Management of viral hepatitis B&C in Slovenia

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Slovenia

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SLOVENIA

2 million inhabitants

Prevalence in general population: HBV estimated <1%
HCV estimated 0.5%

Gross national income per capita: 26,530 int. $

Life expectancy at birth: 76 E/82 Cyears

Probability of dying under five: 3 per 1000 live births

Total expenditure on health per capita: 2,552 Intl $

Total expenditure on health: 9.4 % of GDP

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ACUTE and CHRONIC hepatitis B and C

INCIDENCE / 100 000 inhabitants

HEPATITIS B

HEPATITIS C

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Characteristics of HBV infection

- **Prevalence HBsAg:**
  - general population: <1%
  - blood donors: 0.02%

- **Chronic hepatitis B:**
  - HBeAg-negative: majority
  - genotype D: 95%

- **HDV co-infection:** none

- **HCV co-infection:** 5%

- **HIV co-infection:** 3%

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Prevalence of HBsAg in injecting drug users

SLOVENIA 2000-2010

Anti-HCV prevalence by selected groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Average Proportion Anti-HCV Positive (%)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injecting Drug Users</td>
<td>30% (N=1050)</td>
<td></td>
</tr>
<tr>
<td>Hemophiliacs</td>
<td>26.7% (N=374)</td>
<td></td>
</tr>
<tr>
<td>Prison inmates</td>
<td>26% (N=378)</td>
<td></td>
</tr>
<tr>
<td>HIV-positives</td>
<td>5% (N=300)</td>
<td></td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>1.1% (N=1343)</td>
<td></td>
</tr>
<tr>
<td>Health care workers</td>
<td>0.7% (N=281)</td>
<td></td>
</tr>
<tr>
<td>General Population Adults</td>
<td>estimated 0.5% (N=2 mill)</td>
<td></td>
</tr>
<tr>
<td>Blood donors</td>
<td>0.025% (N=1.4 mill)</td>
<td></td>
</tr>
</tbody>
</table>

Kastelic A et al. 2nd Slovenian Conference on HCV Infection in IDUs, 2007.
SLOVENIA 2000-2010

Anti-HCV prevalence by selected groups

- Injecting Drug Users: 30% (N=1050) HCV RNA: 15.6%
- Hemophilliacs: 26.7% (N=374)
- Prison inmates: 26% (N=378)
- HIV-positives: 5% (N=300)
- Hemodialysis: 1.1% (N=1343)
- Health care workers: 0.7% (N=281)
- General Population Adults: estimated 0.5% (N=2 mill)
- Blood donors: 0.025% (N=1.4 mill)

Kastelic A et al. 2nd Slovenian Conference on HCV Infection in IDUs, 2007.
Prevalence of anti-HCV among IDUs in Europe

Data for the years 2007 and 2008. Black squares are samples with national coverage; blue triangles are samples with subnational (local or regional) coverage. Differences between countries have to be interpreted with caution owing to differences in types of settings and study methods; national sampling strategies vary. Source: Reitox national focal points.
SLOVENIA 1993-2007
Dynamics of HCV-1 and HCV-3 genotypes
N=1504

SLOVENIA 1993-2007
Dynamics of HCV-1 and HCV-3 genotypes
N=1504

**genotype 1 = blood transfusion**
OR, 3.28 [95% CI, 2.18-4.95]; P < 0.0001

**genotype 3 = IDUs**
OR 3.71 [95% CI, 2.97-4.65]; P < 0.0001

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Management of viral hepatitis B and C

- Institute of Public Health:
  Surveillance of communicable diseases (includes prevention of HBV&HCV infections)

- National Viral Hepatitis Expert Group:
  National strategy for the complex management of HBV&HCV
  Action plan
  Operation
HEPATITIS B
Clinical criteria: Not relevant for surveillance purposes.
Epidemiological criteria: Not relevant for surveillance purposes.

Laboratory criteria:
- Positive results on at least one or more of the following tests or combination tests:
  1. IgM hepatitis B core antibody (anti-HBc IgM)
  2. hepatitis B surface antigen (HBsAg)
  3. hepatitis B e antigen (HBeAg)
  4. hepatitis B nucleic acid in serum (HBV DNA).

Case classification
- Possible case: not applicable.
- Probable case: not applicable.
- Confirmed case: any person meeting the laboratory criteria.

HEPATITIS C
Clinical criteria: Not relevant for surveillance purposes.
Epidemiological criteria: Not relevant for surveillance purposes.

Laboratory criteria:
- At least one of the following three:
  1. detection of hepatitis C virus nucleic acid (HCV RNA)
  2. detection of hepatitis C virus core antigen (HCV core)
  3. hepatitis C virus antibody (anti-HCV Ab) confirmed by an antibody test (e.g. immunoblot) in patients older than 18 months without evidence of resolved infection.

Case classification
- Possible case: not applicable.
- Probable case: not applicable.
- Confirmed case: any person meeting the laboratory criteria.

DEFINITIONS for surveillance (available on: http://www.ivz.si/gradiva_nalezljive_bolezni)
Institute of Public Health
Prevention of HBV and HCV infections

### HBV
- Surveillance of hepatitis B and contact tracing (general population)
- **Vaccination programme:**
  - birth cohorts from 1992 (at age 5-6 y)
  - persons at risk
- Screening of **pregnant women** (s.1994)
- **Safe blood** (HBV DNA testing)
- Work place safety (health care workers)
- Promotion of safe sex
- Harm reduction programmes

### HCV
- Surveillance of hepatitis C and contact tracing (general population)
- **Safe blood** (HCV RNA testing)
- **Work place safety** (health care workers)
- Harm reduction programmes

http://www.ivz.si/gradiva_nalezljive_bolezni
HEPATITIS B VACCINATION PROGRAMME

National programme of immunoprophylaxis, Office Gazette, 2012

Vaccination of birth cohorts from 1992 on with hepatitis B vaccine at age of 5-6 years (0-1-6),

Vaccination coverage (3rd dose): generally high

Regional differences:
The capital: 85,6 %
Eastern, rural part: 98 %

<table>
<thead>
<tr>
<th>School-year</th>
<th>Vaccination coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004/2005</td>
<td>98,1 %</td>
</tr>
<tr>
<td>2005/2006</td>
<td>97,8 %</td>
</tr>
<tr>
<td>2006/2007</td>
<td>97,3 %</td>
</tr>
<tr>
<td>2007/2008</td>
<td>97,4 %</td>
</tr>
<tr>
<td>2008/2009</td>
<td>97,1 %</td>
</tr>
<tr>
<td>2009/2010</td>
<td>97,0 %</td>
</tr>
<tr>
<td>2010/2011</td>
<td>92,2 %</td>
</tr>
</tbody>
</table>
Institute of Public Health

Prevention of HBV and HCV infections

HBV
- Surveillance of hepatitis B and contact tracing (general population)
- Vaccination programme:
  - birth cohorts from 1992 (at age 5-6 y)
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HCV
- Surveillance of hepatitis C and contact tracing (general population)
- Safe blood (HCV RNA testing)
- Work place safety (health care workers)
- Harm reduction programmes

http://www.ivz.si/gradiva_nalezljive_bolezni
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National Viral Hepatitis Expert Group

- Founded: in 1997, self-initiative

- Multidisciplinary team:
  - infectologists, gastroenterologists-hepatologists
  - clinical virologists
  - addiction specialists
  - epidemiologists
  - transfusiologyists
  - clinical pharmacists
  - pathologist
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National Viral Hepatitis Expert Group

- National strategy for the complex management of HBV&HCV infections:
  - **Testing**: special populations: case finding, surveillance
  - general population: anonymous free-of-charge testing (routine+campaigns)
  - **Treatment**: availability, access, process, follow-up
    - systematical analysis of treatment efficacy and safety (since 1997)
  - National consensus **guidelines** on the overall management of HBV, HCV infected
  - **Research**
  - **Education** (professionals, general population)
  - **Mass media campaigns** (World Hepatitis Day, etc.)

- National strategy for the management of HCV&HBV in IDUs

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Clinical management of patients with HBV&HCV infection at 5 Centers for Viral Hepatitis

Refferential institution:
Clinic for Infectious Diseases nad Februle Illnesses, UKC Ljubljana
SLOVENIA
Clinical management of patients with HBV&HCV infection

CLINICIANS:
- Infectologists: the majority of cases
- Gastroenterologists/hepatologists: liver failure, HCC

THERAPY for HCV:
- IFN (1993)
- IFN/RBV (1999)
- PEG/RBV (2001)
- BOC/TPV (2012)
- Liver transplantation (1998)

THERAPY for HBV:
- lamivudine (1999)
- adefovir (2003)
- entecavir (2006)
- telbivudine (2008)
- tenofovir (2009)

FINNANCING of HBV&HCV management:
- Basic Health Insurance System:
  - Nominated specialists to prescribe P/R, PI, NUCs
  - National guidelines for the management of HBV&HCV infection
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National management of HBV&HCV infection

- **1997**: Slovenian Viral Hepatitis Expert Group
  National Guidelines for the Management of HCV Infection

- **1999**: National Guidelines for the Management of HCV Infection – An Update

- **2007**: National guidelines for the clinical management of HCV infection in IDUs

- **2007**: Healthcare Network for the Management of HCV infection in IDUs

- **2008**: National consensus guidelines for the prevention of HBV reactivation in patients on immunosuppressive therapy

- **2009**: National guidelines for the clinical management of HCV infection - An update

- **2009**: National guidelines for the clinical management of HBV infection - An update

- **2006-2011**: National Slovenian Conferences on HCV Infection

- **2012**: National consensus guidelines for HCV treatment with protease inhibitors

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Network of 18 Centres for Prevention and Treatment of Drug Addiction

Slovenia: estimated 10 000 IDUs
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No of IDUs managed per year

Network of 18 Centres for Prevention and Treatment of Drug Addiction

Coordination of Centers for Prevention and Treatment of Illicit Drug Abuse, Slovenia 2011.
SLOVENIA

No of IDUs managed per year

Network of 18 Centres for Prevention and Treatment of Drug Addiction

15.6% HCV RNA positive
3% treated for HCV

Coordination of Centers for Prevention and Treatment of Illicit Drug Abuse, Slovenia 2011.
Hepatitis C in drug users on substitution treatment:

National guidelines for clinical management and treatment

March 2007
Healthcare network for the multidisciplinary management of HBV&HCV infections in IDUs

5 Viral Hepatitis Centers and 18 Centers for Prevention and Treatment of Drug Addiction

Referential: Clinic for Infectious Diseases nad Februle Illnesses, University Medical Centre Ljubljana
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Healthcare network for management of hepatitis B&C virus infections in IDUs

COMBINING:
- Viral hepatitis centers: 5
- Drug treatment centers: 18

Centers for Prevention and Treatment of Drug Addiction

Multidisciplinary team:
- Viral hepatitis specialists
- Addiction specialists
- Psychiatrists/therapists
- Other clinical specialists (dermatologist, thyroid specialist)
- Councillors (specially trained nurses, social workers)
- Peers (former HCV+ IVDUs): personally, on-line
- Other support system (familly, friends, co-workers, etc.)

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Healthcare network for management of IDUs with hepatitis C virus infection

National Conferences “HCV in IDUs” for providers:

- **1st Slovenian Conference on HCV Infection in IVDU (Jan 2006):**
  basic medical and supportive education strategies, interventions

- **2nd Slovenian Conference on HCV Infection in IVDU (Mar 2007):**
  set up National guidelines for the management of HCV in IVDUs

- **3rd Slovenian Conference on HCV Infection in IVDU (Apr 2008):**
  vulnerable groups

- **4th Slovenian Conference on HCV Infection in IVDU (Feb 2010):**
  experiences/improvements of the National guidelines
  future perspectives

- **5th Slovenian Conference on HCV Infection in IVDU (Dec 2011):**
  role of addiction programmes, new drugs for HCV, HIV and IVDUs in Slovenia
SLOVENIAN CONSENSUS GUIDELINES 2007

Current strategy for management of HCV infection in IDUs

- **Un-infected**: counselling to prevent HCV infection
  - regular testing for HCV infection
  - HBV vaccination

- **Acutely infected**: identification as soon as possible

- **Chronically infected**: identification
  - evaluation of readiness
  - medical evaluation
  - clinical management
  - counselling, motivation
  - treatment

MANAGEMENT OF CHRONIC HCV INFECTION IN IDUS

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MULTIDISCIPLINARY APPROACH
- to combine Drug Treatment Centers and Viral Hepatitis Centers
- implement already existing facilities into the most appropriate model for local resources

NATIONAL GUIDELINES
- Identification of IDUs who may benefit from referral for further management of HCV infection (Drug Treatment Centre)
- Evaluation of IDUs before treatment (Drug Treatment Centre, Viral Hepatitis Centre)
- Optimization of HCV treatment before and during treatment (Viral Hepatitis Centre, Drug treatment Centre)
- Support during treatment (medical, psychological, social, peers)

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**Cooperation**
between viral hepatitis specialist and drug addiction therapist

- **Viral hepatitis specialist**
  - Drug user
    - HCV RNA +
  - First visit
  - Follow up visits
  - Treatment of hepatitis C
  - Monthly

- **Drug addiction therapist**
  - Drug user
    - HCV RNA +
  - First visit “fill-in form”
  - Follow up “fill-in form”
  - “Fill-in form” on psychical condition, adherence
  - If necessary introduction of psycho-socio-pharmacotherapy
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Evaluation of HCV treatment

Systemic review → Recommendations → Guidelines → Protocol → Decision making → Intervention → Evaluation

Source: Annie Coppel, NICE.
**SLOVENIA**

Four prospective national studies on currently recommended SOC treatment of all naive patients with chronic hepatitis C

<table>
<thead>
<tr>
<th>SOC Therapy</th>
<th>Period</th>
<th>All pts (N)</th>
<th>IDUs (%)</th>
<th>Sustained Viral Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFN</td>
<td>1997-1999</td>
<td>80</td>
<td>5%</td>
<td>28%</td>
</tr>
<tr>
<td>IFN/R</td>
<td>1999-2001</td>
<td>63</td>
<td>16%</td>
<td>43%</td>
</tr>
<tr>
<td>PEG/R</td>
<td>2001-2004</td>
<td>134</td>
<td>36%</td>
<td>64%</td>
</tr>
<tr>
<td>PEG/R optimised</td>
<td>2008-2010</td>
<td>130</td>
<td>78%</td>
<td>80%</td>
</tr>
</tbody>
</table>

SLOVENIA 2008 - 2010
Patients with chronic hepatitis C that finished optPEG/R
Risk factors for HCV infection

SLOVENIA 2008 - 2010

Patients with chronic hepatitis C that finished optPEG/R

Risk factors for HCV infection


IDUs: 6% non-adherent
88% SVR

N=130

n=101

IVDU

88% SVR
SLOVENIA

Management of HCV (in 2013)

Known HCV-positive: 2978

- Detection rate: app. 28%
- Treatment rate: 37%
  IDUs 13%
Management of viral hepatitis B&C in Slovenia

CONCLUSIONS

- **Institute of Public Health:**
  General surveillance and prevention

- **National Viral Hepatitis Expert Group:**
  National strategy for the complex management of viral hepatitis

- **Multidisciplinary Healthcare network for the management of infected IDUs:**
  Combining Drug Treatment Centers and Viral Hepatitis Centers is EFFECTIVE

- **Implementation of already existing facilities into the most appropriate model for local resources is reasonable and effective**
European study on how to improve life for 25 million Europeans with hepatitis (ELPA)

Ranking performance among 30 countries