Optimization of Screening Strategies

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Agenda

Screening Criteria

Screening Roles

Essential Components of Screening Programs

Technical and Operational Research
Public Health Screening Criteria

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

Wilson Junger, WHO 1968. [www.who.int](http://www.who.int)
Role of Screening

• Prevention of transmission

• Prevention of disease and mortality

• Policy and planning

• Public health surveillance and program evaluation
HBV Testing

Detect evidence of infection

Patient Population

Detect antibody protection

Total anti-HBc

Anti-HBs quantitative

Detect active infection
Lab-based or Point of Care

Reactive HBsAg

Non-reactive

Reactive/Non-reactive

Detect evidence of infection

HBV DNA testing
Lab based

HBV DNA >20,000
Treat

HBV DNA <20,000
Monitor
HCV Testing

- HCV: Antibody + PCR testing
- Lab based and Point of Care
Role of HBV and HCV Screening in Prevention of Transmission

Blood Bank Screening (HBsAg, anti-HCV, PCR testing)

- 99% reduction in transmission since 1980s
- 7-14% risk to 1/488,000 (HBV) and 1/1,200,000 (HCV)

Maternal HBsAg testing improves perinatal HBV prevention

- HBIG/HepB superior to vaccine alone (RR 0.08 vs. 0.28)
- Maternal anti-viral prophylaxis (i.e., > 6 log_{10} HBV copies/mL)

Other

- Vaccination of household and other susceptible persons
- Enhance infection control (e.g., HBsAg testing of patients on dialysis, occupational exposures)
- Enhance harm reduction—(behavior change)

Antiviral Therapy Can Reduce HCV Prevalence Among Injecting Drug Users

Annually treating 10 HCV infections per 1000 IDU and achieve SVR of 62.5%

Projected to result in a relative decrease in HCV prevalence over 10 years of 31%, 13%, or 7% for prevalence of 20%, 40%, or 60%, respectively

HCV Cure as Prevention

Martin et al. Journal of Hepatology 2011 vol. 54 j 1137–1144
Benefits of HBV and HCV Screening: Linkage to Care and Treatment

• HBV treatment- long term viral suppressive therapy
  • Reduced risk of liver cancer- 50%
  • Reduced risk of all cause mortality- 40%
  • Generic tenofovir $32 per year.

• HCV treatment- >90% cure with 8-12 weeks of therapy
  • Reduced risk of liver cancer- 80%
  • Reduced risk of all cause mortality- 75%
  • Licensed generics per course ~ $200
  • Less for others –e.g., $68 Ukraine; $75 Pakistan

• Cost- effective or cost-saving

Greatest Challenge to Elimination of Pre-mature Mortality Testing and Early Treatment of HBV and HCV Infection

HBV 257 million
Global: Diagnosed 9%; on treatment 1%

HBV 740,000-2.2M
US: Diagnosed 60% on treatment 15%

HCV 71 million
Global: Diagnosed: 20%; Treated 4%

HCV 3.5 M
US: Diagnosed 50%; Treated 25%

cdc.gov/hepatitis
Components of Effective Screening Programs

• Strategic information to assess disease burden and health system capacity
• Testing policies and plan for implementation
• Civic and political support for implementing partners and target populations
• Capacity to deliver interventions to target populations
• Strategic data to monitor program performance
• Technical and operational research
WHO Recommendations for HBV and HCV Testing and Treatment

- Testing
  - Risk populations- exposures, clinical illness
    - Exposures- blood, and sexual and household (HBV)
  - All blood donors
  - General population- $\geq 2\%$ or $\geq 5\%$ prevalence including HBsAg for pregnant women;
  - Sub-population
    - Birth cohorts
- Treat all persons with HCV
HBV Screening in the United States

850,000–2.2 million persons with chronic HBV
- 50% are Asian/Pacific Islanders (API); 6-fold mortality risk for API
- HBV testing recommended for persons from countries with >2% prevalence (i.e., Asia, Africa)
- Others at risks - e.g., injection drug use
- Strategies
  - Culturally approach outreach
  - Peer support and navigation
  - Need new strategies to keep persons in care

HBV Linkage to Care Cascade, Three Programs, United States, 2014–2016

HBV Testing and Linkage to Care - The Gambia

Community screening
- Engaged community leaders
- Door-to door solicitation
- Point-of-care HBsAg testing
- Participants
  - Low HBV knowledge
  - No prior testing

Blood bank screening - 90% men

Most inactive chronic carriers- need ongoing monitoring
Of 47 recommended for treatment
- All accepted
- 12 month adherence- 81%
- Loss of HBV DNA- 91%
One HCV Testing for Persons Born 1945-1965 United States

- 3.5 M persons living with HCV
- 81% are persons born 1945-1965

70% of Baby Boomers have Moderate to Severe Liver Disease

Rising HCV mortality - 19,659 Deaths

Proportion of HCV infected Persons by Year of Birth - 16 Countries

Gane et al. ,J Viral Hepatitis,
HCV Burden of Disease, HCV Testing and Treatment Cost - Thailand

Total HCV infected 356,670
> 30 yrs of age 343,698 (96%)  
52% have advanced liver disease  
Focus testing on persons > 30 yrs, born before 1983

HCV treatment cost $250 per course  
HCV diagnosis $79 (anti-HCV, PCR)  
HCV monitoring $90-180 (PCR)

https://doi.org/10.1371/journal.pone.0202991  
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0202991
Strategies that Expand Access to HCV Testing, Care and Cure - United States

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


68,440,635 unique enrollees
Educating Providers and Communities
Reflex HCV Testing

Public-Private Partnerships

RNA follow-up testing within 30 days of Ab+ result

Quest changes policy and tests all anti-HCV+ specimens

LabCorp – continues requirement for second specimen

Total tested: Quest 415,000; LabCorps 319,000

CDC, unpublished data
Eliminating Hepatitis C Among US Military Veterans- VA

- Implementing strategies
  - Standing testing orders/reminders
  - Care algorithms
  - Program evaluation and staff accountability
  - Resources for HCV treatment

- Status
  - 78.8% of Veterans born 1945-1965 screened for HCV
  - >90% diagnosed; ~15,500 undiagnosed
  - 87,000 treated with all-oral DAAs; 90-95% cure
  - 58,000 remain eligible for treatment; most difficult to engage in care

Tim Morgan viralhepatitisaction.org/summit-presentations
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, NGOs

% Cure: 85%
% Treatment: 71%
% Evaluation: 75%
% Screening: 55%

Elimination Programs Improve Access
Country of Georgia Example

- ~150,000 HCV RNA+ persons; 5.4% prevalence
- Goal: 90% diagnosed; 95% treated; 95% cured by 2020
- 40,000 HCV RNA+ persons treated (5/15-10/2017)
- Key tools
  - National planning
  - Data to guide and evaluate program
  - Health system strengthening
  - Political support
  - Partnerships – Gilead, Abbott, CDC, State, WHO,

Nasrullah M, Nat Rev Gastroenterol Hepatol. 2017 Jul
Evaluate Quality of Hepatitis Laboratory Testing WHO Assessment Tool Hep-LAT (10 Quality System Elements)

<table>
<thead>
<tr>
<th>Laboratory Systems Republic of Georgia</th>
<th># of Labs</th>
<th>Hep-LAT Indicator Mean (Range)</th>
<th>Total Annual Test Volume (2014 estimated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCDC Public Health Labs</td>
<td>10</td>
<td>85% (79%-92%)</td>
<td>5,000</td>
</tr>
<tr>
<td>Clinical Laboratories</td>
<td>9</td>
<td>64% (42%-92%)</td>
<td>50,000</td>
</tr>
</tbody>
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- 1-building facilities...
- 2-biosafety, hygiene...
- 3-specimen collection...
- 4-equipment
- 5-reagents and supply
- 6-analysis and test...
- 7-laboratory staff &...
- 8-total quality
- 9-reporting, analysis &...
- 10-outbreak...

DVH WIP | June 13, 2017
Increase Priority for Neglected Populations: The Incarcerated

- Incidence 16.4 per 100py
- Prevalence -26%; 2.2M
- Testing/treatment cost-effective $20-29K/QALY
- Only 6 studies to guide HCV testing
- Fewer studies of care and treatment


March 18, 2018


New Target Populations: HCV Infected Mothers

- Increased HCV among pregnant women
- In 2014, 1 of 308 U.S. births were to HCV+ mothers
  - 1 of 63 in Kentucky (high incidence state)

- 6-12% transmission risk for infants
- ~1700 HCV+ infants born in 2015
- Consider routine testing of pregnant women
- New strategies for implementation
- One clinical trial of anti-viral treatment of pregnant women NCT02683005

Consider Screening All Adults for HCV infection

- Response to large increases in HCV incidence (United States)
- Increase opportunities for treatment as prevention
- Recognized benefits of early treatment
- Integrate with other strategies - i.e., HIV
- Cost-effective
  - United States
    - $28,000/QALY with 280,000 additional cures
    - $11,378/QALY gained when HCV prevalence > 0.07%
  - France - €31,100/QALY.

Improve Tests for Current HCV infection

- HCV core antigen testing: low sample volume, less pristine sampling; rapid turn around (1 hour), CE marked
- High correlation with HCV RNA
- High sensitivity/ specificity; in 33 studies – 93% /99%
- Reduced sensitivity at <3000 HCV RNA
- Not widely commercially available

- Point of care PCR: rapid turn around (105 minutes vs 5 hours for lab-based) limit of detection (10 to 10^8) similar to lab based PCR no biosafety handling, CE marked
- Sensitivity/ specificity 100%/94%
- Need POC
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Task Force for Global Health Program for Viral Hepatitis Elimination