

# Measles in Europe: an epidemiological assessment

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## Summary

**Background** Measles persists in Europe despite the incorporation of the measles vaccine into routine childhood vaccination programmes more than 20 years ago. Our aim was therefore to review the epidemiology of measles in relation to the goal of elimination by 2010.

**Methods** National surveillance institutions from 32 European countries submitted data for 2006–07. Data for age-group, diagnosis confirmation, vaccination, hospital treatment, the presence of acute encephalitis as a complication of disease, and death were obtained. 30 countries also supplied data about importation of disease. Clinical, laboratory-confirmed, and epidemiologically linked cases that met the requirements for national surveillance were analysed. Cases were separated by age: younger than 1 year, 1–4 years, 5–9 years, 10–14 years, 15–19 years, and older than 20 years. Countries with indigenous measles incidence per 100,000 inhabitants per year of 0, less than 0·1, 0·1–1, and more than 1 were grouped into categories of zero, low, moderate, and high incidence, respectively.

**Findings** For the 2 years of the study, 12,132 cases of measles were recorded with most cases (n=10,329; 85%) from five countries: Romania, Germany, UK, Switzerland, and Italy. Most cases were unvaccinated or incompletely vaccinated children; however, almost a fifth were aged 20 years or older. For the same 2 years, seven measles-related deaths were recorded. High measles incidence in some European countries revealed suboptimum vaccination coverage. Of the 210 cases that were reported as being imported, 117 (56%) came from another country within Europe and 43 (20%) from Asia.

**Interpretation** The suboptimum vaccination coverage raises serious doubts that the goal of elimination by 2010 can be attained. Achievement and maintenance of optimum vaccination coverage and improved surveillance are the cornerstones of the measles elimination plan for Europe.

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## Introduction

Although the measles vaccine has been part of routine national childhood vaccination programmes throughout Europe for at least 20 years, measles remains a public health concern. Between 2006 and 2007, several countries reported high numbers of cases and outbreaks. The largest outbreaks took place in Switzerland,<sup>1</sup> Germany,<sup>2</sup> Spain,<sup>3</sup> and Romania,<sup>4</sup> and mostly affected the general population. Other outbreaks have been described in particular groups such as the Roma and Sinti communities in Italy,<sup>5</sup> Roma and immigrant families in Greece,<sup>6</sup> orthodox Jewish communities in Belgium<sup>7</sup> and the UK,<sup>8</sup> and traveller communities in the UK<sup>9</sup> and Norway.<sup>10</sup> Increased measles transmission continued to be recorded in 2008, particularly in Italy,<sup>11</sup> Switzerland,<sup>12</sup> Austria,<sup>13</sup> and the UK.<sup>14</sup> Such a situation in Europe underscores the need for concerted efforts to reach WHO's goal laid out in the strategic plan to eliminate measles from the European region by 2010.<sup>15</sup> Our aims were to review the epidemiology of measles in Europe, discuss the feasibility of elimination by 2010, and address methods to reach this goal.

## Methods

### Participants

Measles surveillance data were submitted to the European surveillance network for vaccine-preventable diseases (EUVAC.NET) hub from the national public health or

surveillance institutions of each of the network's participating countries: the 27 EU member states together with Croatia, Iceland, Norway, Switzerland, and Turkey. Cases meeting the requirements for national surveillance, including clinical, laboratory-confirmed, and epidemiologically linked cases, were analysed. During the study period, no changes in the national systems for measles surveillance or the methods for reporting data were identified for the participating countries, except Italy. For 2007, measles data from Italy were derived from a newly established special surveillance system intended to improve timeliness and completion of reporting.<sup>16</sup>

We did not regard ethical approval or informed consent to be necessary since the data are anonymous and are collated under a decision of the European Parliament and the Council of the EU for the epidemiological surveillance and control of communicable diseases in the European Community.<sup>17,18</sup>

### Procedures

All 32 participating countries submitted data for the study period 2006–07. Case-based data were provided by 30 countries, 29 of which obtained the data through national mandatory notification systems. Belgium provided case-based data gathered through both a national voluntary notification system and a mandatory system applied to schools. Case-based reports provided data for disease onset

dates, age, diagnosis confirmation, vaccination, importation, hospitalisation, the presence of acute encephalitis as a complication of measles, and death. Variables for which no data were available in the case-based reports were converted to unknown status. Aggregated data were provided by Romania and Turkey, and consisted of the number of cases in specified age-groups categorised by vaccination, diagnosis confirmation, and hospitalisation variables. The number of cases with complications including death was also supplied.

We defined indigenous cases as those that were not recorded as imported from another country. Those with unknown importation status were also regarded as indigenous cases. Data for imported cases indicated the most probable country to have been the source of infection. For countries supplying aggregated data, the importation status was not reported and therefore all cases were regarded as indigenous. Countries were grouped into categories of zero, low, moderate, and high incidence for the corresponding indigenous measles incidence per 100,000 inhabitants per year of 0, less than 0.1, 0.1–1, and more than 1, respectively.

### Statistical analysis

Cases with disease onset dates in 2006–07 were analysed. Case-based reports with absent or unknown disease onset dates were included in the analyses because the date of notification or the date of collection of the laboratory sample was during the corresponding years. Incidence was calculated with the number of cases of reported measles as the numerator and the country population obtained from Eurostat<sup>19</sup> as the denominator. We expressed incidence of disease as measles cases per 100,000 inhabitants per year, and that of death as the total per 1000 measles cases per year. We included all reported cases (i.e., including indigenous cases, imported cases, and those with unknown importation status) when calculating crude incidences. To test for potential differences in the overall crude and age-specific incidence in 2006 compared with 2007, we used Poisson regression with the PROC GENMOD procedure in SAS software (version 9.1).

### Role of the funding source

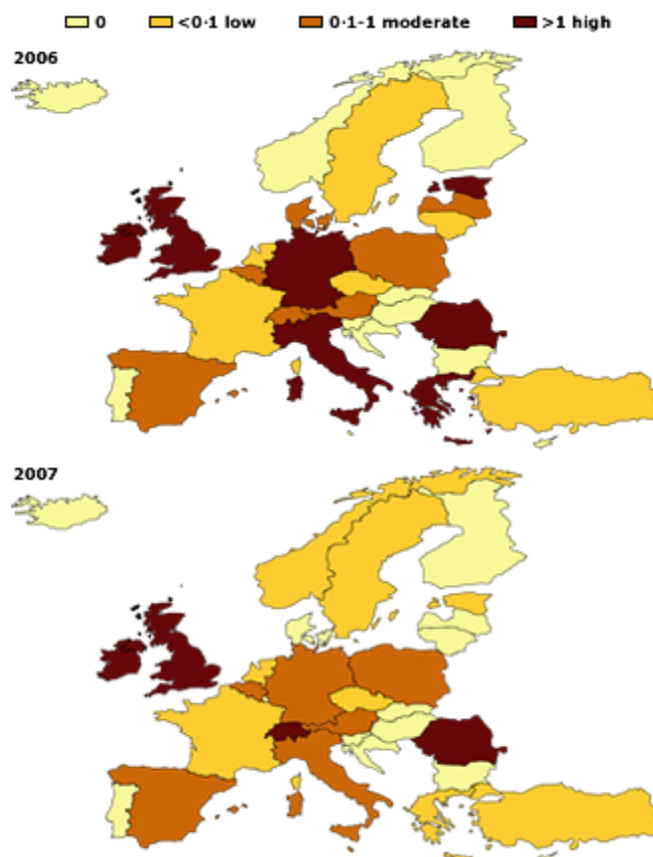
The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

### Results

During 2006 and 2007, a total of 12,132 measles cases was reported and included 3061 (36%) case-based reports with absent or unknown disease onset dates for both years. Most cases (n=10,329; 85%) were from five countries: Romania, Germany, the UK, Switzerland, and Italy (table 1). The largest numbers of cases in 2006 were reported from Romania (39% of the total) and Germany (28%), and the highest crude incidences were in Romania and Greece. In 2007, the overall crude incidence of measles fell significantly (p<0.0001) compared with the previous year. Switzerland and the UK reported the largest numbers of cases—each contributing 27% and 26%, respectively, of the

total—and the highest crude incidences. In both 2006 and 2007 the incidence of indigenous measles cases varied substantially among countries (figure 1). Nine countries reported no indigenous measles cases for both years: Bulgaria, Croatia, Cyprus, Finland, Hungary, Iceland, Portugal, Slovakia, and Slovenia.

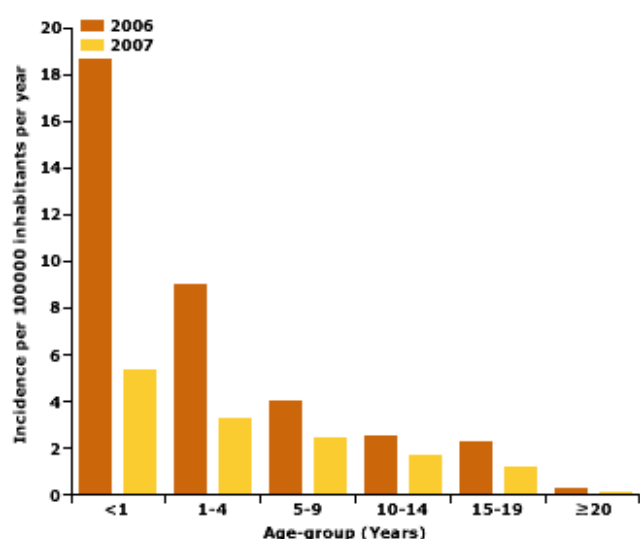
Figure 1: Geographical incidence of indigenous measles in Europe for 2006 and 2007



Data show incidence per 100 000 inhabitants per year. For Romania and Turkey the crude incidence was used because the aggregated dataset did not supply importation status and therefore all cases were regarded as indigenous.

The age-group was known for 99% (n=8121) and 98% (3845) of cases in 2006 and 2007, respectively. Overall, the age distribution of measles in 2007, compared with 2006, changed significantly (p<0.0001), mainly because of a substantial decrease of infected children under age 5 years and only a small decrease of those 20 years or older (figure 2). Infants (younger than 1 year) had the highest age-specific incidence per 100,000 inhabitants for 2006 (18.6 [95% CI 17.5–19.6]) and 2007 (5.3 [4.8–5.9]). For both years, 15% (n=1223) and 9% (357) of the total number of cases were infants, 29% (2352) and 23% (868) were 1–4 years of age, 38% (3110) and 49% (1896) were 5–19 years of age, and 18% (1436) and 19% (724) were 20 years or older. In 2006, Romania had an incidence per 100,000 inhabitants of 341.4 (95% CI 317.7–366.8) in infants and 142.3 (134.5–150.6) in children aged 1–4 years, corresponding to 61% (n=745) and 51% (1194) of the total cases in the respective age-groups.

Figure 2: Incidence of reported measles cases by age-group (2006-07)



In 2007, Switzerland had the highest incidence per 100,000 inhabitants of 78.8 (95% CI 70.4–88.1) in children aged 5–9 years, followed by 58.2 (51.4–65.9) in those aged 10–14 years. In the same year in the UK, infants had the highest incidence per 100,000 inhabitants of 14.3 (11.8–17.3), followed by 11.1 (9.9–12.4) in children aged 1–4 years.

The status of measles vaccination was known in 89% (n=7333) and 92% (3582) of all reported measles cases in 2006 and 2007, respectively (table 2). In 2006, 2820 (91%) cases aged 5–19 years had known vaccination status, of whom 2058 (73%) were unvaccinated, 452 (16%) had received a single dose of vaccine, and 39 (1%) had been vaccinated with an unspecified number of doses. The following year, 1796 (95%) cases from the same age-group had known vaccination status, of whom 1567 (87%) were unvaccinated, 156 (9%) had received a single dose, and two (0.1%) had been vaccinated with an unspecified number of doses. For both years, the remaining cases had received two or more doses.

Table 1: Incidence of measles in 32 participating European countries (2006-07)

	Number of cases		Crude incidence		Laboratory-confirmed cases		Epidemiologically linked cases	
	2006	2007	2006	2007	2006	2007	2006	2007
Austria	25	20	0.3	0.2	15 (60%)	15 (75%)	0	0
Belgium	15	58	0.1	0.5	8 (53%)	14 (24%)	1 (7%)	36 (62%)
Bulgaria	1	1	0.01	0.01	1 (100%)	1 (100%)	0	0
Croatia	1	0	0.02	0	0	..	0	..
Cyprus	0	0	0	0	..	..	..	..
Czech Republic	6	2	0.1	0.02	6 (100%)	2 (100%)	0	0
Denmark	27	2	0.5	0.04	26 (96%)	2 (100%)	1 (4%)	0
Estonia	27	1	2	0.1	27 (100%)	1 (100%)	0	0
Finland	0	0	0	0	..	..	..	..
France	44	40	0.1	0.1	17 (39%)	24 (60%)	1 (2%)	0
Germany	716	571	0.9	0.7	835 (36%)	280 (49%)	640 (28%)	207 (36%)
Greece	519	2	4.7	0.02	214 (41%)	0 0	0	0
Hungary	1	0	0.01	0	1 (100%)	..	0	..
Iceland	0	0	0	0	..	..	..	..
Ireland	83	52	2	1.2	23 (28%)	14 (27%)	0	6 (12%)
Italy	595	420	1	0.7	0	154 (37%)	0	0
Latvia	7	0	0.3	0	6 (86%)	..	0	..
Lithuania	1	0	0.03	0	0	..	0	..
Luxembourg	7	0	1.5	0	0	..	0	..
Malta	0	2	0	0.5	..	0 0	..	0
Netherlands	1	10	0.01	0.1	1 (100%)	10 (100%)	0	0
Norway	0	20	0	0.4	..	17 (85%)	..	3 (15%)
Poland	120	43	0.3	0.1	88 (73%)	29 (67%)	3 (3%)	1 (2%)
Portugal	0	0	0	0	..	..	..	..
Romania	3196	352	14.8	1.6	2830 (89%)	344 (98%)	169 (5%)	0
Slovakia	0	0	0	0	..	..	..	..
Slovenia	0	0	0	0	..	..	..	..
Spain	343	265	0.8	0.6	296 (86%)	235 (89%)	34 (10%)	20 (8%)
Sweden	19	1	0.2	0.01	18 (95%)	0 0	0	0
Switzerland	71	1040	1	13.9	41 (58%)	421 (40%)	6 (8%)	125 (12%)
Turkey	34	3	0.05	0.004	34 (100%)	3 (100%)	0 0	0
UK	773	1004	1.3	1.6	769 (99%)	972 (97%)	4 (1%)	32 (3%)
<b>Total</b>	<b>6632</b>	<b>3909</b>	<b>1.14*</b>	<b>0.67†</b>	5256 (64%)	2538 (65%)	859 (10%)	430 (11%)

Data show number of measles cases, incidence per 100 000 inhabitants, and % of total cases. For some countries, minor discrepancies might arise with nationally reported data if these include cases by year of notification rather than year of disease onset. \*95% CI 1.38–1.44. † 95% CI 0.65–0.69.

Six measles-related deaths were reported in 2006, which corresponded to a death rate per 1000 measles cases of 0.7 (0.3–1.6). Pneumonia was the cause of death in three patients from Romania and one from the UK. The fatal cases from Romania were a 9-month-old male infant below the recommended age for measles vaccination, a 20-month-old girl who had received one dose of vaccine, and a 23-month-old unvaccinated girl. The fatal case reported from the UK was an unvaccinated 13-year-old boy who had an underlying lung condition and was receiving immunosuppressive drugs.<sup>20</sup> Acute encephalitis was the cause of death in an infant and a 2-year-old child, both reported from Germany. One patient acquiring measles in 2007 died (0.26 per 1000 measles cases [0.04–1.82]) due to pneumonia. The death was reported from Italy and occurred in a 10-year-old girl with a congenital immunodeficiency disorder.<sup>11</sup> All fatal cases were laboratory confirmed. In 2006, acute encephalitis caused two deaths and was reported in a further eight cases: five from Germany, one from Greece, one from Switzerland, and one from the UK. The non-fatal cases were distributed between age-groups with one younger than 1 year, two aged 1–9 years, two aged 15–19 years, and three older than 20 years. Six cases were not vaccinated against measles, one was vaccinated with a single dose, and vaccination status was unknown in the remaining case. In 2007, seven cases of acute encephalitis were reported: five from Switzerland, one from Germany, and one from the UK. They were distributed between age-groups with two aged 5–9 years, one aged 10–14 years, two aged 15–19 years, and two older than 20 years. None had been vaccinated against measles.

Information about admission to hospital was available in 92% (n=7601) of measles cases in 2006; 55% (4202) of these cases were admitted, of which 66% (2777) were from Romania. Of the 95% (3732) of cases with known hospitalisation status in 2007, 805 (22%) were admitted.

Known importation status was reported in 70% (3508) and 54% (1912) of cases from countries supplying case-based data in 2006 and 2007, respectively. 126 and 84 of these cases were imported for the 2 years, corresponding to 4% of cases with known importation status for each year. In 2006, 64 (51%) cases were imported from another European country and 62 (49%) from outside Europe: 30 from Asia, 14 from the Middle East, 16 from Africa, one from South America, and one from Australia. In 2007, 53 (63%) cases were imported from another European country and 31 (37%) from

outside Europe: 13 from Asia, seven from the Middle East, seven from Africa, three from North America, and one from Australia. The panel shows the top ten countries implicated as sources of imported measles cases.

## Discussion

Our findings show widely varied incidence of measles in the 32 European countries. Although some countries reported rates per 100,000 inhabitants of less than 0.1, suggesting near-elimination of measles, others reported unacceptably high rates in an era of expected elimination of the disease from Europe.

Since most measles cases were unvaccinated or incompletely vaccinated, the differences in incidence between countries could reasonably be attributed to varying degrees of success with national vaccination programmes. Vaccination coverage and seroprevalence rates also indicate the performance of vaccination programmes. Achievement and maintenance of the WHO-recommended minimum of 95% vaccination coverage with two doses is necessary for measles elimination.<sup>15</sup>

Suboptimum measles vaccination coverage over a long period has indeed been reported by countries with high measles incidence. Switzerland reported vaccination coverage of about 82% between 1991 and the beginning of this decade, with substantial variations among its 26 cantons.<sup>12</sup> In the UK, measles vaccination coverage for children at 2 years of age was less than 90% (1999–2006), and was below 85% (2002–05),<sup>21</sup> whereas in Ireland, coverage increased from less than 80% (1999–2003) to below 90% (2004–06).<sup>22</sup> For the same age-group in Germany, vaccination coverage for children born between 1996 and 2003 was consistently about 70%, with substantial regional differences.<sup>23</sup> In Italy, national vaccination coverage in children at 2 years of age increased from below 85% (2001–03) to below 90% (2004–06), with large variations among regions.<sup>24</sup> The high incidence of disease in Greece in 2006 was caused by a large outbreak originating in 2005, which mostly affected Roma and immigrant families.<sup>6</sup> Estimates of vaccination coverage for 2003–05 were very low in Roma children (2–12%) and low in immigrant children (80–90%). In Romania, a seroprevalence study on samples from 2002 showed high susceptibility of children aged 2–4 years of about 24%.<sup>25</sup>

Table 2: Measles cases with known vaccination status (2006-07)

	<1 years	1–4 years	5–9 years	10–14 years	15–19 years	≥20 years	Unknown age	Total
<b>2006</b>								
Unvaccinated	1092 (93%)	1469 (68%)	883 (71%)	650 (77%)	525 (72%)	968 (84%)	31 (97%)	5618 (77%)
Vaccinated with single dose	78 (7%)	606 (28%)	266 (21%)	97 (11%)	89 (12%)	137 (12%)	0	1273 (17%)
Vaccinated with at least two doses	0	51 (2%)	79 (6%)	91 (11%)	101 (14%)	30 (3%)	1 (3%)	353 (5%)
Vaccinated with unspecified number of doses	2 (0.2%)	31 (1%)	16 (1%)	11 (1%)	12 (2%)	17 (1%)	0	89 (1%)
<b>2007</b>								
Unvaccinated	343 (98%)	663 (81%)	683 (86%)	526 (90%)	358 (85%)	520 (86%)	11 (73%)	3104 (87%)
Vaccinated with single dose	7 (2%)	137 (17%)	75 (9%)	39 (7%)	42 (10%)	72 (12%)	4 (27%)	376 (10%)
Vaccinated with at least two doses	0	16 (2%)	34 (4%)	17 (3%)	20 (5%)	7 (1%)	0	94 (3%)
Vaccinated with unspecified number of doses	0	1 (0.1%)	1 (0.1%)	1 (0.2%)	0	5 (1%)	0	8 (0.2%)

By contrast, countries with zero indigenous measles incidence reported consistently high measles vaccination coverage for long periods. In Finland, studies that have been undertaken every 2 years on birth cohorts from 1995 to 2003 showed that vaccination coverage was consistently above 95%.<sup>26</sup> In Iceland, the coverage for two measles vaccine doses ranged between 90% and 99% (1999–2006); (Gudnason T, Iceland Directorate of Health, personal communication). Measles vaccination is obligatory in Slovenia, Slovakia, and Hungary. For children aged 2 years, coverage for first vaccination (1996–2006) ranged between 94% and 96% in Slovenia,<sup>27</sup> and was consistently above 99% in Slovakia<sup>28</sup> and Hungary.<sup>29</sup> A seroprevalence study also showed that Slovenia, Slovakia, and Hungary had low susceptibility levels.<sup>25</sup>

*Panel:* Top ten countries identified as a source of measles importation into Europe (2006–07)

**Number of cases (2006)**

Ukraine (17), Thailand (13), Italy (11), Pakistan (8), India (8), Romania (6), Spain (6), Germany (5), Morocco (4), Ethiopia (4)

**Number of cases (2007)**

Switzerland (13), UK (10), Germany (9), Spain (7), Italy (6), India (5), Pakistan (4), Thailand (4), China (3), Ethiopia (3)

Almost one in five patients were aged 20 years and older for both 2006 and 2007, and therefore measles cannot be regarded solely as a childhood disease. Nearly half the measles cases in 2007 were 5–19 years of age, of which more than 80% were unvaccinated, although the measles vaccine has been part of routine national childhood vaccination throughout Europe since the 1980s. Although we did not seek detailed vaccination coverage data, this finding is most probably a reflection of the suboptimum uptake of the vaccine particularly by these birth cohorts. Moreover, vaccination coverage levels might have varied enough throughout the years to result in susceptible populations of different ages, as exemplified by Switzerland and the UK. However, since the first dose of measles vaccine is generally offered after the first year of life, infants remain the most vulnerable group in the absence of herd immunity. Consequently, the very high incidence seen in Romanian infants in 2006 was a result of intense measles transmission in the country that year.

Although measles in Europe might be perceived as a mild disease,<sup>30</sup> it still causes deaths; seven deaths were reported during the 2 years of the study. The full extent of mortality is not completely apparent in the short term because the fatal complication subacute sclerosing panencephalitis, although rare, can develop years after acute measles infection.<sup>31</sup> Moreover, measles mortality could be underestimated since most surveillance systems do not systematically obtain outcome data, and measles might not be noted on death certificates. Indeed, death certification errors are well recognised.<sup>32,33</sup>

We acknowledge that although we reported acute encephalitis as a complication of measles, other complications such as pneumonia were recorded only in relation to deaths. Our data for hospitalisation should be interpreted with caution since no definition of hospitalisation was used. The term generally signifies inpatient admission to hospital, but could also be interpreted to include outpatient ambulatory care at a hospital. The high rate in 2006 compared with 2007 was mostly caused

by the large number of cases in Romania, where admission of measles cases is a legal requirement. Future surveillance should gather more comprehensive data to describe measles morbidity and mortality more accurately. The form of the data available meant that we could not use a denominator of susceptible persons only. However, use of country population as the denominator, means that the incidences are comparable with the outcome indicators used by WHO.<sup>34</sup> Comparisons between countries should be made with caution because of different reporting procedures—some countries reported only laboratory-confirmed and epidemiologically linked cases, whereas others reported clinical cases without laboratory confirmation. Absence of laboratory confirmation could cause overestimation of incidence especially in countries with few and sporadic cases, because low disease incidence results in a poor positive predictive value of clinical diagnosis of measles.<sup>35</sup> Conversely, passive routine surveillance systems are notorious for under-reporting and delayed reporting despite the statutory obligation to report measles in almost all the 32 participating countries, which poses further limitations on accuracy of comparisons. We might have overestimated the indigenous measles incidence since our data included cases with unknown importation status. Data for countries identified as sources of infection should also be interpreted cautiously because no universal definition for importation was used. Nevertheless, several strains of measles virus have been identified as imported with improved surveillance by better identification techniques.<sup>4</sup> Importation of measles has emphasised the presence of pools of susceptible individuals in the general population, as occurred in Denmark,<sup>36</sup> and in particular groups, as in Belgium.<sup>7</sup> Several countries such as Belgium, Denmark, and the UK, recommend pre-travel measles vaccination to unvaccinated travellers, without a history of the disease, who intend to visit measles-endemic countries and those where measles outbreaks occur.

Despite an overall reduction in measles cases in 2007 compared with 2006, the continued emergence of outbreaks and persistently high incidence in some European countries have indicated suboptimum vaccination coverage, which will threaten the success of the measles elimination plan for the region by 2010. Since imported cases are a potential source of outbreaks, countries should be aware of possible transmission within Europe and from other continents to ensure that appropriate control measures are implemented in a timely manner. Surveillance networks and formal channels of communication—e.g., WHO's International Health Regulations<sup>37</sup> and the EU Early Warning and Response System<sup>17,38</sup>—are important for exchange of relevant information, including a travel history.

For achievement of the measles elimination goal, awareness of the disease and commitment by decision makers and public health authorities in all European countries are essential to strengthen vaccination programmes. WHO's strategic plan for the European region between 2005 and 2010,<sup>15</sup> stipulates that vaccination programmes should achieve and sustain a minimum of 95% coverage with two doses of vaccine and better target susceptible individuals in the general population and high-risk groups. We need to identify barriers for measles vaccine uptake and explore methods to target vulnerable populations that have been hard to reach with standard programmes. Records of measles vaccination uptake are also important to monitor progress and allow early identification of

suboptimum vaccination coverage.

Strengthening of surveillance systems is also necessary for elimination, which requires suspected measles cases to be thoroughly and quickly investigated. Both epidemiological and laboratory investigations are essential for identification of transmission patterns to improve contact tracing and ensure that spread of disease is swiftly controlled. Improved surveillance, including measles virus genotyping, is also

important to ascertain trans-mission chains and to assess country-specific risk. Molecular characterisation for virus identification has been useful,<sup>39</sup> particularly for documentation of the interruption of endemic measles transmission.<sup>36,40</sup> Failure to implement these elimination strategies by all European countries raises concerns for the successful and continued interruption of measles virus transmission.

#### Contributors

MM had primary responsibility for coordinating EUVAC.NET's measles surveillance activities and analysed data, reviewed literature, and wrote the report. HB gathered and validated the data, and produced the graphics. JW did the statistical analysis and reviewed the report. SG and KM reviewed and commented on the final version of the report. The EUVAC.NET group processed and supplied national measles data, and commented on the final version of the report.

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#### Conflict of interest statement

We declare that we have no conflict of interest.

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