Country examples

GREECE (2007)

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Presentation outline

• Comparison of viral hepatitis epidemiology and strategies between 2007 - 2014
• Identification of progress made and remaining gaps
  – Surveillance
  – Treatment
  – Prevention
Meeting 2007 main conclusions

Strengths

• Viral hepatitis identified as a public health burden
• Universal infant HBV vaccination since 1998
• Large nationwide cohort study (hepnet-study) was initiated in 2003
Meeting 2007 main conclusions

Challenges identified

- Absence of national hepatitis seroprevalence data
- Absence of reliable surveillance systems
- Shortage of data of immunization status of HCW
- Higher HAV, HBV and HCV incidence in immigrants
- High involvement of private sector in HC services leads to social inequalities
- Although high vaccination coverage against HBV, significant delays of first HBV dose
Surveillance

- Surveillance of Viral Hepatitis in Greece is based on the mandatory notification system.
- Have **not** been able to switch to laboratory based notification system.
Successes and remaining challenges
Hepatitis A
Seropidemiology of hepatitis A in Greece

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>No of subjects</th>
<th>Age (y)</th>
<th>%anti-HAV (+)</th>
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<tbody>
<tr>
<td>Papaevangelou and Frosner</td>
<td>1978</td>
<td>83</td>
<td>10-19</td>
<td>52</td>
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<td>Mavromichalis et al</td>
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<td>155</td>
<td>10-19</td>
<td>40</td>
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<td>10-14</td>
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<td>Kremastinou et al.</td>
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<td>436</td>
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<td>Arvanitidou et al</td>
<td>1989</td>
<td>255</td>
<td>6-14</td>
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<td>Mamasi et al</td>
<td>1989</td>
<td>478</td>
<td>10-15</td>
<td>13.4</td>
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<td>1989</td>
<td>115</td>
<td>16-20</td>
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<td>Basoukou P. et al</td>
<td>1990</td>
<td>593</td>
<td>10-20</td>
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Hepatitis A vaccination in Greece

• 1999: HAV vaccine available in the market

• Vaccination was provided by private pediatricians but not reimbursed
Vaccination coverage in children <14 yo (2006)

Ethnicity

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Vaccinated</th>
<th>Natural Immunity</th>
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<tbody>
<tr>
<td>greek</td>
<td>35.51</td>
<td>15.97</td>
</tr>
<tr>
<td>immigrants</td>
<td>29.16</td>
<td>16.36</td>
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</tbody>
</table>

p < 0.01

Kyrka A JMV 2009
Vaccination coverage in children <14 yo (2006)

Urban versus rural areas

Vaccine coverage
Natural Immunity

p = 0.012

urban
rural

Kyrka A JMV
2009
Successes and remaining challenges
Hepatitis A

Intervention analysis showed
- no significant effect of the release of HAV vaccine in 1999 (p=0.808) or
- its introduction to the routine childhood immunization program in 2008 (p=0.837)

Mellou K et al. PLOS ONE accepted
Hepatitis A incidence

Mellou K et al. Plosone accepted
Age distribution of HAV cases 2004 - 2012

30% among Roma
10% among travelers
5.5% immigrants

Mean age of cases among general population increased:
< 2008 : 21.2yrs (SD=3) versus
> 2008 : 30.6 yrs (SD=3.3)

www.keelpno.gr
New outbreaks in 2013

Mellou K et al. PLOS ONE accepted
Remaining challenges
Hepatitis A

• Strong discussions in recent Advisory Committee for Immunization Practices over possible withdrawal of full reimbursement for hepatitis A vaccine based on:
  – No significant reduction in incidence post 2008
  – Increase in mean age of cases
  – Possible need to spend recourses in targeting high risk groups (as all other EU countries)
Successes and remaining challenges
Hepatitis B and C

In Greece:

• 1970s: prevalence of hepatitis B was 5%
  • 25% of those also infected with HDV

• Currently prevalence of
  – HBV: estimated at 2.2% (1.2% among Greeks)
    • 5% of those also HDV
  – HCV: 1-2%

with implementation of:
  ▪ vaccination
  ▪ preventive technologies for post-transfusion hepatitis
  ▪ health education
  ▪ general improvement of health conditions
Annual mean number of new cases of Hep B and Hep C per risk factor, Greece 2004-2014

Average annual number of cases, 2004-2014, Greece

- Vulnerable population group
- Epidemiological link
- Foreign nationality
- Tattoo
- Health professional
- Dental procedure
- Haemodialysis
- Transfusion
- Surgical procedure

Confirmed anti-HCV positive (1st diagnosis)  | Hepatitis C, acute  | Hepatitis B, acute

Keelpno.gr
HBV Vaccination

National Immunization Program

- Hepatitis B vaccine since 1998
- 3 doses up to 12-18 months

Table 2: Greek NIP [6]

<table>
<thead>
<tr>
<th>Vaccines</th>
<th>Age</th>
<th>Birth</th>
<th>1 month</th>
<th>2 months</th>
<th>4 months</th>
<th>6 months</th>
<th>12 months</th>
<th>15 months</th>
<th>18 months</th>
<th>2 years</th>
<th>3 years</th>
<th>4-6 years</th>
<th>7-12 years</th>
<th>13-18 years</th>
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<tbody>
<tr>
<td>Hepatitis B (Hep B)¹</td>
<td>HEP B</td>
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<td>HEP B</td>
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<tr>
<td>Diphtheria, Tetanus, Pertussis (DTP)²</td>
<td>DTP</td>
<td>DTaP</td>
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<td>DTaP</td>
<td>DTaP</td>
<td>TdaP²,³,⁴</td>
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<tr>
<td>Polio (IPV)³</td>
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<td>Haemophilus Type B³</td>
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<td>Meningococcal C (MCC)³</td>
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<td>MCC</td>
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<td>Pneumococcal (PCV)⁴</td>
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<td>PCV</td>
<td>PCV</td>
<td>PCV (PCV)³,⁴</td>
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<td>Measles-Mumps-Rubella (MMR)⁵</td>
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<td>Chickenpox (Var)⁶</td>
<td>Var</td>
<td>Var</td>
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<tr>
<td>Hepatitis A (Hep A)⁷</td>
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<td>Hep A (2 doses)</td>
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<td>Tuberculosis (BCG)⁸</td>
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<td></td>
<td>BCG</td>
<td>Mantoux</td>
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<tr>
<td>Flu (INFL)⁹</td>
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</table>

Vaccination Schedule for children and adolescents.

Vaccines presented under the intermitted line are suggested for selective vaccination.

Vaccination Age Range. The parenthesis shows the number of doses (more than one). Age range sets the opportunity of using monovalent or polypotent (combined) vaccines and/or combination monovalent polypotent.

Age range when vaccination has not been done according to the suggested scheme of age and doses.
Vaccination coverage for Hep B

National study by NSPH-HCDCP (2012)

- Cohort of children born 2005
- Coverage for Hep B vaccine 98-99%
- 3 doses by 12 months, only 36%!
Vaccination coverage for Hep B

- National vaccination coverage survey (2013) of children 2-3 years old (N= 2539) attending daycare centers (n=187)
  - Distributed over the country
  - General population, immigrants (5.5%) & Roma (0.4%)

<table>
<thead>
<tr>
<th>Doses (HEP B)</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 dose Hep</td>
<td>99.4</td>
</tr>
<tr>
<td>2 doses Hep</td>
<td>98.8</td>
</tr>
<tr>
<td>3 doses Hep</td>
<td>96.2</td>
</tr>
</tbody>
</table>

Source: Dept for Surveillance & Intervention, KEELPNO

<table>
<thead>
<tr>
<th>Doses (HEP B)</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 up to 6 months of age</td>
<td>53.3</td>
</tr>
<tr>
<td>3 up to 12 months of age</td>
<td>52.2</td>
</tr>
<tr>
<td>3 up to 24 months of age</td>
<td>84.6</td>
</tr>
</tbody>
</table>
HEP B Vaccination coverage
(children 2-3 years old, attending day care centers, Greece 2013)

- High vaccination coverage from 96-99%
- Significant delay in initiation & completion, but eventually reaches very high levels of vaccination coverage

Source: Dept for Surveillance & Intervention, KEELPNO
HBV vaccination remaining challenges

- After identifying the delay in HBV vaccination in infants: a birth dose was recommended (2011) to all high risk newborns (immigrants, Roma..)
- Emphasis on utilization of hexavalent vaccines.
- Recent austerity measures has resulted in decreased access to health care services affecting mainly children and immigrants.
- HCW vaccination is suboptimal (56-69%).

Maltezou E et al. J Infect 2012
Maltezou E et al. PIDJ 2012
HepNet Cohort

• HCDCP coordinates and sponsors the nationwide Hepnet cohort study for Hepatitis B and C from 2003 (HepNet.Greece)

• Retrospective-prospective study. Started in 2003 with retrospective recording of all patients followed since 1997.

• The aim of this study is to evaluate the epidemiology, the course and outcome of chronic viral hepatitis B and C infection with and without treatment.
HepNet Cohort

- 23 participating departments all over Greece:
  - Athens (metropolitan area): 12
  - Piraeus (metropolitan area): 2
  - Thessaloniki (north Greece): 5
  - Patra (Peloponnese): 1
  - Larissa (central Greece): 1
  - Alexandroupolis (Thrace): 1
  - Rhodes (South Aegean): 1

- HBV: 6,403
  - Greeks: 70%
  - IDUs: 2.1%

- HCV: 5,666
  - Greeks: 76.8%
  - IDUs: 34%
Changes in HCV

Change in HCV genotype distribution

Changing routes of HCV transmission

Raptopoulou et al, Hippokratia, 2011
1600% increase of HIV reported cases among IDU
Followed by increase in HCV prevalence among IDUs

HCV prevalence among IDUs

HCV prevalence among “new” IDUs

Paraskevis D et al PLOS ONE 2013
Prevention among IDUs

• Provision of clean needles & syringes:
  – 2013: >400,000 syringes distributed through outreach & fixed sites, an estimated **133 syringes per IV drug user** in Athens

• “Open doors” project: Day center for health & psychosocial support of sex workers & vulnerable population groups

<table>
<thead>
<tr>
<th></th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>SYRINGES/STERILE TISSUES</td>
<td>102.790</td>
</tr>
<tr>
<td>WATER FOR INJECTION</td>
<td>85.200</td>
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<td>SWABS</td>
<td>35.400</td>
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<tr>
<td>CONDOMS</td>
<td>15.850</td>
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<tr>
<td>INFORMATIONAL LEAFLETS</td>
<td>750</td>
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</table>

KEELPNO: (01/12/2011– 01/07/2012)

Source: OKANA
Treatment of Hep B & C in Greece

January 2007:

- Treatment for the patients with chronic hepatitis B and C free of charge

- Currently conventional treatment provided
BLOOD SAFETY
Molecular testing with NAT in 3,240,394 blood units (2007-2012)

<table>
<thead>
<tr>
<th></th>
<th>HBV-DNA</th>
<th></th>
<th>HCV-RNA</th>
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<th>Total</th>
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<tbody>
<tr>
<td></td>
<td>NAT positive only</td>
<td>(HBsAg negative)</td>
<td>NAT positive only</td>
<td>(Anti-HCV negative)</td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>Rate</td>
<td>n</td>
<td>Rate</td>
<td>n</td>
<td>Rate</td>
</tr>
<tr>
<td>368</td>
<td>1:8,805</td>
<td>15</td>
<td>1:216,026</td>
<td>383</td>
<td>1:8,461</td>
</tr>
</tbody>
</table>

- Prevalence of Occult HBV: 1:8,805
- 957 blood components prepared from the 383 positive blood units were discarded and NOT transfused
- Transfusion transmitted hepatitis 2004-2013: Zero cases

(source: SKAE)
Remaining challenges

Conclusions

• Surveillance system not updated according to ECDC guidelines
• HAV: close follow up of epidemiology
• HBV: reinforcing birth dose in high risk newborns and timely vaccination for all
• HCW vaccination for HBV
• Decrease access to health care due to economic crisis
• HCV: controlling recent outbreak among IDUs
• New era in HCV treatment and cost
Good news

• Increased awareness
• Stakeholders such as KEELPNO, MOH, Academia and Patient Associations have been very active and devoted in working on viral hepatitis challenges
Good news

• Increased awareness
• Stakeholders such as KEELPNO, MOH, Academia and Patient Associations have been very active and devoted in working on viral hepatitis challenges

Thank you for your attention
Recent telephone survey

• Involved about 10,000 subjects
• Almost 50% of chronic HBV and 80% of chronic HCV patients in Greece may be unaware of their infection,
• Only 32% and 58% of diagnosed chronic HBV or HCV patients, respectively, have been ever treated.

Papatheodoridis G et al J Viral Hepat. 2014