Optimization of Screening Strategies for Viral Hepatitis

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Optimization of Hepatitis C Screening

• Strategic information

• Policy development

• Financial planning (budgetary, cost-effectiveness)

• Feasible/effective implementation

• Technology
Criteria to Guide Public Health Screening

1. The condition sought should be an important health problem.
2. There should be an accepted treatment
3. Facilities for diagnosis and treatment should be available.
4. There should be a recognizable latent or early symptomatic stage.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition should be adequately understood.
8. There should be an agreed policy on whom to treat as patients.
9. The cost of case-finding should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case-finding should be a continuing process

In response to the growing threat, the World Health Assembly set goals for reductions in transmission and mortality for 2030

Global Health Sector Strategy on Viral Hepatitis, 2016-2021

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

**Health outcome targets:**

- Reduce the incidence from 1.75 M cases of chronic HCV infection to less than 200,000 infections by 2030
- Reduce the annual deaths from chronic hepatitis from 400,000 to less than 150,000 deaths by 2030
There are five key interventions to reach HCV elimination

Five interventions with 2030 performance targets

- Injection safety
- Blood safety
- Harm reduction (syringe exchange, drug treatment)
- HCV testing
- HCV treatment

Only 20% of people living with HCV have been diagnosed and 7% treated

Source: WHO Global Health Sector Strategies: Roadmaps to Elimination, 2016-2021
All-oral, curative HCV therapies are a medical breakthrough and have evolved to allow for simple delivery of care and treatment

✓ **Transformational medicine:**
  - Cure > 95 % with 1-3 pills/day/8-12 wks
  - Excellent safety profile
  - 75%-80% reduction in mortality risk
  - Treatment as prevention reduces transmission risk

✓ **Allow for public health approach:**
  - Delivery can be co-located in high prevalence settings (e.g. HIV, TB) and primary care
  - Shift management to mid–level providers (e.g., pharmacists)
Cost of HCV treatment is no longer the major barrier to elimination

62% of persons with HCV live in countries with access to HCV medication < $150

## HCV testing challenges

<table>
<thead>
<tr>
<th>Algorithm</th>
<th>• Current two step testing – anti-HCV (exposure) + viral testing (PCR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Utilization</td>
<td>• Central lab requires patient or specimen transport</td>
</tr>
<tr>
<td></td>
<td>• Point of care (e.g., Genexpert PCR) improves access; 92% of TB, HIV programs use &lt; 50% of Genexpert capacity</td>
</tr>
<tr>
<td></td>
<td>• Lack of policies to guide testing</td>
</tr>
<tr>
<td></td>
<td>• Lack of data to monitor test volume and results</td>
</tr>
<tr>
<td>Cost</td>
<td>• Varied costs $5-200 (PCR)– because of diverse procurement mechanisms, lack of price transparency, and uncertain purchase volumes</td>
</tr>
<tr>
<td></td>
<td>• Volume as reaching health targets will require near universal screening</td>
</tr>
<tr>
<td>Technology</td>
<td>• Research priority: Move from two step to a single test to diagnose HCV infection</td>
</tr>
<tr>
<td></td>
<td>• Prime candidate- HCV core-antigen test</td>
</tr>
</tbody>
</table>

Source: CHAI and FIND. Diagnostics landscape. (2017)
WHO Recommendations for HCV Testing and Treatment

• Testing
  • All blood donors- 95% of donors globally
  • Risk populations- exposures, clinical illness
  • Sub-population- i.e. birth cohorts
  • General population- > 2% or > 5% prevalence

• Treat all persons with HCV
Risk-based Testing
HCV Testing for Persons Who Inject Drugs

- Global prevalence 60%
- Drug treatment, syringe services programs reduce risk by 71%
- Addition of HCV testing/treatment reduces risk by 90%
- In US HCV testing 79% of syringe service programs
  - 88% of drug treatment programs offer
  - Linkage to care is the issue
- HCV treatment
  - Good adherence and response to therapy
  - Reinfection is relatively low 0.0 to 6.4 /100 person years
- Routine testing (annual)

90% reduction in HCV incidence by 2030

Risk-based Testing
Incarcerated Populations

Global: 13% have HCV (8-95%)
North America – 15%
Europe 18-23%

Opportunity to Test, Cure and eliminate HCV

Micro-elimination program demonstrate the feasibility of HCV elimination

Routine testing
Education
Treatment on site
Barriers include cost, systematic and jurisdictional issues

HCV prevalence
Lotus Glen Correctional Center

Risk-based Testing
Persons with HIV

Global 2.3M (6.4%) persons with HIV/HCV; 1.4M PWID

HIV accelerates HCV disease progression

Liver disease leading cause of death for HIV+ persons

For MSM, HCV incidence 19X greater if HIV+
  • HCV cure decreases mortality risk for HIV+ persons
  • Integrate care- set “micro-elimination” targets

HCV infection among persons with HIV
Risk-based Testing with Linkages to Care Spain -2015-2017

Indicator- HCV RNA + prevalence
- HCV testing- risk based- ~ 26,000/yr.
- HCV all oral treatment

HCV Prevalence
- 1960s birth cohort- 52% of cases
- HIV- 19%
- HCV Rate change from 2.4 to 1.3/1000 (2015-2017)

47% decline in HCV RNA Prevalence

General Population Screening

1945-1965 Birth Cohort Strategy in the United States

- 81% of the HCV infected population
- ~3% anti-HCV prevalence (2010)
- 50% moderate severe liver disease
- 50% reported no risks- health care and drug use exposures in the distant past
- Non-stigmatizing
- Cost-effective $32000 per QALY
- Baby boomer cohort a recognized entity to public
- Policy intended to be time limited

Recommendation for all adult testing (18-79yrs ) pending
Potential impact: 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)

Strategies that Expand Access to HCV Testing - United States

- Policy
- Provider education
- Clinical decision tools (table)
- Reflex RNA testing
- 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>
</thead>
<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>10%</td>
</tr>
</tbody>
</table>

Declines in HCV Prevalence - United States

2.4 million HCV infected persons

- 2003-2010: 4.4 million
- 2013-2016: 2.1 million

- 73% decline
- 57% decline

Hofmeister M, Hepatology 2018
General Population HCV Testing
Essential components of effective elimination programs: Egypt

Political commitment
- 10 yrs of small-scale program
- External assistance obtained (e.g., USCDC, World Bank, industry)
- President launches HCV campaign to test all persons 18-59 yrs.

Negotiating affordable diagnostics/medications

<table>
<thead>
<tr>
<th></th>
<th>Prices in US $</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2017</td>
</tr>
<tr>
<td>HCV antibody Elisa</td>
<td>5</td>
</tr>
<tr>
<td>HCV antibody rapid test</td>
<td>5</td>
</tr>
<tr>
<td>HCV RNA RT-PCR</td>
<td>20</td>
</tr>
<tr>
<td>Treatment (12 weeks</td>
<td>80</td>
</tr>
<tr>
<td>(sofosbuvir + daclatasvir)</td>
<td></td>
</tr>
</tbody>
</table>

Decentralization: Broad-based screening & treatment
- Testing in clinical and community (mobile) settings
- No co-pays
- Network of 60 treatment centers

Source: Egyptian national HCV program data courtesy of Dr. Imam Waked
General HCV Testing
Pakistan is a High Burden Country Beginning Development of an HCV Elimination Program

Achievements to date

Phase 1: Political commitment
- Recent political commitment
- National plan
- Local coalition of stakeholders

Phase 2: Set the foundation
- Negotiated affordable HCV medications <US$ 40 per course
- Field studies of HCV testing and treatment
- Identified effective screening and treatment strategies (modeling)

Phase 3: Challenges to achieving scale

- Test 25 m /year
- Treat 700,000 year

Potential impact of reaching 2030 targets

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>2030</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td>8.27M</td>
<td>89,000</td>
</tr>
<tr>
<td>Incidence</td>
<td>281,000</td>
<td>9200</td>
</tr>
<tr>
<td>Mortality</td>
<td>93,300/ yr</td>
<td>323,000 (averted)</td>
</tr>
<tr>
<td>DALYs total</td>
<td>60.74M</td>
<td>13M (averted)</td>
</tr>
<tr>
<td>Cost</td>
<td>$684M/yr</td>
<td>$2.6b (saved)*</td>
</tr>
</tbody>
</table>

Challenges for phase 1 and 2 persist

- Strategic information for planning
- Provincial-level government buy-in
- Need policy of one time HCV testing of all adults
- Limited partnerships to date (except CDC)

- Monitoring and accountability system
- Negotiate affordable diagnostic costs
- Reduce or eliminate costs for patients
- Health promotion campaign

This scale-up could lead to...

Only with point-of-care anti-HCV and PCR

Chhatwal JAMA Online 2019, Saeed Hamid, personal communication
Models can Guide Selection of Cost-effective Testing Strategies

Pakistan

Table. Different Hepatitis C Virus Testing Algorithms Evaluated to Scale Up Interventions in Pakistan

<table>
<thead>
<tr>
<th>Testing Algorithm</th>
<th>Screening Test</th>
<th>Detection of Viremia</th>
<th>Assessment of Hepatitis C Treatment Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 (base case)</td>
<td>Laboratory based</td>
<td>Nucleic acid test</td>
<td>Nucleic acid test</td>
</tr>
<tr>
<td>T2</td>
<td>Laboratory based</td>
<td>HCVAg test</td>
<td>Nucleic acid test</td>
</tr>
<tr>
<td>T3</td>
<td>Point of care</td>
<td>Nucleic acid test</td>
<td>Nucleic acid test</td>
</tr>
<tr>
<td>T4</td>
<td>Point of care</td>
<td>GeneXpert</td>
<td>GeneXpert</td>
</tr>
<tr>
<td>T5</td>
<td>Point of care</td>
<td>HCVAg test and nucleic acid test if HCVAg test result is negative</td>
<td>HCVAg test</td>
</tr>
<tr>
<td>T6</td>
<td>Point of care</td>
<td>HCVAg test and nucleic acid test if HCVAg test result is negative</td>
<td>Nucleic acid test</td>
</tr>
<tr>
<td>T7</td>
<td>Laboratory based</td>
<td>GeneXpert</td>
<td>GeneXpert</td>
</tr>
</tbody>
</table>
Coalition for Global Hepatitis Elimination
A community of practice to improve information sharing and assist future actions

www.globalhepatitisedition.org
CGHE Developing a Web-based Tool for Budget Based Planning HCV Testing and Treatment

**Inputs**
- Prevalence
- Interventions

**Outputs**
- Screening
- Costs

**Policy brief**
- Temporal trends in hepatitis C-related costs for Alabama
  - Cumulative spending on hepatitis C treatment between 2019 and 2030 is an estimated $49.7 million
  - Cumulative spending on hepatitis C screening between 2019 and 2030 is an estimated $311.1 million
  - Cumulative spending on hepatitis C disease management between 2019 and 2030 is an estimated $843 million

Note: The results begin in 2019 but the plot includes 2018 as a reference point.

Temporal trends in chronic and cured hepatitis C infections for Alabama
- Estimated number of individuals cured of hepatitis C infections at the end of 2030 is 25,500
- Estimated number of individuals living with diagnosed chronic hepatitis C infections at the end of 2030 is 2,360
- Estimated number of individuals living with undiagnosed chronic hepatitis C infections at the end of 2030 is 11,800

Note: The numbers change, depending on the subpopulations selected. The default includes all subpopulations.

https://www.hepcsimulator.org/
### High-priority project: core Ag test to enable test and treat approach

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Current status</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMPLEMENTATION SETTINGS</td>
<td>Levels 0-1</td>
</tr>
<tr>
<td>PLATFORM FORMAT</td>
<td>Lateral flow</td>
</tr>
<tr>
<td>DETECTION</td>
<td>2 prototypes: 1) Colorimetric (visual readout) 2) Fluorimetric (reader device)</td>
</tr>
<tr>
<td>SENSITIVITY (target 85%)</td>
<td>70%</td>
</tr>
<tr>
<td>SPECIFICITY (target 98%)</td>
<td>95%</td>
</tr>
<tr>
<td>Sample pretreatment</td>
<td>Plans to integrate sample preparation into an easy-to-use, manually actuated rotocol (ongoing)</td>
</tr>
<tr>
<td>Test costs (production costs, estimated)</td>
<td>&lt; 2 US $</td>
</tr>
</tbody>
</table>

- HCV core antigen level correlates well with HCV RNA level
- HCV core antigen can be used for diagnosis of active infection and to document cure
- A point-of-care test could be used to detect HCV and start treatment in single visit
- Main technical challenge: antigen-antibody separation
- High analytical sensitivity requirements unlikely to be met in RDT format

**Project timeline:**
- Design-lock assay: end 2020
- Regulatory submission Q3 2021

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Slide provided by Elena Ivanovar
Optimization of Hepatitis C Screening

- **Strategic information** –
  - Plan - surveillance, serologic surveys, clinical data
  - Evaluate – test volume, results

- **Policy development** – HCV testing policies are needed at national level
  - Target – minimum
  - Scale up to population-based testing as appropriate

- **Financial planning** (budgetary, cost- effectiveness)
  - Negotiate affordable costs
  - Model test options for budget planning

- **Feasible/ effective implementation**
  - Tailor best practices to meet local needs
  - Integrate into existing health systems

- **Technology**
  - Assure quality
  - Efficient use of existing platforms
Let's Work Together to Eliminate Viral Hepatitis

IT TOOK US 25 YEARS TO BRING HIM TO HIS KNEES... NOW LET'S FINISH HIM OFF!...