Surveillance of Varicella and Herpes Zoster in Europe

As of November 2010

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Table of contents

Executive summary .................................................................................................................................. 4
Introduction .............................................................................................................................................. 6
    Clinical disease and complications .................................................................................................. 6
    Vaccine and Vaccination ............................................................................................................... 6
Objectives of the report ..................................................................................................................... 7
Methods ................................................................................................................................................ 7
    Validation of results .................................................................................................................... 7
Results ................................................................................................................................................ 8
Epidemiology and Vaccination .......................................................................................................... 8
    Epidemiology of Varicella in Europe ............................................................................................ 8
    European vaccination Policies ..................................................................................................... 9
Surveillance systems ............................................................................................................................ 10
    Surveillance systems for varicella ............................................................................................... 10
    Future changes in surveillance of varicella ............................................................................... 10
    Countries with more than one surveillance system for varicella............................................. 11
    Surveillance systems for zoster ..................................................................................................... 11
Frequency of data submission and variables .................................................................................. 12
    Frequency of data submission to EUVAC.NET ......................................................................... 12
    Review of variables available for reporting varicella at European level .................................... 12
Case definitions ................................................................................................................................... 14
    Type of cases reported ............................................................................................................... 14
    Proposed standard case definition for varicella and herpes zoster ........................................ 14
EUVAC.NET proposal for case definition and classification for the surveillance of
varicella/herpes zoster at EU level .................................................................................................. 16
Discussion ............................................................................................................................................ 18
Conclusions ......................................................................................................................................... 19
Recommendations .............................................................................................................................. 19
References .......................................................................................................................................... 20
Annex 1. EUVAC.NET participants .................................................................................................. 21
Annex 2. Questionnaire used for the survey on surveillance system .............................................. 24
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**Date of update:** 31 August 2011 (after collaboration with VENICE project which undertook a similar survey)

**List of Abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>EU</td>
<td>European Union</td>
</tr>
<tr>
<td>ECDC</td>
<td>European Centre for Disease Prevention and Control</td>
</tr>
<tr>
<td>EUVAC.NET</td>
<td>Surveillance Community Network for Vaccine-preventable Diseases</td>
</tr>
<tr>
<td>MMR-V</td>
<td>Measles, mumps, rubella, and varicella vaccine</td>
</tr>
<tr>
<td>PCR</td>
<td>Polymerase chain Reaction</td>
</tr>
<tr>
<td>VZV</td>
<td>Varicella Zoster Virus</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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</tbody>
</table>
Executive summary

EUVAC.NET is a European network for surveillance of vaccine preventable diseases and has collected surveillance data on varicella for the period 2000-07. A total of 5,435,223 cases of varicella were reported by 15 countries with mandatory notification that could provide data for the whole period 2000-07, corresponding to an average incidence of 319 per 100,000 inhabitants. Highest incidences were reported among those aged 1-4 years and those aged 5-9 years (respectively 2,588 and 1,943 cases per 100,000). Data collection and report preparation for 2008-09 are currently ongoing.

Varicella is not included in the EU list of mandatory reportable diseases. After consultation with disease experts and using the information derived from the participating countries, in 2008 EUVAC.NET proposed a EU case definition for varicella and herpes zoster, which includes a three tier case classification (possible, probable and confirmed case), and a suggestion to report probable and confirmed cases at EU level.

The aim of this report is to provide an overview of the surveillance systems in place for varicella and herpes zoster as of November 2010, and to discuss possible and future strategies for varicella and zoster surveillance in Europe.

As part of EUVAC.NET Work Area 3 a survey was carried out in 2007 on surveillance systems for varicella and herpes zoster among 32 EUVAC.NET countries. The information derived from the survey forms the basis of the present report; in addition, the information from the EUVAC.NET survey on sentinel surveillance systems from 2008 and vaccination schedules from the EUVAC.NET website were included. Results have been re-validated by EUVAC.NET country gatekeepers in November 2010 and amended as necessary.

Three European countries have introduced a universal varicella vaccination program (Germany, Greece, Latvia), and two countries in some regions (Italy and Spain). In additional eleven countries varicella vaccination is recommended to susceptible adolescents and adults and high risk groups. Twenty-six of 32 countries have a surveillance system in place for varicella, of these six and England and Wales have a sentinel system and the other 19 and Northern Ireland have a system covering the whole population. Six countries and Scotland do not have surveillance in place for varicella. Of the 19 countries with a surveillance system for varicella covering the whole population, information on the number of cases is the only variable on which all countries can report at European level; nine countries are able to provide data aggregated by age-groups. Only eight countries have access to more detailed information (hospitalisation, vaccination status, laboratory confirmation) at national level.

Countries reported different classification of cases to EUVAC.NET (clinical, epidemiological, laboratory confirmed cases) and the case definitions in use vary greatly. Fourteen countries have a surveillance system in place for herpes zoster, of these six have a sentinel system. Eighteen countries have no surveillance for herpes zoster.

To monitor the effect of vaccine introduction in the national immunisation schedule, it is important that background epidemiologic data are available, and that surveillance systems, either sentinel or mandatory, have the possibility to assess its effect on the burden of disease once the vaccine is introduced. If only a few countries have introduced varicella vaccine in the schedule now, the situation might change in the future, especially when MMR-V will be available in more European countries. The same applies to the vaccine for herpes zoster, which has just recently been granted EMA authorisation.
The survey highlights that:

- There is need to better understand the epidemiology of varicella and herpes zoster in Europe
- There is need for data that reflects varicella incidence and that is comparable between countries
- There is need to identify standardized surveillance methodologies to improve data comparability in the European Member States

Based on the data and information currently available, we recommend that:

- An EU case definition and classification of varicella should be adopted
- An EU case definition and classification of herpes zoster should be adopted
- Countries should use the EU case definitions of varicella and zoster for reporting at EU level once they are approved
- If varicella is considered to be introduced in a childhood vaccination programme, a disease surveillance strategy should also be integrated to validate the impact of vaccination introduction on the burden of disease
- Surveillance of herpes zoster at European level should be investigated further to identify strengths and weaknesses of existing surveillance systems
- Concerted efforts to identify high quality and feasible surveillance methodologies could be a timely and valuable tool to strengthen surveillance of varicella and herpes zoster in Europe.
Introduction

EUVAC.NET is a European surveillance network for vaccine preventable disease. The network incorporates all 27 EU Member States together with Croatia, Iceland, Norway, Switzerland and Turkey. The hub is based at the Statens Serum Institut in Copenhagen. Work Package 5 deals with surveillance of varicella, and this report constitutes one of the deliverables of the project in the year 2010.

According to the Framework Partnership Agreement (grant number 2008/005), it was agreed that “The hub will actively prepare a comprehensive plan in collaboration with ECDC, based on a broad consultation with experts from Member States and key stakeholders on how best to develop the surveillance of varicella and zoster in Europe. This will include a review of the data variables on varicella and zoster required to monitor these diseases, frequency of data submission and publishing of surveillance reports.”

Clinical disease and complications

Varicella is caused by varicella-zoster virus (VSV), a member of the alpha herpesvirus family. The illness is usually of short duration; it has a characteristic vesicular rash, usually accompanied by fever and malaise, and is very contagious. The incubation period is between 2 and 3 weeks. The disease can be serious in older age groups and in the immunocompromised, with the most common complication being bacterial skin superinfections (1). Complications such as varicella pneumonia and encephalitis, although rarely, may occur, and lead to persistent sequelae or death. After infection, the virus becomes latent in dorsal root ganglia and can reactivate later in life as a localised manifestation termed herpes zoster (shingles). Serological studies across Europe conducted via the European sero-epidemiology network have shown that antibodies to varicella are mostly acquired before 15 years of age, but also that there are substantial differences in VSV sero-epidemiology within the European region, which will need to be taken into account in designing national policies regarding VZV vaccination (2).

Vaccine and Vaccination

In Europe two combined Measles Rubella Mumps Varicella (MMR-V) vaccine were licensed in 2006, Priorix-Tetra® and ProQuad®. Monovalent vaccines have been available for more 20 years. A vaccine against herpes zoster was also licensed in Europe in 2006, Zostavax®. This vaccine was issued a marketing authorisation for people aged 60 years and above and is licensed for the prevention of herpes zoster and post herpetic neuralgia.

Universal vaccination with one dose of varicella was introduced in US in 1995, with a second dose added in 2006, and has led to a large reduction in incidence and complications (3). In 2008 the Advisory Committee on Immunization Practices recommended Zoster vaccine for all persons aged >60 years who have no contraindications.

In a position paper WHO states that routine childhood immunization against varicella may be considered in countries where this disease is a relatively important public health and socioeconomic problem, where the vaccine is affordable, and where high (85%-90%) and sustained vaccine coverage can be achieved. Indeed, childhood immunization with lower coverage could theoretically shift the epidemiology of the disease and increase the number of cases with severe disease in older children and adults (4).
Objectives of the report

The objectives of the present report are:

- To give an overview of the epidemiology of varicella and varicella vaccination strategies in the EUVAC.NET participating countries
- To give an overview of the surveillance systems in place for varicella and herpes zoster in the EUVAC.NET European Countries
- To report the EUVAC.NET proposal on standard varicella and herpes zoster case definition
- To address and discuss future strategies for surveillance of varicella and herpes zoster in Europe

Methods

A surveillance system and vaccination programme questionnaire (Annex 2) was e-mailed to 32 countries (UK divided into 3 units: England and Wales, Scotland and N. Ireland) participating in EUVAC.NET in 2007. The questionnaire contained structured questions on details of varicella surveillance, case definitions used for reporting and varicella vaccination programme in place or planned, and the presence of a surveillance system in place for herpes zoster.

Additional information on sentinel systems was extracted from the EUVAC.NET Sentinel Systems for the Surveillance of Vaccine-Preventable Diseases in Europe (5), and the EUVAC.NET website (page on vaccination schedules).

The responses of the questionnaire and the information extracted from the sentinel systems report and EUVAC.NET website were validated again in the first two weeks of November 2010 and the updated information is included in the current report.

Validation of results

All 32 countries have validated the following report in November 2010. In February 2011, some inconsistencies were noted in the answers collected in a similar survey undertaken by the project VENICE. For this reason, gatekeepers were contacted and asked to clarify their answer. Inconsistencies mainly related to table 1, recommendations for varicella vaccine to high risk groups.

Nevertheless the update, this report refers to the status of varicella and zoster surveillance and vaccination policies as of November 2010.
Results

Epidemiology and Vaccination

Epidemiology of Varicella in Europe
The epidemiology of varicella in Europe has been presented in the last EUVAC.NET report (6) covering the years 2000-07. Data collecting and report preparation for 2008-09 are currently ongoing.
During 2000-07, there were 5,435,223 cases of varicella reported from the 15 countries with mandatory notification systems that could provide data for the whole period (UK represented by Scotland), (Figure 1). This corresponds to a cumulative average incidence of 319 varicella cases per 100,000 inhabitants for 2000-07, which is shown in Figure 1.
The incidence, based on data reported by nine countries (Czech Republic, Croatia, Estonia, Hungary, Italy, Malta, Romania, Slovakia, Slovenia) for the whole period 2000-07, was higher in children aged 1-4 years and in those aged 5-9 years, respectively 2,588 and 1,943 cases per 100,000 (Figure 2).

Figure 1. Average incidence category of reported varicella cases per 100,000 inhabitants in EUVAC.NET countries, 2000-07

Figure 2. Average age-specific incidence of varicella cases, 9 countries, 2000-07
European vaccination Policies
Most European countries do not include varicella in the routine childhood immunisation program (table 1), but have recommendations for susceptible individuals (children and/or adolescence and/or adults) and/or specific high-risk groups (such as those suffering from malignancy and/or immuno-suppressed).

Table 1. Vaccination policies for varicella in European countries (last update through EUVAC.NET gatekeepers on November 2010). Recommendation implies recommendation by the National Health Authority

<table>
<thead>
<tr>
<th>Universal varicella vaccination (year of start of the programme)</th>
<th>Only recommended vaccination for susceptible individuals and/or high risk groups</th>
<th>No policy on varicella vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Germany (2004)</td>
<td>Austria</td>
<td>Bulgaria</td>
</tr>
<tr>
<td>Greece (2006)</td>
<td>Belgium</td>
<td>Croatia</td>
</tr>
<tr>
<td>Latvia (2008)</td>
<td>Estonia</td>
<td>Denmark</td>
</tr>
<tr>
<td>Spain (4 Autonomic regions, Madrid, Navarra, Ceuta and Melilla) (2006-2009)</td>
<td>Finland</td>
<td>Hungary</td>
</tr>
<tr>
<td></td>
<td>France</td>
<td>Netherlands</td>
</tr>
<tr>
<td></td>
<td>Iceland</td>
<td>Norway</td>
</tr>
<tr>
<td></td>
<td>Ireland</td>
<td>Portugal</td>
</tr>
<tr>
<td></td>
<td>Italy (national)</td>
<td>Romania</td>
</tr>
<tr>
<td></td>
<td>Lithuania</td>
<td>Slovakia</td>
</tr>
<tr>
<td></td>
<td>Luxemburg</td>
<td>Sweden</td>
</tr>
<tr>
<td></td>
<td>Malta</td>
<td>Turkey</td>
</tr>
<tr>
<td></td>
<td>Poland*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Slovenia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spain (national)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Switzerland</td>
<td></td>
</tr>
<tr>
<td></td>
<td>United Kingdom</td>
<td></td>
</tr>
</tbody>
</table>

*Poland. There is a recommended varicella vaccination since 2002 and mandatory varicella vaccination for susceptible individuals and/or high risk groups in 2010 vaccination schedule.
Surveillance systems

Surveillance systems for varicella
As of November 2010, 81% (26/32) of European countries have a surveillance system in place for varicella (UK conducts varicella surveillance in England and Wales and Northern Ireland). Of these, 19 have a national mandatory surveillance system. Table 2 gives an overview of the situation in each country.

Finland has laboratory based surveillance system which does not separated clinical disease and therefore includes both varicella and herpes zoster

Future changes in surveillance of varicella
Six countries are considering changes to their surveillance of varicella in the near future (indicated with an * in the table 2). Of these, four countries already have national mandatory surveillance. One of these five describes that case-based data will be collected in the future at national level (Estonia), another that introduction of reporting of varicella in adults is being considered (Austria). Scotland implemented a change in the surveillance system from 1 January 2010: varicella ceased to be notifiable.

Table 2. Type of surveillance system in place in 32 European Countries for varicella (UK is divided into three units: England and Wales, Scotland and Northern Ireland for the purpose of varicella surveillance). Last update in November 2010 through EUVAC.NET gatekeepers. Some country has more than one system in place, if so they are here placed according to the system covering the largest population

<table>
<thead>
<tr>
<th>Surveillance systems covering the whole country</th>
<th>Case-based data at national level from mandatory reports</th>
<th>Aggregated data at national level from mandatory reports</th>
<th>Laboratory-based mandatory reports</th>
<th>Only Sentinel surveillance</th>
<th>No surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Croatia</td>
<td>Bulgaria</td>
<td>Finland</td>
<td></td>
<td>Austria*</td>
<td>Denmark</td>
</tr>
<tr>
<td>Cyprus</td>
<td>Estonia*</td>
<td>Norway</td>
<td></td>
<td>Belgium</td>
<td>Iceland</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>Lithuania*</td>
<td></td>
<td></td>
<td>England and Wales</td>
<td>Luxemburg</td>
</tr>
<tr>
<td>Germany†</td>
<td>Malta</td>
<td>Northern Ireland</td>
<td></td>
<td>France</td>
<td>Scotland</td>
</tr>
<tr>
<td>Greece</td>
<td></td>
<td>Poland*</td>
<td></td>
<td>Portugal*</td>
<td>Sweden</td>
</tr>
<tr>
<td>Hungary</td>
<td></td>
<td>Romania</td>
<td></td>
<td>Netherlands</td>
<td>Switzerland</td>
</tr>
<tr>
<td>Italy</td>
<td></td>
<td>Spain*</td>
<td></td>
<td>Ireland</td>
<td>Turkey</td>
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<tr>
<td>Latvia</td>
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<tr>
<td>Malta</td>
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<tr>
<td>Slovakia</td>
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<td></td>
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<tr>
<td>Slovenia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>9</td>
<td>2</td>
<td>7</td>
<td>7</td>
</tr>
</tbody>
</table>

*countries which are considering a change in the surveillance system for varicella
†regional mandatory reporting in 5 out of 16 Federal states
Countries with more than one surveillance system for varicella

Italy, Cyprus, Germany and Greece have two surveillance systems in place for varicella. All three countries have both national mandatory surveillance system and a sentinel system. The national mandatory surveillance system in Greece collects information only on cases of varicella with complications, and the sentinel system on cases of varicella.

In Germany, case based notifications are mandatory in 5 out of the 16 Federal States. Sentinel surveillance is countrywide but not population based with aggregated cases by age group and case based reporting for complications and vaccinated cases.

Surveillance systems for zoster

Fourteen countries have some form of surveillance in place for herpes zoster (UK represented by England and Wales). Six countries conduct sentinel surveillance, for all countries the system is clinician-based. Seven other countries conduct other forms of surveillance. Of these, Slovakia has a system covering the whole country with clinical mandatory notification. Finland has laboratory based surveillance system which does not separate clinical disease and therefore includes both varicella and herpes zoster. Spain is currently implementing surveillance of herpes zoster, following an agreement between national and regional health authorities from 2007.

Eighteen countries, Northern Ireland and Scotland have no surveillance for herpes zoster.

Table 3. Presence of a surveillance system for herpes zoster, last update November 2010. UK is divided into three units for the purpose of herpes zoster surveillance: England and Wales, Northern Ireland, Scotland.

<table>
<thead>
<tr>
<th>Sentinel Surveillance clinician-based</th>
<th>Other forms of surveillance</th>
<th>Plans to introduce surveillance</th>
<th>No surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belgium</td>
<td>Austria</td>
<td>Spain</td>
<td>Bulgaria</td>
</tr>
<tr>
<td>England and Wales</td>
<td>Croatia</td>
<td></td>
<td>Cyprus</td>
</tr>
<tr>
<td>France</td>
<td>Czech Republic</td>
<td></td>
<td>Denmark</td>
</tr>
<tr>
<td>Germany</td>
<td>Finland</td>
<td></td>
<td>Estonia</td>
</tr>
<tr>
<td>Ireland</td>
<td>Malta</td>
<td></td>
<td>Greece</td>
</tr>
<tr>
<td>Netherlands</td>
<td>Slovakia</td>
<td></td>
<td>Hungary</td>
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<tr>
<td></td>
<td>Slovenia</td>
<td></td>
<td>Iceland</td>
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<td></td>
<td></td>
<td></td>
<td>Italy</td>
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<td></td>
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<td>Latvia</td>
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<td></td>
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<td>Lithuania</td>
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<td></td>
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<td>Luxemburg</td>
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<td></td>
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<td></td>
<td>Northern Ireland</td>
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<td></td>
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<td>Norway</td>
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<td></td>
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<td>Poland</td>
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<td></td>
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<td>Portugal</td>
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<td>Romania</td>
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<td>Scotland</td>
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<td>Switzerland</td>
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<td></td>
<td></td>
<td></td>
<td>Turkey</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>20</td>
</tr>
</tbody>
</table>
Frequency of data submission and variables

Frequency of data submission to EUVAC.NET
EUVAC.NET has been collecting varicella surveillance data from participating countries. Data was collected for the first time in 2007 (for the period 2000-07), and again in 2010 for the periods 2008-09. Data was collected in an aggregated format, consisting of number of cases aggregated by age groups and categorised by vaccination status, laboratory confirmation, hospitalisation and complications.

Review of variables available for reporting varicella at European level
Based on the surveillance varicella data reporting to EUVAC.NET for the years 2000-07, most countries are able to report only on a limited set of variables at European level. The only information that all countries with a mandatory surveillance system covering the whole country population could provide was the total number of cases of varicella (table 4). Countries that collect data on hospitalisation status and complications have provided additional details on their surveillance system (Table 5).

Table 4. Data available from countries with national mandatory surveillance covering the whole population that could provide data for all years on a series of variables 2000-07.

<table>
<thead>
<tr>
<th>Data provided</th>
<th>No. countries</th>
<th>Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of cases</td>
<td>18</td>
<td>Bulgaria, Croatia, Cyprus, Czech Republic, Estonia, Finland, Greece, Hungary, Italy, Latvia, Lithuania, Malta, Poland, Romania, Scotland, Slovakia, Slovenia, Spain</td>
</tr>
<tr>
<td>By modified EU-defined age groups (&lt;1, 1-4, 5-9, 10-14, 15-19, 20+*)</td>
<td>11</td>
<td>Czech Republic, Croatia, Cyprus, Greece, Estonia, Hungary, Italy, Malta, Romania, Slovakia, Slovenia</td>
</tr>
<tr>
<td>Vaccination status of cases</td>
<td>6</td>
<td>Bulgaria, Croatia, Cyprus, Greece, Italy, Slovenia</td>
</tr>
<tr>
<td>Hospitalisations</td>
<td>7</td>
<td>Hungary, Cyprus, Greece, Italy, Poland, Slovakia, Slovenia</td>
</tr>
<tr>
<td>Complications</td>
<td>4</td>
<td>Greece, Hungary, Slovakia, Slovenia</td>
</tr>
<tr>
<td>Lab confirmed cases</td>
<td>3</td>
<td>Finland, Hungary, Slovenia</td>
</tr>
</tbody>
</table>

Cyprus and Finland started a surveillance system in 2004, and therefore data is available for 2004-07. For Greece, total number of varicella cases was provided from the national mandatory surveillance system for the years 2000-03.
Table 5. Information provided by seven countries that are able to report data on hospitalizations and complications, 2010.

<table>
<thead>
<tr>
<th>Type of surveillance system</th>
<th>Country</th>
<th>Hospitalisations</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mandatory, national case-based data</td>
<td>Slovenia</td>
<td>According to Act of Communicable Diseases (Official Gazette 69/95) and amendments to law with revised list of notifiable ID), proposal of new Law in Aug 2007, and Bylaws (Communicable Disease Reporting Act, Official Gazette 16/99); notification of varicella is obligatory within three days after diagnosis. Doctors and laboratories notify it to regional Institutes of Public Health (IPH). From regional IPH electronic notifications sent to national IPH. Notification form includes basic data on hospitalization (whether patient was hospitalized, whether he has died or not). There is another data base, which is for the time is not connected with our data base with more data on hospitalizations, but we can get data from it as well.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cyprus</td>
<td>Hospitalisation data gathered because n/a Varicella is included in the list of Mandatory Notifiable diseases. It is reported to the Surveillance Unit by the MD who makes the diagnosis. Reporting is done through a reporting form in which data such as age and sex of the patient, vaccination status, if imported case, hospitalisation, treatment outcome etc.</td>
<td></td>
</tr>
<tr>
<td>Mandatory, national aggregate data</td>
<td>Hungary</td>
<td>According to the Decree No 63/1997(XII. 21.) of the Minister of Welfare on the Regulation of Notification of Communicable Diseases notification of varicella is mandatory within 24 hours after diagnosis. GPs, hospital doctors notify it to the local PH institutes, where is the data entry to the web-based national reporting system. After that in the regional PH institutes and in the National Center for Epidemiology the data are immediately available. The paper based notification form includes the date of hospitalization. In case complication or death, the doctors have to send &quot;deregistration form&quot; with the basic information. The information flows in the same ways.</td>
<td></td>
</tr>
<tr>
<td>Mandatory, national aggregate data</td>
<td>Poland</td>
<td>Receive aggregate data on how many people had the disease, their sex and age, place of residence (city, country) and seasonal distribution of disease and how many were hospitalized. Have a separate hospital registry database from which we could potentially withdraw data on hospitalized cases.</td>
<td>n/a</td>
</tr>
<tr>
<td>Sentinel, case based data</td>
<td>Netherlands</td>
<td>The number of hospitalizations due to varicella is collected by the National Medical Register of Prismant (registration of discharge diagnosis, ICD-9 code, national surveillance) in addition to the GP sentinel system</td>
<td></td>
</tr>
<tr>
<td>Sentinel, aggregate data</td>
<td>France</td>
<td>n/a</td>
<td>Sentinel GP system (aggregate data)</td>
</tr>
<tr>
<td>Sentinel aggregated as well as Sentinel case based data since 2006</td>
<td>Germany</td>
<td>Aggregated number of varicella cases with complications and case based description of the majority of these cases, including underlying disease, symptoms, outcome and including information on hospitalisation.</td>
<td></td>
</tr>
<tr>
<td>Mandatory, national aggregate data</td>
<td>Germany</td>
<td>Aggregated registry on hospitalizations by ICD-10 code (Hospital statistics)</td>
<td></td>
</tr>
</tbody>
</table>
**Case definitions**

Varicella is not included in the list of EU list of diseases for Surveillance (Commission Decision of 28/IV/2008). Therefore currently each country is not bound to a standard case definition.

**Type of cases reported**

Countries vary with respect to the classification of cases reported at national level (clinical, laboratory confirmed and epidemiologically linked), and to the description of the definition associated to each category. Table 6 gives an overview of the type of cases reported at national level, for the countries with a surveillance system for varicella.

Thirteen countries stated that they have case definitions of varicella for reporting purposes. Seven countries provided the definition of a clinical case, which included different ways of describing the rash, and other clinical signs such as acute onset and fever. A full description of the clinical picture can be found in table 7. Five countries provided the definition of laboratory confirmed case; this included confirmation via DNA detection, virus isolation, IgG serum or antibody and antigen detection.

Two countries have additional differences in the case definitions for reporting. In Norway, only laboratory cases of varicella encephalitis are reported, and in Greece since 2004 only cases with complications are reported to the mandatory surveillance system.

*Table 6. Summary of type of cases reported at national level in the countries with varicella surveillance (n=26), November 2010.*

<table>
<thead>
<tr>
<th>Clinical &amp; laboratory</th>
<th>Laboratory</th>
<th>Clinical &amp; laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>Finland</td>
<td>Belgium</td>
</tr>
<tr>
<td>Croatia</td>
<td></td>
<td>England and Wales*</td>
</tr>
<tr>
<td>Czech republic</td>
<td></td>
<td>Cyprus</td>
</tr>
<tr>
<td>Northern Ireland</td>
<td></td>
<td>Poland</td>
</tr>
<tr>
<td>Estonia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>France</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td></td>
<td></td>
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<tr>
<td>Greece</td>
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<tr>
<td>Hungary</td>
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<tr>
<td>Ireland</td>
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<td>Italy</td>
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<td>Latvia</td>
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<td>Lithuania</td>
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<tr>
<td>Netherlands</td>
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<td>Malta</td>
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<td>Portugal</td>
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<td>Romania</td>
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<td>Slovakia</td>
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<tr>
<td>Slovenia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spain</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*England and Wales, from Oct 2010 all lab confirmed VZV are notifiable

**Proposed standard case definition for varicella and herpes zoster**

Bases on the information collected through the survey, EUVAC.NET, in collaboration with disease experts, has proposed standard EU case definitions for varicella and herpes zoster which include a three tier case classification (possible, probable and confirmed case), and a suggestion to report probable and confirmed cases at EU level (page 16 and 17)
Table 7. Clinical case definition used by EUVAC.NET countries (Belgium, Bulgaria, Croatia, Estonia, Germany, Portugal, Spain), 2000-07.

<table>
<thead>
<tr>
<th>Clinical description</th>
<th>No. countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash/exanthema</td>
<td>7</td>
</tr>
<tr>
<td>Maculopapular/papular</td>
<td>6</td>
</tr>
<tr>
<td>Vesicular</td>
<td>6</td>
</tr>
<tr>
<td>Progressive stages</td>
<td>4</td>
</tr>
<tr>
<td>Diffuse</td>
<td>3</td>
</tr>
<tr>
<td>Concomitant stages</td>
<td>2</td>
</tr>
<tr>
<td>Pruritic</td>
<td>1</td>
</tr>
<tr>
<td>Generalised</td>
<td>1</td>
</tr>
<tr>
<td>Itchy</td>
<td>1</td>
</tr>
<tr>
<td>Single rash elements detected on mucous membranes</td>
<td>1</td>
</tr>
<tr>
<td>Cannot be explained by other symptoms</td>
<td>1</td>
</tr>
<tr>
<td>Acute onset of symptoms</td>
<td>4</td>
</tr>
<tr>
<td>Fever</td>
<td>3</td>
</tr>
<tr>
<td>Crust/scabs</td>
<td>2</td>
</tr>
<tr>
<td>Pustules/blisters</td>
<td>1</td>
</tr>
<tr>
<td>Malaise</td>
<td>1</td>
</tr>
<tr>
<td>Mild constitutional symptoms</td>
<td>1</td>
</tr>
</tbody>
</table>
EUVAC.NET proposal for case definition and classification for the surveillance of varicella/herpes zoster at EU level

Varicella

Clinical Criteria
Any person with ► an acute onset of generalised maculo-papulovesicular rash.

Laboratory Criteria
At least one of the following three:
- Isolation of varicella virus from a clinical specimen
- Detection of varicella virus ► nucleic acid in a clinical specimen
- Detection of specific varicella virus IgM antibody by ► specific IgM antibody response

Laboratory results need to be interpreted according to the vaccination status

Epidemiological criteria
An ► epidemiological link by ► human to human transmission

Additional information
Incubation period 2-3 weeks, commonly 14-16 days

Case Classification
A. Possible case
NA
B. Probable case
Any person ► meeting the clinical criteria
C. Confirmed case
Any person not vaccinated and ► meeting the clinical and the laboratory criteria or ► with an epidemiological linked to a confirmed or probable case of varicella or herpes zoster

In case of recent vaccination:
Any person with identification of wild-type varicella zoster virus

To be reported at EU level
Probable and confirmed cases should be reported at EU level

For countries with laboratory based reporting where no clinical information is available, laboratory confirmed cases should be reported

Note: In vaccinated persons who develop varicella more than 42 days after vaccination (breakthrough disease), the disease is almost always mild and of shorter duration. The rash may also be atypical in appearance (maculo-papular with few or no vesicles).
Herpes zoster

Clinical Criteria
Any person with at least one of the following two:
► an acute onset of localised maculo-papulovesicular unilateral rash, involving at least one dermatome.
► an acute onset of disseminated maculo-papulovesicular rash, beyond the involvement of one dermatome.

Laboratory Criteria
Detection of specific varicella virus antibody by ►specific antibody response

AND

At least one of the following three:
- Isolation of varicella virus from a clinical specimen
- Detection of varicella virus ►nucleic acid in a clinical specimen
- Detection of varicella virus antigen by ELISA or immunofluoresce test

Laboratory results need to be interpreted according to the vaccination status

Epidemiological criteria
none

Additional information
none

Case Classification
A. Possible case
NA
B. Probable case
Any person ►meeting the clinical criteria
C. Confirmed case
Any person not vaccinated and ►meeting the clinical and the laboratory criteria.

In case of recent vaccination:
Any person with identification of wild-type varicella zoster virus

To be reported at EU level
Probable and confirmed cases should be reported at EU level

For countries with laboratory-based reporting where no clinical information is available, laboratory-confirmed cases should be reported

Acknowledgements: EUVAC.NET hub, Dr Pierre van Damme (University of Antwerp, Belgium). Prof Birthe Høgh (Hvidovre Hospital, Copenhagen, Denmark) and Lars Peter Nielsen (Statens Serum Institut, Denmark)
Discussion

There is a large heterogeneity in varicella surveillance systems in European countries in relation to the type of surveillance system (national mandatory or sentinel), the type of data collected (case-based or aggregate) and the case classification (clinical, laboratory and/or epidemiologically linked) reported. Six of 32 countries have no surveillance for varicella. The great majority of systems operate using reports of clinical cases. When comparing countries that are reporting similar cases (e.g. clinical) problems may still be encountered as the case definitions used vary widely and a standardised European case definition is not currently available.

To date there are two main concerns about infant varicella vaccination: that it could lead to an increase in adult disease, and/or it could lead to a temporary increase in the incidence of herpes zoster (7). These patterns have already been experienced by countries where vaccine was introduced. After a decade of experience with the vaccine in the USA, the peak of incidence of disease shifted to older age-groups (from 3-6 years to 9-10 years of age) (8); this supported the introduction of a second dose which is now recommended for all varicella vaccines. In Australia an ecologic study conducted five years after the introduction of varicella vaccine in the national immunisation schedule has suggested preliminary evidence for an increase in the incidence of herpes zoster in adults aged ≥ 20 years (9). Another American study has also suggested an increase of 63% in incidence of herpes zoster in the 10-19 year age group. The authors state that such a finding must be confirmed with the use of other data sources (10). In general, the findings must be weighted against the overall decreasing number of varicella cases and deaths which are attributable to the disease in the post-vaccination area (11), and an observed 55% decrease in the incidence of herpes zoster in children aged less than 10 years (10).

It is therefore important that countries have baseline data for varicella and herpes zoster before the introduction of varicella vaccine in the immunisation programme and that the epidemiology of varicella can be compared between countries; an added value would then be also to share the lessons learned.

A case-based mandatory surveillance system is ideal to collect base-line data as it is in place in European countries for most vaccine preventable diseases. Nevertheless, sentinel systems can provide sufficient information for making public health decisions and for detecting long-term trends. Being generally less costly than universal surveillance systems, sentinel surveillance is particularly useful for diseases that occur frequently such as varicella. If a sentinel systems cover all ages groups it can contribute to monitor changes in the age distribution of varicella cases, and assess changes in incidence of herpes zoster. Hospitalisation and complication data are important to assess the severity of varicella cases; and sentinel hospital-based systems could be useful in assessing disease burden and complications due to varicella infection.

Some countries reported that they are considering changes to their varicella surveillance systems, and more would be expected to follow in the future. Concerted efforts to identify high quality and feasible surveillance methodologies could therefore be a timely and valuable tool to strengthen surveillance of varicella and herpes zoster in Europe.
Conclusions

There is a large heterogeneity in varicella and Herpes Zoster surveillance among European countries, with 26 of 32 countries performing surveillance for varicella, and 14 of 32 surveillance for herpes zoster. From the limited data that is available and comparable at European level, varicella had a high and relatively stable incidence in recent years (2000-07).

Only few European countries could at this stage report an extensive set of variables, and only nine countries were able to report on number of cases in specified age groups (data 2000-07). Data reporting on herpes zoster has not been undertaken by EUVAC.NET and therefore it is not possible to draw further conclusions related hereto.

Recommendations

The survey highlights that:

- There is need to better understand the epidemiology of varicella and herpes zoster in Europe
- There is need for data that reflects varicella incidence and that is comparable between countries
- There is need to identify standardized surveillance methodologies to improve data comparability in the European Member States

Based on the data and information currently available, we recommend that:

- An EU case definition and classification of varicella should be adopted
- An EU case definition and classification of herpes zoster should be adopted
- Countries should use the EU case definitions of varicella and zoster for reporting at EU level once they are approved
- If varicella is considered to be introduced in a childhood vaccination programme, a disease surveillance strategy should also be integrated to validate the impact of vaccination introduction on the burden of disease
- Surveillance of herpes zoster at European level should be investigated further to identify strengths and weaknesses of existing surveillance systems
- Concerted efforts to identify high quality and feasible surveillance methodologies could be a timely and valuable tool to strengthen surveillance of varicella and herpes zoster in Europe.
References


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Annex 2. Questionnaire used for the survey on surveillance system

Chickenpox (Varicella) Surveillance Systems Questionnaire

This one-page questionnaire is intended to identify which surveillance systems for chickenpox (varicella) (with one specific question at the end for shingles (herpes zoster)), and what types of reporting are in operation in the different European countries. Kindly cross the appropriate answer with an “x”. More than one answer may apply.

1. What level of surveillance system operates for chickenpox (varicella) in your country?
   - Nationwide surveillance [ ]
   - Regional surveillance [ ]
   - None [ ]
   - Other [ ]
   If other, please state:
   ……………………………………………………………………………..

2. What type of data for chickenpox (varicella) are available:
   (i) at national level?   (ii) at regional level?
   - Case-based [ ]
   - Aggregated [ ]
   - No data [ ]

If nationwide surveillance exists for chickenpox (varicella) and data are available at national level:

3. What is the legal basis of reporting?
   - Mandatory* reporting [ ]
   - Voluntary reporting [ ]

4. What type of surveillance system exists?
   - Comprehensive (total population) [ ]
   - Sentinel surveillance (sample points) [ ]

5. What is the source of reporting?
   - Clinician or health care worker [ ]
   - Laboratory [ ]

6. What type of cases are reported?
   - Clinical cases [ ]
   - Laboratory confirmed cases [ ]
   - Epidemiologically-linked cases to a lab-confirmed case [ ]

7. Is there a case definition of chickenpox (varicella) for reporting purposes?
   - Yes [ ]
   - No [ ]
If yes, please state:  
…………………………………………………………………………………………………………………………

8. Are there any plans for changes of the surveillance system for *chickenpox* (varicella) in the future?  
Yes []    No []

9. Are there any plans to introduce *chickenpox* (varicella) vaccination in the national childhood vaccination programme the future?  
Yes []    No []    Already in place []

If yes, further details (e.g. age-groups & date of implementation)……………………………………
……………………………………………………………………………………………………………………………

10. Are there any plans to introduce surveillance for *shingles* (herpes zoster) in the future?  
Yes []    No []    Already in place []

**Additional comments:**  
____________________________________________________________________________________

____________________________________________________________________________________