RAPID RISK ASSESSMENT

Ongoing outbreak of measles in Romania, risk of spread and epidemiological situation in EU/EEA countries

3 March 2017

Main conclusions and options for response

A measles outbreak in Romania has been ongoing since February 2016 and cases continue to be reported despite implemented and ongoing response measures at national level through reinforced vaccination activities. As of 17 February 2017, 3 071 cases had been reported to the National Institute of Public Health in Romania since the end of September 2016.

In 2016, measles outbreaks were seen in a number of EU/EEA countries; and an increase in the number of cases continues to be observed in 2017. Previous and ongoing measles outbreaks in three other EU countries have been epidemiologically linked to the current outbreak in Romania. However, additional knowledge on genotypic characterisation of the virus is needed to allow further insight into the epidemiological investigations.

The latest available vaccination coverage data from the World Health Organization (WHO) in 2015 show that vaccination coverage was above the 95% target in 17 EU/EEA countries for the first dose of measles-containing vaccines (MCV) (range: 85–99%). In eight countries, vaccination coverage for the second dose of MCV was at least 95% (range: 74–99%). Therefore, the vaccination coverage in many EU/EEA countries remains suboptimal.

Given the size of the current outbreak in Romania, the recent historical trends, and that vaccination coverage for the first and second dose of MCV in Romania is below 90%, there is a high risk of continued measles transmission within the country. This poses a risk of potential repeated exportation to other EU/EEA countries and possible continuous transmission in some where vaccination coverage is suboptimal. Response efforts are continuing in Romania and should help ensure that pockets of susceptible individuals are adequately vaccinated.

Immunisation is the only effective preventive measure against measles. All countries in the EU/EEA have measles vaccination policies in place with two doses of the measles, mumps and rubella (MMR) vaccine. Catch-up programmes exist in a number of countries for individuals having missed vaccination or being too old to have been targeted by routine programmes. Routine immunisation needs to be strengthened by facilitating access to vaccination, and mechanisms to identify people who are not or are incompletely vaccinated are needed. Additional opportunities for immunisation should be promoted and provided through a variety of supplemental immunisation activities (SIA) in countries with suboptimal vaccination coverage and/or pockets of susceptible populations.

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Vaccination coverage of ≥95% of the general population at national and subnational levels with two doses of MCV is recommended and necessary to ensure that measles circulation is interrupted, and that the introduction of measles cases does not result in secondary cases. This has not yet been achieved in all EU/EEA countries according to available vaccination coverage figures. The assessment of vaccination coverage and the availability of data at subnational level would allow geographical areas where targeted actions may be needed to be identified.

Strengthening and ensuring high quality surveillance, including monitoring the changing epidemiology of measles, helps guide public health actions. All suspected cases should be detected and investigated in order to break chains of transmission as soon as possible, and performing epidemiological investigations, including an assessment of the susceptibility of contacts to consider necessary control measures. Adequate laboratory investigation is essential because data on viral genotype are needed to track transmission chains.

Source and date of request

Official request from the European Commission on 24 February 2017.

Public health issue

Risk of spread of measles and sustained transmission in EU/EEA countries related to an ongoing outbreak in Romania and the epidemiological situation in the EU/EEA.

Consulted experts

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Experts from the World Health Organization (WHO) Regional Office for Europe contributed to this risk assessment. Although experts from WHO reviewed the risk assessment, the views expressed in this document do not necessarily represent the views of WHO.

All experts have submitted declarations of interest and a review of these declarations did not reveal any conflicts of interest.

Disease background information

Measles is an acute illness caused by *morbillivirus*. The disease is transmitted via airborne respiratory droplets, or by direct contact with nasal and throat secretions of infected individuals. Measles is highly infectious and it is estimated that 90% of non-immune people exposed to an infective individual will contract the disease.

The main symptoms are fever, rash, cough, runny nose and inflammation of the eye. The first symptoms appear on average 10 days after exposure, but with a range of 7–21 days from exposure to onset of fever. A rash usually appears four days after the start of the first symptoms, and patients are contagious from about 4 days before eruption of the rash until 4 days after eruption.

Complications can include pneumonia, encephalitis, otitis media, diarrhoea, laryngotracheo-bronchitis and secondary bacterial infections. Subacute sclerosing panencephalitis (SSPE), a severe but rare and slowly progressing degenerative disease of the central nervous system, characterised by behavioural and intellectual deterioration and seizures may develop six to eight years after primary infection.

Infants and immunocompromised individuals are at higher risk of complications, severe disease and death following measles infection.

Measles frequently results in widespread outbreaks, mainly among unvaccinated individuals. The disease is preventable by vaccination, which provides lifelong immunity in most recipients. Vaccine uptake of at least 95% with two doses of measles containing vaccine (MCV) is considered to be necessary to ensure the level of immunity required in the population to interrupt disease circulation and achieve elimination.

For a more complete background of the disease and its epidemiology in the EU, please refer to the ECDC health topic page on measles [1].

Event background information

Since February 2016, an increase in the number of measles cases has been reported by Romania (Table 1 and Figure 1).

The National Institute of Public Health in Romania has been updating its website with situation reports at regular intervals since 23 September 2016 [2].

As of 17 February 2017 [2], 3 071 cases had been reported to the National Institute of Public Health, with 2 341 since October 2016 (Figure 2). These cases are either laboratory-confirmed, or have an epidemiological link to a laboratory-confirmed case. Cases have been reported in 36 districts with the districts of Caras Severin (n=703), Arad (n=617) and Timis (n=566) having reported the highest number of cases (Figure 3).

To date, 16 deaths have been reported, all of which occurred in persons who were immunocompromised or had other co-morbidities.

Infants <1 year old (n=549) and children 1–4 years old (n=1 247) made up the majority of cases. Ninety-six percent of cases were unvaccinated (n=2 958), 80 cases had received one dose of MCV and 33 had received two doses.

The measles genotype identified was B3 which is not the usual strain circulating in Romania but was circulating in other EU/EEA countries in 2015. Genotype D4 was identified in previous outbreaks in Romania.

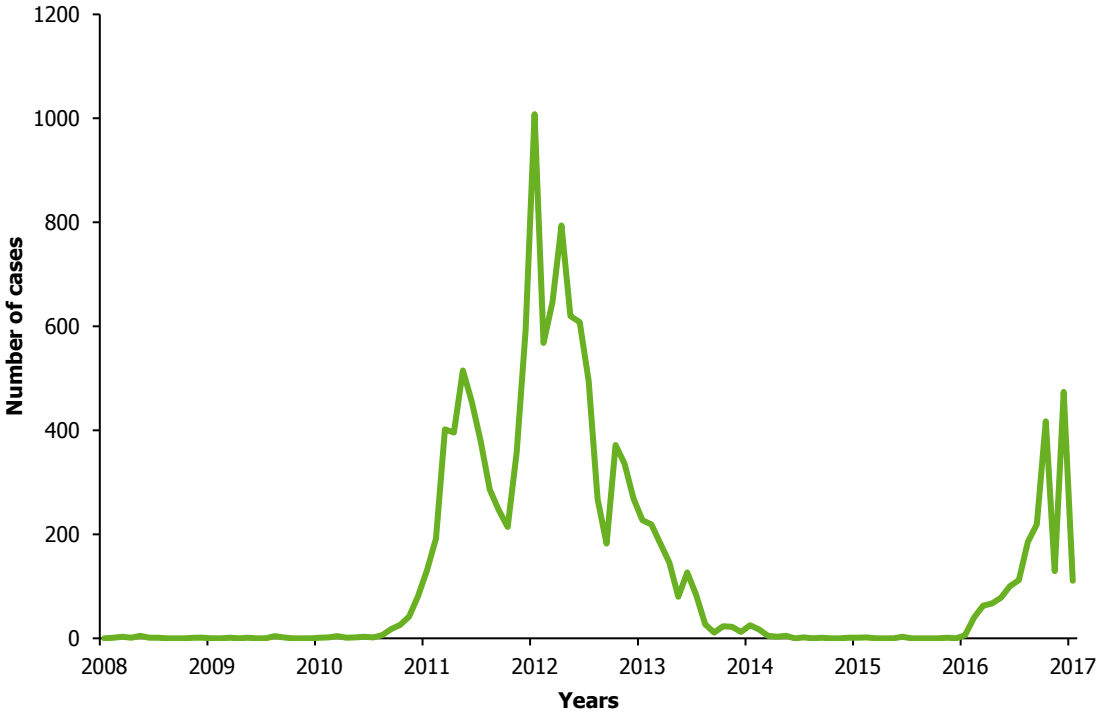
As part of the action plan to respond to the outbreak, an intensified vaccination campaign is ongoing and Romania has lowered the age of administering the first vaccine dose from 12 months to nine months. It was also recommended that all children up to nine years of age are vaccinated according to the National Immunisation Programme recommendation, and that all children under five years of age should receive one dose of MMR (measles–mumps–rubella) vaccine and children aged five to nine years receive two doses. The second dose of MMR is usually recommended to be administered at five years of age. In order to implement these measures, family doctors are registering eligible children between nine months and nine years of age who have not been vaccinated, and those aged five to nine years who have received a single dose of vaccine. It is reported that supplies of MMR vaccines are sufficient to respond to the outbreak [3]. A network of community nurses was involved to mobilise children mainly in vulnerable population groups. The campaign was sustained by providing posters, leaflets and booklets for family doctors and the general population in order to increase awareness. Since 31 January 2017 the coverage data shows that 36% of children received the first dose and 31.6 % of eligible children received the second dose.

Table 1. Number of measles cases by year, Romania, 2005–2016

Year	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Number of cases	5 647	3 196	352	14	8	188	4 165	6 166	1 159	59	7	1 890

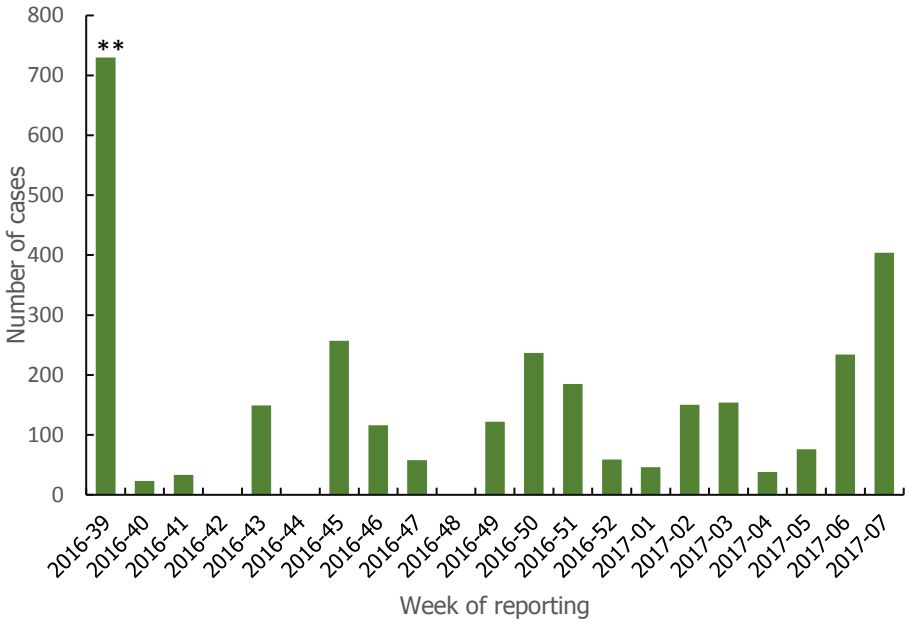
Source: The European Surveillance System - ECDC. The discrepancy in the number of measles cases reported to ECDC in 2016 and published by the National Institute of Public Health in Romania may be explained by the delay in case-based reporting to ECDC, compared to the aggregated data regularly published by the National Institute of Public Health.

Figure 1. Number of measles cases by month, Romania, 1 January 2008–31 January 2017



Source: The European Surveillance System - ECDC

Figure 2. Measles cases per week*, week 2016–39 to 2017–07, Romania

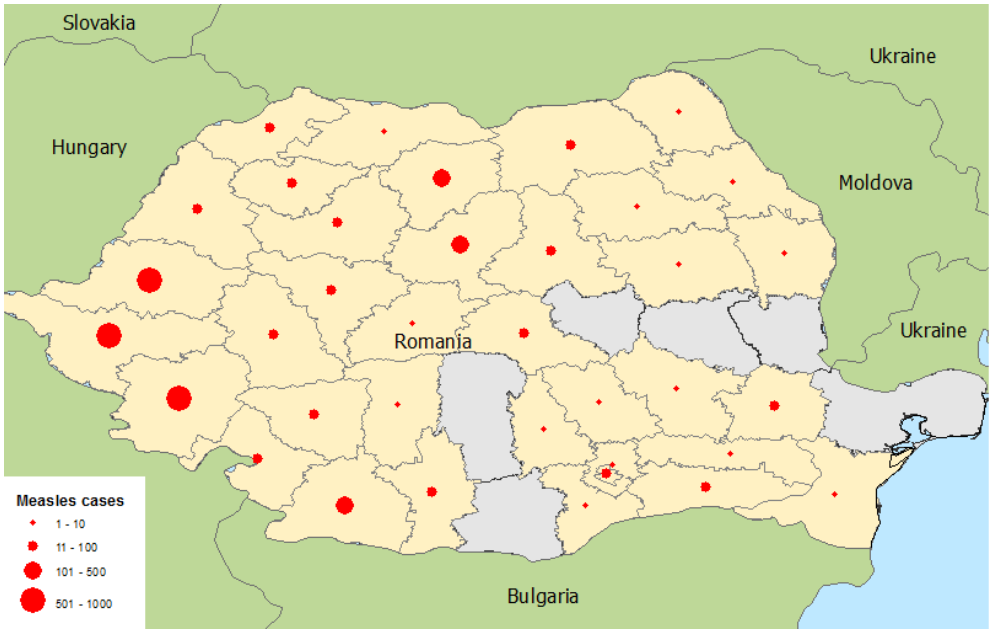


Source: National Institute of Public Health. Situatia rujeolei in Romania 2017 [update as of 17 February 2017]. Available from: http://www.cnscbt.ro/index.php/informari-saptamanale/rujeola-1.

**Cases per week are calculated by subtracting total number of cases published by the National Instite of Public Health from the total number of cases published with the previous update.*

*** Cumulative number of cases in 2016 until week 39, first date of NIPH updates (no weekly data available)*

Figure 3. Geographical distribution of measles cases in Romania, (depicting the situation between 2016–17/02/17)



Source: National Institute of Public Health. Situatia rujeolei in Romania 2017 [update as of 17 February 2017]. Available from: http://www.cnscbt.ro/index.php/informari-saptamanale/rujeola-1.

The current measles outbreak in Romania follows a pattern of previous large outbreaks in 2005–2006, and from late 2010 to early 2014 according to data reported to ECDC. The numbers of measles cases reported to ECDC by Romania by year from 2005–2016 are presented in Table 1. Monthly data available since 2008 are presented in Figure 1.

The predominant age groups affected during both outbreaks (2005–2006 and 2010–2014) have been the same compared to the current outbreak, i.e. infants <1 year of age and young children 1-4 years old had the highest notification rates, and also comprised the majority of cases. In 2011, in reponse to the outbreak, an additional MMR vaccination campaign was started in affected areas targeting all children aged between seven months and seven years, irrespective of their measles vaccination status [4]. In 2005–2006, the response to the outbreak also included an additional campaign using a monovalent measles vaccine targeting all children aged between seven months and seven years.

Historically, the measles vaccination policy in Romania has been implemented as follows:

- In 1979, monovalent measles vaccine was introduced for children aged 9–11 months.
- In 1994, the second measles vaccine dose was introduced for children aged between six and seven years.
- In 2004, the MMR vaccine replaced the first dose of monovalent measles vaccine, and was recommended for children aged 12–15 months. The second dose of MMR vaccine was recommended for children aged between six and seven years from October 2005 as part of school-based vaccination.
- In 2015, the second dose of MMR was moved down in the vaccination schedule to five years of age and vaccination now occurs in health centres rather than being school-based.

Vaccination coverage for the first and second dose of MMR was ≥95% in the early 2000s, however since 2010 it has decreased and vaccination coverage for the first dose in 2015 was 86% (Table 2). The latest reported national coverage estimate for the second dose (2014) was 88% [5]. In 2014, vaccination coverage across the districts ranged from 71–98% for the first dose of MMR, and 53–95% for the second dose [5].

Table 2. Vaccination coverage of MCV dose 1 and MCV dose 2, 2005–2015, Romania (country estimates)

Year	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014*	2015
MCV 1	97	95	97	-	-	95	93	94	92	89	86
MCV 2	96	96	96	95	-	93	91	-	88	-	-

Source: WHO vaccine-preventable diseases: monitoring system. 2016 global summary [Internet]. Available from: http://apps.who.int/immunization_monitoring/globalsummary/coverages?c=ROU

** MCV2 coverage of 88% is reported in Kriss JL, Stanescu A, Pistol A, Butu C, Goodson JL. The World Health Organization Measles Programmatic Risk Assessment Tool-Romania, 2015. Risk Anal. 2016.*

Measles situation in the EU in the last 12 month period

From 1 February 2016 to 31 January 2017, 30 EU/EEA countries conducting measles surveillance reported 4 484 cases to ECDC. This is similar to the number of cases reported in the calendar years 2014 (n=3 656), 2015 (n=4 003) and overall in 2016 (n=4 099). The countries reporting the highest proportion of cases vary from year to year, which influences the epidemiology of measles at the European level (Figure 4)[i].

In 2016, measles outbreaks were described in other EU/EEA countries with published reports from France [7], Ireland [8], England and Wales [9] and Italy [10].

In the EU/EEA countries, measles outbreaks are currently ongoing in:

- Austria: a total of 68 cases have been reported since the last week of 2016. In comparison, 28 cases were reported in 2016 [11].
- Germany: as of 16 February, the Robert Koch Institut (RKI) reported 43 measles cases for 2017. RKI highlights that the true number of cases is likely to be underestimated. Infections have occurred in the areas of Frankfurt, Lahn-Dill, Leipzig, Berlin and Duisburg. Forty-seven cases were reported to ECDC for the month of January 2017, compared to six cases reported in January 2016 [12].
- Italy: 238 cases were reported to ECDC for the month of January 2017, compared to 73 cases reported in January 2016.

According to data reported to ECDC, in the 12 month period from 1 February 2016 to 31 January 2017, eight EU/EEA countries (Austria, the Czech Republic, France, Germany, Ireland, Italy, Spain and the United Kingdom) reported a total of 34 measles cases whose probable country of infection[ii] was Romania, 30 of the cases were reported since September 2016. . Furthermore, EU/EEA countries reported 63 additional cases imported from other EU/EEA countries, and 169 cases imported from non-EU/EEA countries during the 12 month period.

Previous and ongoing measles outbreaks in other EU countries have been epidemiologically-linked to the current outbreak in Romania. However more extensive information on strain sequencing may allow a deeper insight into the current findings:

- An outbreak in Ireland between April and June 2016 resulted in at least 27 cases (22 laboratory-confirmed). The primary case was in Romania for 17 days before symptom onset, and stayed in an area with reported measles transmission [8]. All cases sequenced from the outbreak were genotype B3, however the distinct sequence data were inconclusive to establish a link with the outbreak in Romania.
- In Belgium[iii], between 20 December 2016 and 24 February 2017, 75 cases, of which 30 were laboratory-confirmed, were reported in the region of Wallonia. Five cases were among healthcare workers. All cases were infected with a genotype B3 strain, the same strain that was reported to have circulated in Austria, Italy and Romania at the end of 2016. The index case visited Romania during the incubation period [14].
- In Austria, a cluster of nine cases was reported between the last week of 2016 and 1 February 2017, the index case had travelled to Romania during the incubation period and had contact with a measles case. The genotype identified in eight cases was B3-4741 (measles RNA positive samples were genotyped at the National Reference Laboratory for measles at the Clinical Institute of virology, Medical University Vienna).

The latest available vaccination coverage data from WHO (2015 data) show that vaccination coverage was above the 95% target in 17 EU/EEA countries for the first dose of MCV (range: 85–99%). In eight countries, vaccination coverage for the second dose of MCV was at least 95% (range: 74–99%). Five countries did not submit data for the second dose for 2015 or 2014 (Figure 5, see also the Annex).

[i] For the latest update of measles cases reported in the EU, please refer to the ECDC website and the Surveillance Atlas of Infectious Diseases [6]

[ii] Defined as a case with virological or epidemiological evidence, or both, of exposure outside the region or country during the 7–18 days prior to rash onset 13. World Health Organisation. Surveillance Guidelines for Measles, Rubella and Congenital Rubella Syndrome in the WHO European Region [internet]. 2012 Dec. [cited 2017 Feb. 28]. Available from: http://www.euro.who.int/__data/assets/pdf_file/0018/79020/e93035-2013.pdf?ua=1..

[iii] Belgium is not included in the list of countries who reported imported cases from Romania in the 12 month period from 1 February 2016 to 31 January 2017, as Belgium reports aggregated measles data to ECDC, which do not include data on the origin of infection.

Figure 4. Number of measles cases by month, EU/EEA countries, 1 January 2008–31 January 2017

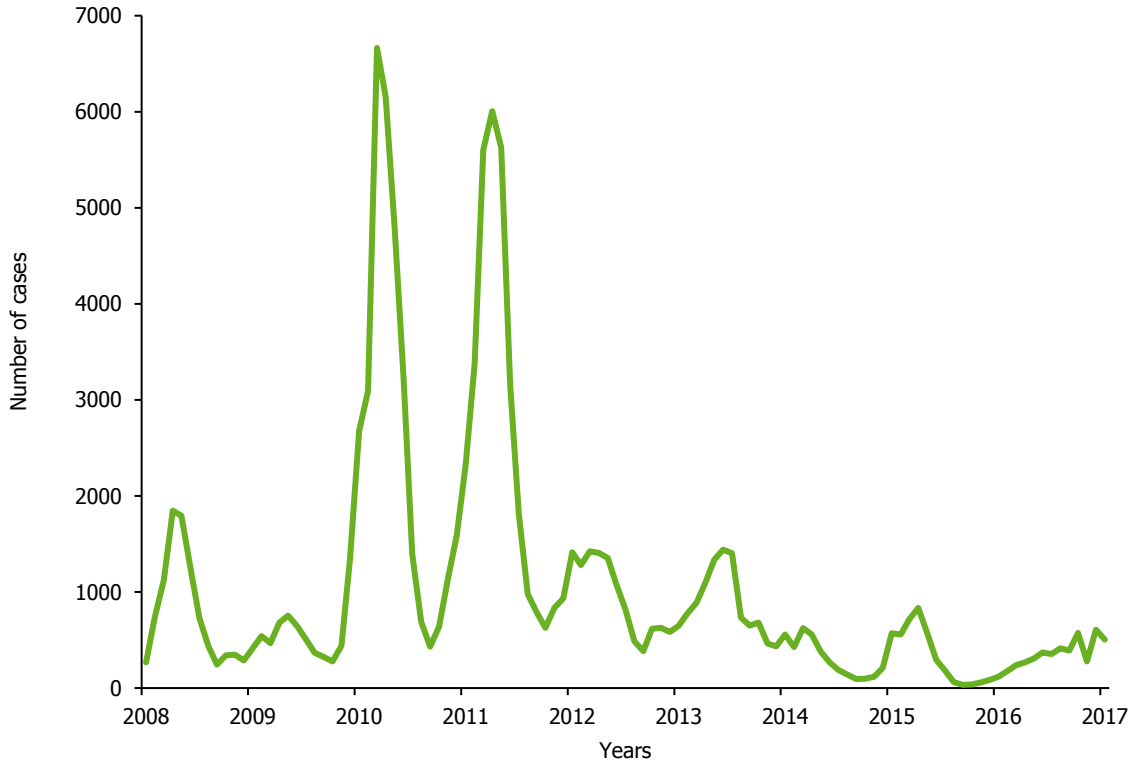
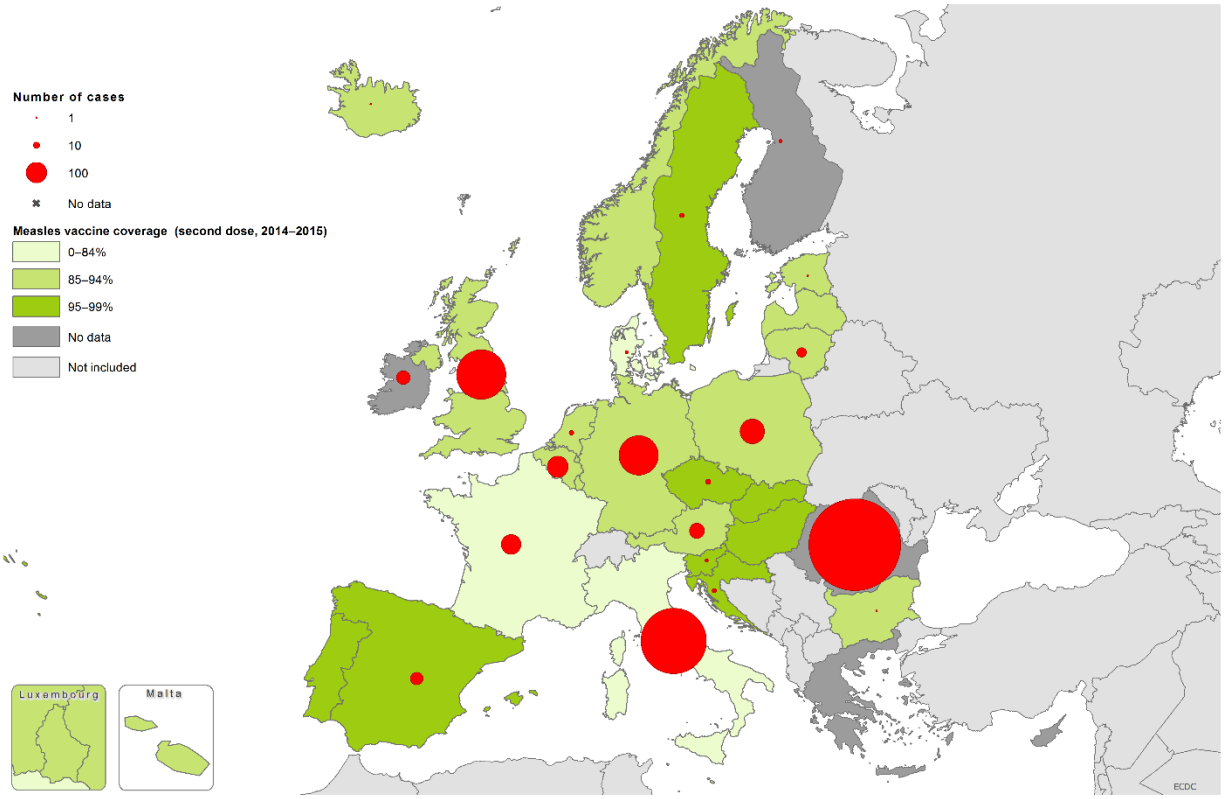


Figure 5. Number of measles cases between 1 February 2016 and 31 January 2017, and vaccination coverage with the second dose of MMR (2014–2015, WHO*), EU/EEA countries



Source: Coverage figures (%) are official national figures reported via the annual WHO/UNICEF Joint Reporting Form [15]. Case data are extracted from ECDC/TESSy

ECDC threat assessment for the EU

From 1 February 2016 to 31 January 2017, 4 484 measles cases were reported in 22 out of 30 EU/EEA countries and multiple outbreaks were identified [6]. In spite of the outbreaks varying in size, duration and setting, the affected groups are consistently predominantly unvaccinated individuals or those who have not completed their primary series.

The progress towards elimination of measles in the European Region of WHO is assessed by The European Regional Verification Commission for Measles and Rubella Elimination (RVC). Member States of the WHO European Region are making steady progress towards the elimination of measles. At the fifth meeting of the RVC for Measles and Rubella in October 2016, of 53 countries in the WHO European Region, 24 (15 of which are in EU/EEA) were declared to have reached the elimination goal for measles, and an additional 13 countries (nine in EU/EEA) were concluded to have interrupted endemic transmission for less than 36 months, meaning they are on their way to achieving the elimination goal. However, six EU/EEA countries were judged to still have endemic transmission of measles: Belgium, France, Germany, Italy, Poland, Romania (Table 3) [16].

Table 3. Elimination status of EU/EEA Member States, based on 2015 data review, formed from RVC meeting report

Elimination status	Country
EU/EEA Member States judged to have **eliminated the disease** (≥36 months without endemic transmission)	Bulgaria, the Czech Republic, Cyprus, Estonia, Finland, Hungary, Latvia, Luxembourg, Malta, the Netherlands, Norway, Portugal, Slovakia, Slovenia, Sweden (15)
EU/EEA Member States judged to have **interrupted endemic transmission** for between 24 and 35 months	Croatia, Denmark, Greece, Iceland, Lithuania, Spain, the United Kingdom (7)
EU/EEA Member States judged to have **interrupted endemic transmission** for between 12 and 23 months	Ireland (1)
EU/EEA Member States which have provided **evidence of interrupted endemic transmission for less than 12 months**, evidence of interruption for a full 12 months or longer is expected in the annual status update for 2016	Austria (1)
EU/EEA Member States judged to have **endemic transmission**	Belgium, France, Germany, Italy, Poland, Romania (6)

Source: Meeting report of the Fifth Meeting of the European Regional Verification Commission for Measles and Rubella Elimination (RVC) [16]

The current measles outbreak in Romania has been ongoing since February 2016 and cases continue to be reported despite implemented and ongoing response measures at national level through reinforced vaccination activities.

A programmatic risk assessment conducted in 2015 to guide measles elimination programme activities in Romania classified 27 out of 42 districts in the country as being at a high or very high risk of a measles outbreak, including the districts most affected by the current outbreak. Low vaccination coverage and insufficient surveillance quality were identified as driving factors behind these classification. A survey of parents conducted in 2015 found that the most common reasons for them not to vaccinate their child were failure to attend a healthcare clinic, and refusal of vaccines [5].

As the current outbreak evolves, and considering its size and geographical spread, the likelihood of exportation of measles cases from Romania is high. Likewise, the potential for exportation applies for any area where measles transmission is occurring. Molecular investigation of circulating measles strains allows clarification of the origin of the virus. The size and duration of outbreaks are to a large extent determined by the overall population immunity, population density, timeliness of the detection, public health response to the outbreak, and whether the outbreak affects pockets of under-vaccinated and vulnerable populations. In that sense, the interval between the end of the previous outbreak (2011–2014) and the beginning of the current one, illustrates the dynamic of the disease in a low vaccine coverage area, where the susceptible cases are accumulating before the start of a new outbreak.

Given that the national vaccination coverage is less than 95% for the second dose of MMR in the majority of EU/EEA countries (Figure 5), the risk of spread and sustained transmission in areas with susceptible populations is high. In addition, in 13 EU countries the vaccination coverage is less than 95% for the first dose. Immunity profiling of other EU/EEA countries would be needed to estimate the exact risk of importation and magnitude of spread.

Even in countries with high national vaccination coverage, pockets of individuals susceptible to measles may still exist since the number of measles-susceptible persons increases over time, as successive cohorts of unvaccinated individuals add to the pool of susceptible individuals.

Individuals susceptible to measles are present in all EU/EEA countries also due to:

- the window of susceptibility in infants between waning of maternal antibodies and the time when the first dose of MMR is provided, a time period lasting about 6 to 12 months depending on the immunisation schedule [17]
- lack of or limited catch-up campaigns for non-immune individuals of all ages since measles immunisation programmes were initiated
- groups of individuals who cannot be vaccinated with a live attenuated vaccine for medical reasons, e.g. immunosuppressive treatment, chemotherapy for cancer, or organ transplantation. This group remains dependent on protection through herd immunity
- sub-optimal immunisation coverage in certain population groups due to certain cultural traditions, religious beliefs, fear of adverse effects of the vaccine or lack of confidence in public authorities.

Conclusions and options for response

Immunisation is the only effective preventive measure against acquiring measles. All countries in the EU/EEA have measles vaccination policies in place with two doses using an MMR vaccine. Catch-up programmes for individuals having missed vaccination or being too old to have been targeted by routine programmes exist in a number of countries. Strengthening routine immunisation through facilitating access to vaccination, and mechanisms to identify people not or incompletely vaccinated are needed. Promoting and providing additional opportunities for immunisation through a variety of supplemental immunisation activities (SIA) may be needed in countries with suboptimal coverage and/or pockets of susceptible individuals.

Vaccination coverage of at least 95% of the general population at national and subnational levels with two doses of MCV is recommended and necessary to ensure that measles circulation is interrupted, and that introduction of measles cases does not result in secondary cases. This has not yet been achieved in all EU/EEA countries according to available vaccination coverage figures. The assessment of vaccination coverage and the availability of data at subnational level would allow geographical areas where targeted actions may be needed to be identified.

Strengthening and ensuring high-quality surveillance, including monitoring the changing epidemiology of measles helps guide public health actions. All suspected cases need to be detected and investigated in order to break chains of transmission as soon as possible, and performing epidemiological investigations including an assessment of the susceptibility of contacts to consider necessary control measures [18]. Adequate laboratory investigation is essential as data on viral genotype are needed to track transmission chains.

In light of the current outbreak, travellers to Romania who have not been immunised with two doses of MCV are at risk of being exposed and contracting measles, in the same way as when travelling to any area where measles transmission is occurring. As the vaccine is highly effective, healthcare providers should consider recommending vaccination for all eligible travellers who are not, or not fully immunised, in line with the national recommendations. Any encounter with the healthcare system should be used as an opportunity for a catch-up vaccination against measles as well as other vaccine-preventable diseases.

Given the size of the current outbreak in Romania, the recent historical trends, and that vaccination coverage for the first and second dose of MCV is below 90%, there is a high risk of continued measles transmission within Romania. This poses a risk of potential repeated exportation to other EU/EEA countries and consequently continuous transmission in some of them, where vaccination coverage is suboptimal. Response efforts are continuing in Romania and should help ensure pockets of susceptible individuals are adequately vaccinated.

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Annex

Vaccination coverage with the first and second dose of MMR (2014–2015, WHO*), EU/EEA countries

	MCV1		MCV2	
Country	**2015**	**2014**	**2015**	**2014**
Austria	-	96	-	87
Belgium	96	96	85	85
Bulgaria	92	93	87	89
Croatia	93	94	96	97
Cyprus	90	86	-	-
Czech Republic	-	99	99	96
Denmark	91	90	80	84
Estonia	93	93	92	93
Finland	95	-	-	-
France	-	90	-	74
Germany	97	97	93	93
Greece	97	97	-	-
Hungary	99	99	99	99
Iceland	93	90	94	93
Ireland	93	93	-	-
Italy	85	87	83	83
Latvia	96	95	92	89
Lithuania	94	93	92	92
Luxembourg	99	99	86	86
Malta	89	98	91	94
Netherlands	95	96	92	93
Norway	95	94	91	92
Poland	96	97	94	95
Portugal	98	98	95	96
Romania	86	89	-	-
Slovakia	95	97	98	98
Slovenia	94	94	96	94
Spain	96	96	95	93
Sweden	98	97	95	95
United Kingdom	95	93	91	89

Coverage figures (%) are official national figures reported via the annual WHO/UNICEF Joint Reporting Form [15].