ($20 per cure)
Expand HCV testing

Corporate Coalition for Viral Hepatitis Elimination in
Pakistan (CCVHEP) launched on WHD 2019:

12 leading companies to support the Government of
Pakistan’s effort to eliminate viral hepatitis in Pakistan by
2030

How to apply the Egyptian lessons learned to Pakistan
National Screening Campaign
October 2018-May 2019- Egypt

➢ 49,630,319 screened; 2,229,328 4.61% HCV+
➢ 1.6 M (72%) viremic persons treated with sofosbuvir/ daclatasvir

➢ Essential components
  ➢ Plan with elimination goals by 2020

➢ Political commitment
  ➢ Test all persons 18-59 yrs.
  ➢ Achieve elimination by 2020

➢ Affordable diagnostics (< $5 PCR test); treatment ($50-$120)

➢ Network of 60 treatment centers

➢ Serologic surveys and case registry data

President El Sisi
Good Health for 100 Million
HCV, blood pressure, diabetes, obesity screening

Mobile testing van

http://english.ahram.org https://www.egypttoday.com
Dr. Khaled Kabil
Hepatitis Elimination Champion - Egypt

Since 2006, Executive Director, National Committee for Prevention & Control of Viral Hepatitis

He managed establishment of HCV treatment centers leading to the treatment of more than 2 million patients.

Managed training efforts of physicians in >150 treatment centers.
Egypt Pledges to Provide HCV Testing and treatment for One Million Persons in 18 African countries

- Presidential initiative
- Public-private partnership – government and Egyptian pharma
- Improve access to HCV PCR
- Register Egyptian HCV meds or support local WHO approved drugs
- Technical support by WHO country offices
- Drs. Zeyed and Aceng announced Egyptian support to treat all HCV+ patients in Uganda
Essential Components of Hepatitis Elimination Programs

- Data for planning and monitoring program performance
- Plan of action with time limited numerical targets
- Civic and political support for implementing partners and target populations
- Capacity to deliver appropriate interventions to target populations
- Sustainable models for financing
- Integration of services within existing health systems
- Participation in operational research

Ward J, Gastroenterology 2019
Coalition for Global Hepatitis Elimination

A community of practice to improve information sharing and drive future actions

Partners include:

- Hepatitis B and/or C programs
- Sub-national and national programs
- Technical and implementing partners
- 43 partners have shared program information and resources to date

www.globalhepatitiselimination.org
CGHE technical assistance priorities: Focus on service-coverage and data gaps

WHO Global Hepatitis Strategy targets and service coverage levels

Countries in grey: No published data on Hepatitis prevalence estimates

Polaris Observatory 2017

WHO Global Hepatitis Report 2017
Current therapies effective, safe and relatively inexpensive ($10-15K/yr US; $450/yr. generic global)

Applicability of US/European guidelines questioned; need guidelines for African setting:

Most HBsAg + patients do not need immediate treatment - retention in care for monitoring an issue

Access to lab-based or point-of-care diagnostics varies
Need improve monitoring options
Need models of care

Research for new therapies and functional cure

- Target steps of viral replication
- Interrupt replenishment of cccDNA
- Stimulate immune response
Summary

• HBV and HCV are major causes of liver cancer infections

• HBV and HCV elimination goals are feasible and opportunities for major improvements in health

• Model programs provide examples of best practices

• Information sharing and collaboration will help programs achieve elimination goals