PREVENTION OF HBV AND HCV

ANGELOS HATZAKIS, MD
PROFESSOR OF EPIDEMIOLOGY & PREVENTIVE MEDICINE
ATHENS UNIVERSITY MEDICAL SCHOOL

GEORGE PAPATHEODORIDIS, MD
PROFESSOR IN MEDICINE AND GASTROENTEROLOGY
ATHENS UNIVERSITY MEDICAL SCHOOL

HARRY JANSSEN, MD
PROFESSOR OF MEDICINE, TORONTO WESTERN AND TORONTO GENERAL HOSPITAL,
UNIVERSITY HEALTH NETWORK, TORONTO, CANADA
**PREVENTION**

- HBV Vaccination
- Hepatitis Caused by Drug Use Behaviors
- Health Care Associated Hepatitis
- Screening for HBV and HCV
- Cost-Effectiveness of Birth-Cohort Screening
HBV vaccine Facts (1)

A. 1\textsuperscript{st} gen – Plasma derived (1981)
   2\textsuperscript{nd} gen – Recombinant DNA vaccine (1986)
   3\textsuperscript{rd} gen – Triple antigen vaccine (1992)
B. Efficacy: 95-100%, <90% in immunocompromised
C. Vaccination schedule: 1, 2, 6 months
D. Booster dose: No booster up to 20 years
E. Safety: Excellent
F. WHO, 1991: All countries should introduce universal HBV vaccination into national immunization programmes

G. Worldwide, 2010: Estimated coverage of fully vaccinated infants: 75%.
   Countries integrated HBV vaccine: 92%

H. Europe, 2009: 46 out of 53 countries implement universal HBV immunization, 6 countries implement immunization of high risk sexual and IDU adults.
Global Immunization 1989-2010, 3rd dose of Hepatitis B coverage in infants global coverage at 75% in 2010

Fig. 1 Morbidity rate ($\times 10^5$ inhabitants) of hepatitis B in Italy, according to age (1990–2009).
WHO, UNODC, UNAIDS guidance for universal access of IDUs to HIV prevention, treatment and care

1. Needle and syringe programmes (NSPs).
2. Opioid substitution therapy (OST) and other drug dependence treatment.
3. HIV testing and counseling (T&C).
4. Antiretroviral therapy (ART).
5. Prevention and treatment of sexually transmitted infections (STIs).
6. Condom programmes for IDUs and their sexual partners.
7. Targeted information, education and continuation (IEC) for IDUs and their sexual partners.
8. Vaccination, diagnosis and treatment of viral hepatitis.
Interventions for prevention and control of infectious diseases in IDUs

**Key intervention components**

**Injection equipment:** Provision of, and legal access to, clean drug injection equipment, including sufficient supply of sterile needles and syringes free of charge, as part of a combined multi-component approach, implemented through harm-reduction, counselling and treatment programmes.

**Vaccination:** Hepatitis A and B, tetanus, influenza vaccines, and, in particular for HIV-positive individuals, pneumococcal vaccine.

**Drug dependence treatment:** Opioid substitution treatment and other effective forms of drug dependence treatment.

**Testing:** Voluntary and confidential testing with informed consent for HIV, HCV (HBV for unvaccinated) and other infections including TB should be routinely offered and linked to referral to treatment.

**Infectious disease treatment:** Antiviral treatment based on clinical indications for those who are HIV, HBV or HCV infected. Anti-tuberculosis treatment for active TB cases. TB prophylactic therapy should be considered for latent TB cases. Treatment for other infectious diseases should be offered as clinically indicated.

**Health promotion:** Health promotion focused on safer injecting behaviour; sexual health, including condom use; and disease prevention, testing and treatment.

**Targeted delivery of services:** Services should be combined and organised and delivered according to user needs and local conditions; this includes the provision of services through outreach and fixed site settings offering drug treatment, harm reduction, counselling and testing, and referrals to general primary health and specialist medical services.
Figure 3: Core values of prevention of infections among people who inject drugs

Principles of service provision

- Ensure confidentiality.
- Promote service accessibility.
- Create a user-friendly atmosphere.
- Engage in dialogue with users and promote peer involvement.
- Adopt a practical approach to the provision of services.
- Refrain from ideological and moral judgement.
- Maintain a realistic hierarchy of goals.

A pragmatic approach to health promotion

Public health objectives

The clients’ rights perspective

Guidance based on scientific evidence and expert experience
Health care associated hepatitis (1)

- **Patient to patient transmission**
  - Breaches of infection control and unsafe health care practices

- **Patient to provider transmission**
  - Sharps injuries

- Transfusion of infected blood and blood products

- Transplantation of infected organs
Health care associated hepatitis (2)

- **Patient to patient transmission**
  Breaches of infection control and unsafe health care practices include:

1. Syringe and needle reuse
2. Vial contamination
3. Improper use and handling of blood glucose monitoring equipment
4. Lapses in the reprocessing of patient equipment (e.g. endoscopes)
5. Contamination of equipment, supplies and the environment

1. **Syringe and needle reuse**
   - Injection equipment reuse is negligible in developed world.
   - In developing world persons receive 3.4 injections/year of which 39.8% with reused equipment.
   - Unsafe injection practices is the cause of 31.9% (0.9-58.3%) of HBV infections, 39.9% (0.9-81.7%) of HCV infections and 5.4% (0-24.3%) of HIV infection in developing world.
   - In 2000, contaminated injections caused 21million HBV, 2million HCV and 260.000 HIV infections.
Number of injections per person and per year and proportion of these administered with injection equipment reused in the absence of sterilisation, by region, 2000

Health care associated hepatitis (4)

- **Patient to provider transmission**
  - Worldwide 35 million health care personnel suffer 16,000 HCV and 66,000 HBV infections annually.
  - Risk of HBV infection after percutaneous exposure is 23-62%, dependent on e antigen status and HBV-DNA levels of the source.
  - HBV can remain infective in the environment for more than 7 days.
  - Risk of HCV infection after percutaneous exposure is 1.8%.
  - HCV in dried blood samples can remain infective in the environment for 16 hours.

Prevention of health care associated hepatitis (1)

- Awareness, understanding, implementation and enforcement of best practice guidelines.
  Remain suboptimal.

- Hierarchy of controls to establish priorities for hazard reduction in the workplace.
  Remain suboptimal.

- HBV vaccination of health care personnel.
  Remain suboptimal.

Hatzakis A et al, 2012
Prevention of health care associated hepatitis (2)

- Recognition and containment of health care associated hepatitis.
  Remain suboptimal.

- Screening of blood for prevention of transfusion and transplantation associated hepatitis by serology and nucleic acid testing (NAT).
  Highly successful in developed world.
Prevention of health care associated hepatitis in the US

<table>
<thead>
<tr>
<th>Study period</th>
<th>Agent</th>
<th>Incidence (rate per 10^5 PY)</th>
<th>Infectious window period (days)</th>
<th>Residual risk per donated unit</th>
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<tbody>
<tr>
<td>2007-2008</td>
<td>HIV</td>
<td>3.1</td>
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<td>2007-2008</td>
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<td>2006-2008</td>
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<td>3.4</td>
<td>38-30</td>
<td>1:357,000 to 1:280,000¥</td>
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</tbody>
</table>

¥ Range combines two estimates for the HBsAg-negative window period (38 days vs. 30 days) with two methods for deriving incidence

PY person-years of observation

Epstein JS & Holmberg JA. Transfusion 2010; 50, 1408
### Risk-based screening of HBV

<table>
<thead>
<tr>
<th>Populations recommended or required for routine testing of hepatitis B virus infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons born in regions of high and intermediate HBV endemicity (HBsAg prevalence ≥ 2%)</td>
</tr>
<tr>
<td>US-born persons not vaccinated as infants whose parents were born in regions with HBV endemicity ≥ 8%</td>
</tr>
<tr>
<td>Injection drug users</td>
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<tr>
<td>Men who have sex with men</td>
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<tr>
<td>Injection-drug users</td>
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<tr>
<td>Persons needing immunosuppressive therapy</td>
</tr>
<tr>
<td>Persons with elevated ALT/AST of unknown etiology</td>
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<tr>
<td>Donors of blood, plasma, organs, tissues or semen</td>
</tr>
<tr>
<td>Hemodialysis patients</td>
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<tr>
<td>All pregnant women</td>
</tr>
<tr>
<td>Infants born to HBsAg positive mothers</td>
</tr>
<tr>
<td>Household, needle-sharing or sex contacts of persons known to be HBsAg positive</td>
</tr>
<tr>
<td>Persons who are the sources of blood or body fluids for exposures that might require postexposure prophylaxis (e.g. needlestick, sexual assault)</td>
</tr>
</tbody>
</table>

Weinbaum CM. Hepatology, 2009;49:S35
## Risk-based screening of HCV

<table>
<thead>
<tr>
<th>Updated summary of CDC recommendations for high risk populations for hepatitis C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons who have ever injected illegal drugs, including those who injected only once many years ago</td>
</tr>
<tr>
<td>Recipients of clotting-factor concentrates made before 1987</td>
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<tr>
<td>Recipients of blood transfusions or solid organ transplants before July 1992</td>
</tr>
<tr>
<td>Patients who have ever received long-term hemodialysis treatment</td>
</tr>
<tr>
<td>Persons who have ever known exposures to HCV such as:</td>
</tr>
<tr>
<td>▪ Health-care workers after needlesticks involving HCV-positive blood</td>
</tr>
<tr>
<td>▪ Recipients of blood or organs from donors who later tested HCV-positive</td>
</tr>
<tr>
<td>All persons who have HIV infection</td>
</tr>
<tr>
<td>Patients who have signs or symptoms of liver disease (for example, abnormal liver-enzyme tests)</td>
</tr>
<tr>
<td>Children born to HCV-positive mothers (to avoid detecting antibody, these children should not be tested before the age of 18 months)</td>
</tr>
</tbody>
</table>

*CDC, 2001*
<table>
<thead>
<tr>
<th></th>
<th>Algeria</th>
<th>Egypt</th>
<th>Israel</th>
<th>Jordan</th>
<th>Lebanon</th>
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## Comparative HBV and HCV screening policies in the non-EU Mediterranean countries - **Part B**

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Comparative HBV and HCV screening policies in the non-EU Balkan countries
Considerations for the implementation of successful screening programmes for HBV and HCV (1)

- Develop clear public awareness campaigns targeted at the general public and at risk groups.
- Need a clear clinical strategy to deal with HBV and HCV infected persons.
- Revise clinical guidelines to endorse HBV and HCV screening in specified risk groups and reinforce dissemination of best practices for case finding.
- Integrate screening into existing public health and care practices whenever possible.
Considerations for the implementation of successful screening programmes for HBV and HCV (2)

- Conduct HBV and HCV screening in HIV/STD clinics, prisons, drug user services as well as in primary care clinics.
- Simplify screening criteria, e.g. adopt age-based criteria for HCV, birthplace for HBV with the aim of providing clear guidance to GPs and those screening patients.
- Educate providers about the needs for screening and about the management pathways for HBV- and HCV- infected individuals.
- Always carry out screening in an evidence-based way that defines when and how often screening should be offered and respects the human rights of those screened.
Considerations for the implementation of successful screening programmes for HBV and HCV (3)

- Always accompany screening with appropriate counseling of the individual and his or her family.
- In the case of marginalized or stigmatized groups such as migrants or IDUs, one must ensure that individuals are not stigmatized because of their group membership or their viral hepatitis status.
Key factors necessary for the successful implementation of prevention and management programmes targeting HBV and/or HCV (1)

- Reliable local epidemiological data to communicate with policymakers.
- Clinical leadership from specialist centres as well as from public health, social services and other relevant professional groups.
- Motivation of all those involved in programme using quantifiable goals (e.g. 75% of patients with HepC will be aware of their infection by a given year).
- Inclusion of concrete goals to extend treatment in line with existing –and desired– treatment capacity.
Key factors necessary for the successful implementation of prevention and management programmes targeting HBV and/or HCV (2)

- Recognition of the need and potential of therapeutic developments to confer true patient benefits.
- Strong, continuous patient advocacy.
- Close and ongoing dialogue between patients, clinical leads, public health specialists and policymakers.
- Awareness campaigns to increase testing through GPs and other primary care providers.
- Systematic referral system for individuals screening positive to secondary care.
Key factors necessary for the successful implementation of prevention and management programmes targeting HBV and/or HCV (3)

- Targeted awareness campaigns (e.g. aimed at different immigrant communities).
- Strengthening of network between hospitals, GPs and physicians in special settings (e.g. prisons or sexual health clinics).
- Shared patient management between specialists and GPs to lessen the burden on hospitals.

Hatzakis A et al. JVH 2011; 18, S1
Cost-effectiveness analysis of birth-cohort screening in the US

- HCV infected (birth-cohort 1945-1965): 69% of the total HCV infected
- HCV prevalence (birth-cohort 1945-1965): 3.6%
- Scenarios:
  a) No screening or treatment.
  b) Risk-based screening of individuals unaware of HCV (1% per year for 20 years) and offer of peg-IFN+R.
  d) One time HCV birth-cohort (1945-1965) screening of individuals unaware of HCV and
     1) peg-IFN+R in patients with HCV-2 or 3 and, 2) peg-IFN+R+direct-acting antiviral in
     patients with genotype 1.
- Screening cost per case identified: 2.874 USD
- Incremental cost-effectiveness ratio (ICER):
  - B: 15,700 USD/QALYS
  - C: 15,700 USD/QALYS
  - D: 73,700 USD/QALYS

### Priorities among effective clinical preventive services
(National Committee on Prevention Priorities)

<table>
<thead>
<tr>
<th>Services</th>
<th>CPB</th>
<th>CE</th>
<th>Total</th>
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<tbody>
<tr>
<td>Aspirin chemoprophylaxis</td>
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<td>5</td>
<td>10</td>
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<tr>
<td>Childhood immunization series</td>
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<td>5</td>
<td>10</td>
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<tr>
<td>Tobacco-use screening and brief intervention</td>
<td>5</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Colorectal cancer screening</td>
<td>4</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Hypertension screening</td>
<td>5</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Influenza immunization of adults 50yrs or older</td>
<td>4</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Pneumococcal immunization of adults 65yrs or older</td>
<td>3</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Problem drinking screening and brief counseling</td>
<td>4</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Vision screening of adults 65yrs or older</td>
<td>3</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Cervical cancer screening</td>
<td>4</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Cholesterol screening</td>
<td>5</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Breast cancer screening</td>
<td>4</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Chlamydia screening</td>
<td>2</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Calcium chemoprophylaxis</td>
<td>3</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Vision screening-children</td>
<td>2</td>
<td>4</td>
<td>6</td>
</tr>
</tbody>
</table>

CPB: Clinically Preventable Burden, CE: Cost-Effectiveness

HCV birth cohort (1945-1965) screening
<table>
<thead>
<tr>
<th>Disease</th>
<th>Conditions</th>
<th>Cost per case (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic HBV</td>
<td>Prevalence of HBsAg: 2%</td>
<td>750-3,752</td>
</tr>
<tr>
<td>Chronic HCV</td>
<td>Prevalence of anti-HCV: 3.6% (birth-cohort 1945-1965)</td>
<td>2,874</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>Prevalence of anti-HIV: 1%</td>
<td>2,133 (1,733-3,733)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Two-step glucose</td>
<td>4,064</td>
</tr>
<tr>
<td>Hearing disorders in newborns</td>
<td>Universal newborn screening</td>
<td>16,000</td>
</tr>
<tr>
<td>Metabolic disorders in newborns</td>
<td>Universal mass spectometry screening</td>
<td>68,000</td>
</tr>
<tr>
<td>Down syndrome</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; and 2&lt;sup&gt;nd&lt;/sup&gt; trimester evaluation</td>
<td>690,000</td>
</tr>
</tbody>
</table>

Definitions (1)

**Screening**: A Public Health service in which members of a defined population are asked a question or offered a test to identify those individuals who, by further tests or treatment, will reduce the risk of a disease or its complications (*UK Screening Committee*).

**Efficacy**: The extent to which an intervention produces a beneficial result to an individual under ideal circumstances.

**Effectiveness**: A measure of the extent to which a specific intervention does what is intended to do for a specific population.

**Effectiveness** = **Efficacy** × Treatment Coverage
Continuum of HCV diagnosis, care and treatment

- HCV infected
- Unaware of HCV

- Screening offered
- Screening accepted
- Screening diagnosis
- Screening results offered

- Linked to care
- Retained to care
- Need treatment
- No contraindication
- Treatment cost covered
- On treatment
- Sustained viral response (cure)
Goals of a Hepatitis Screening, Care and Treatment Programme

- **To control HCV:** To decrease incidence of cirrhosis and HCC following reduction of HCV infection.

- **To eliminate HCV:** Zero or near zero incidence of HCV infection with major reduction in the incidence of cirrhosis and HCC in a specific area.

- **To eradicate HCV:** Zero or near zero incidence of HCV infection with major reduction in the incidence of cirrhosis and HCC at global level.
CHALLENGES FOR A SCREENING PROGRAMME TO CONTROL OR ERADICATE HCV
Major challenges for designing an efficient screening programme to control or eradicate HCV

1) Knowledge of HCV epidemiology and burden of disease.

2) Issues related to the screening process (goals, testing algorithms, testing strategy, operational and ethical problems).

3) Improvements in all steps of treatment cascade.

4) Availability of resources for testing, care and treatment (health infrastructure, affordable care and treatment).
A series of publications for 31 countries based on the same natural history model to estimate current and future HCV burden.

The model makes use of epidemiological data from each country to estimate the current and future distribution of chronic HCV by fibrosis stage, under various assumptions concerning prevention and treatment strategies.
HCV Disease Progression Modeling

Acute HCV Infection

F0 – New Cases (NC)
F0 – Total Cases (TC)

Diuretic Sensitive Ascites (NC)
Diuretic Sensitive Ascites (TC)

Variceal Hemorrhage (NC)
Variceal Hemorrhage (TC)

Hepatic Encephal. (NC)
Hepatic Encephal. (TC)

Hepatocellular Carcinoma (NC)
Hepatocellular Carcinoma (TC)

Comp. Cirrhosis (NC)
Comp. Cirrhosis (TC)

Refractory Ascites (NC)
Refractory Ascites (TC)

Liver Related Mortality

Liver Transplantation

Spontaneously Cured

Is elimination of HCV possible?

Important parameters

1) Viremic prevalence
2) Age and sex distribution of HCV
3) Diagnostic rate
4) Distribution of CHC by fibrosis stage
5) Status of primary prevention
6) Treatment rate 2012-2013
7) Increase in the future treatment coverage
8) Efficient testing strategy
9) Availability of resources for testing, care and treatment infrastructure
Viremic Prevalence

Hatzakis A, 2015
Historical Distribution by Age and Gender
Canada, Czech Republic, Denmark and Egypt

Historical Distribution by Age and Gender
Argentina, Finland, Greece and India

Diagnostic Rate (%)
HCC and Decompensated Cirrhosis, 1950-2030
Argentina, Finland, Greece and India

HCC, Decompensated Cirrhosis and Transplant, 1950-2030
England, France, Germany and Portugal

Cirrhosis, 2013-2030
England, France, Germany and Portugal

Cirrhosis, 2013-2030
Ireland, Israel, Luxembourg and Mexico

Estimated Viremic Infections, 2013-2030
Czech Republic, Denmark and Egypt

Estimated Viremic Infections, 2013-2030
Argentina, Finland, Greece and India

Increase in the future treatment coverage

Treated (2014-2020) / Treated 2013

Hatzakis A, 2015
Efficient testing strategy

FIGURE 3: Anti-HCV positive patients according to year of birth

US American baby boomer generation

German baby boomer generation

- IV drug users
- non IV drug users

Percentage of anti-HCV positive patients per age range

n = 1

1945 - 1950
1950 - 1954
1955 - 1959
1960 - 1964
1965 - 1969
1970 - 1974
1975 - 1979
1980 - 1984

Wolffram I et al. JVH 2015 (in press)
Fig. 2 Distribution of the 2013 hepatitis C virus (HCV)-infected population by age as a percentage of total number of cases.
WHO Recommendation on Screening (risk-based)

- It is recommended that HCV serology testing be offered to individuals who are part of a population with high HCV seroprevalence, or who have a history of HCV risk exposure/behaviour.

- It is suggested that nucleic acid testing for the detection of HCV RNA be performed directly, following a positive HCV serological test to establish the diagnosis of chronic HCV infection, in addition to nucleic acid testing for HCV RNA as part of the assessment for starting treatment for HCV infection.
One-time HCV testing is recommended for persons born between 1945 and 1965*, without prior ascertainment of risk (*birth-cohort screening*).

Other persons should be screened for risk factors for HCV infection, and one-time testing should be performed for all persons with behaviors, exposures and conditions associated with an increased risk of HCV infection (*risk-based screening*).

**Risk exposures:**

- Long-term hemodialysis (ever)
- Getting a tattoo in an unregulated setting
- Healthcare, emergency medical and public safety workers after needlesticks, sharps or mucosal exposures to HCV-infected blood
- Children born to HCV-infected women
- Prior recipients of transfusions or organ transplants, including persons who 1) were notified that they received blood from a donor who later tested positive for HCV infection, 2) received a transfusion of blood or blood components or underwent an organ transplant before July 1992, 3) Received clotting factor concentrates produced before 1987
- Persons who were ever incarcerated

*Regardless of country of birth*
<table>
<thead>
<tr>
<th>AASLD Recommendation for HCV Testing (2)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk behaviors:</strong></td>
</tr>
<tr>
<td>• Injection-drug use (current or ever, including those who inject once)</td>
</tr>
<tr>
<td>• Intranasal illicit drug use</td>
</tr>
<tr>
<td><strong>Other:</strong></td>
</tr>
<tr>
<td>• HIV infection</td>
</tr>
<tr>
<td>• Unexplained chronic liver disease and chronic hepatitis, including elevated alanine aminotransferase levels</td>
</tr>
<tr>
<td>• Solid organ donors (deceased and living)</td>
</tr>
</tbody>
</table>
Types of screening programmes

- **Integrated**: Screening programmes that are integrated within already existing health care facilities (STD clinics, HIV/STD service providers, sexual and reproductive health clinics, emergency departments, community centers, prisons, health clinics, public laboratories, occupational physicians etc).

- **Non-integrated**: Screening programmes that are exclusively set up for screening (community health clinics, private practice offices, outreach community screening, city programmes, schools etc).
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Efficacy</th>
<th>Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood screening</td>
<td>&gt;98%</td>
<td>~90%</td>
</tr>
<tr>
<td>Vaccination A and B</td>
<td>&gt;95%</td>
<td>79% (HBV)</td>
</tr>
<tr>
<td>Disposable, single-use syringes</td>
<td>&gt;95%</td>
<td>~60%</td>
</tr>
<tr>
<td>Harm reduction (NSP, OST)</td>
<td>~50-60%</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>Treatment of chronic HBV and HCV</td>
<td>40-90%</td>
<td>&lt;&lt;1%</td>
</tr>
</tbody>
</table>