

# Measles in Italy, July 2009 to September 2010

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Outbreaks of measles continue to occur in Italy, as in other European countries. We present here details of cases reported through the Italian enhanced measles surveillance system from July 2009 to September 2010. In total, 2,151 cases were reported, 42% (n=895) of which were laboratory confirmed. The median age of cases was 18 years and 1,709 of 1,856 cases (92%) were unvaccinated. Many cases with complications were reported (n=305), including three with encephalitis. A total of 652 of 1,822 cases (36%) were hospitalised. Molecular characterisation revealed circulation of a limited number of measles virus genotypes (D4, D8 and B3), which is consistent with the current epidemiology of the disease in Italy. A national measles elimination plan was approved in 2003 with the aim of interrupting endemic measles transmission by 2007. Since elimination was not achieved, the target date was recently moved to 2015. The emphasis of the new elimination plan, approved in March 2011, is on strengthening surveillance, implementing evidence based-interventions to increase measles-mumps-rubella vaccine uptake in children, adolescents and young adults, and implementing communication activities related to the vaccine. The strategies proposed by the plan should be implemented fully and appropriately by all regions in order to meet the elimination goal by 2015.

## Introduction

As in other European countries [1-6], various outbreaks of measles have recently occurred in Italy. Since December 2009, outbreaks have been reported in various regions, including Trentino-Alto Adige (Trento and South Tyrol), Veneto, Piedmont, Emilia Romagna and Liguria in northern Italy, Lazio in central Italy and Calabria, Apulia, Sardinia and Sicily in southern Italy.

A single-antigen measles vaccine was introduced in the country in 1976: measles-mumps-rubella (MMR) vaccine has been recommended since the early 1990s. Initially, a single dose of a measles-containing vaccine was recommended for children aged 15 months. Later,

in 1999, the age of administration of the first dose (of MMR vaccine) was lowered to 12 months. From 1999 to 2003, a second MMR vaccine dose was recommended in regions that had reached a coverage level of 80% or higher for the first dose [7]. Since 2003, the national vaccination schedule has recommended two doses of MMR vaccine in all regions: the first dose at 12–15 months and the second at the age of 5–6 years or 11–12 years.

A national measles elimination plan was launched in 2003, with the aim of interrupting endemic measles transmission (incidence below one confirmed case per 1,000,000 population) by 2007 [8]. Strategies of the plan included strengthening surveillance and increasing vaccination coverage with two doses of MMR vaccine to a minimum of 95%, as recommended by the World Health Organization (WHO) Regional Office for Europe [9]. Since 2003, various actions to improve coverage rates of MMR vaccination have been undertaken, including a supplementary vaccination campaign in 2003 to 2005 targeted at school-age children (1991–1997 birth cohorts).

Vaccination coverage in Italy is routinely measured by the administrative method, using as the numerator the number of vaccine doses administered. The mean national coverage for the first dose of MMR vaccine in children below two years of age was 89.9% in 2009 [10], ranging from 70.8% to 95.5% in the 21 regions of the country (Figure 1, panel A). However, a WHO Expanded Programme on Immunization (EPI)-cluster sampling survey conducted in 2008 in 18 regions [11] revealed that MMR vaccination coverage rates for the first dose at 15 months (73.7%; 95% CI: 71.7–75.7) were substantially lower than those at 24 months (86.5%; 95% CI: 85.1–88.0). This indicates that many children are being vaccinated beyond the age recommended by the national schedule. Coverage for the second dose of MMR vaccine is not routinely measured in Italy but according to the survey, only 53.9% of 16-year-olds (1992 birth cohort) had received two doses of MMR

vaccine. This percentage varied considerably among the regions, ranging from 21.2% to 80.5%. Vaccination coverage in 16-year-olds was found to be low (78.1%) even for the first dose of MMR, ranging from 53.2% to 97.1% (Figure 1, panel B).

Measles has been statutorily notifiable in Italy since 1934. An enhanced surveillance system was introduced in 2007 [12], as proposed by the national measles elimination plan [8], to improve timeliness, completeness of case reporting, and case investigation, including laboratory confirmation of diagnosis. According to this system, physicians are required to report all suspected measles cases to the local health authorities within 12 hours (as opposed to within 48 hours in the statutory notification system). For each suspected case, the local health authorities are required to carry out an epidemiological investigation, including obtaining specimens for laboratory confirmation and genotyping, and to complete a standard measles notification form, which is then to be sent to regional health authorities. The regional authorities forward the forms immediately to the Ministry of Health and to the Infectious Diseases Epidemiology Unit of the National Institute of Health.

Measles incidence has decreased in Italy since measles vaccination was introduced. The mean number of cases reported annually through the statutory notification system was 49,000 in the 1970s (91 per 100,000 population), 46,000 in the 1980s (81 per 100,000 population) and 23,000 in the 1990s (41 per 100,000 population). In 2000 to 2009, a mean of 4,036 cases were reported annually (7 per 100,000 population), ranging from 215 cases (incidence: 0.4 per 100,000 population in 2005) to 18,020 cases (incidence: 32 per 100,000 population in 2002). The previous outbreaks occurred in 2002 to 2003 and in 2007 to 2008 [13,14]. Following the 2008 outbreak, a new resurgence of measles cases was observed starting in December 2009, with outbreaks reported in various regions. In this article we describe measles cases reported to the National Health Institute (through the enhanced measles surveillance system) with a date of rash onset between 1 July 2009 and 30 September 2010.

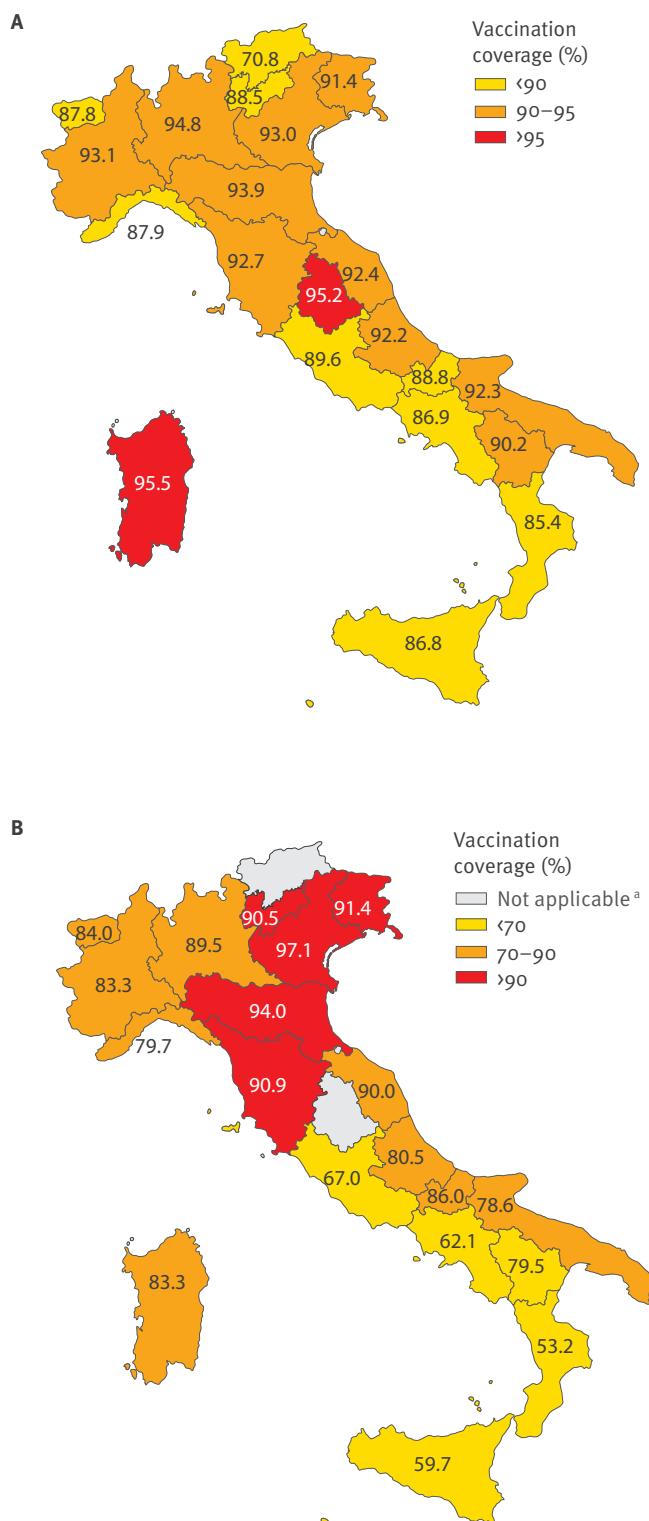
## Methods

The European Union case definition was used to classify cases [15]. Recent vaccination was defined as having received measles or MMR vaccine 6–45 days before onset of rash [16]. Recently vaccinated cases with a positive IgM response were classified as possible or probable cases according to the presence of the defined clinical criteria and/or an epidemiological link to a confirmed measles case. Suspected cases not meeting the clinical criteria were not considered as cases and were discarded.

Cases vaccinated up to and including five days before rash onset were probably incubating the disease at the time of vaccination and were classified either as not vaccinated if they had received only one dose) or as

**FIGURE 1**

Vaccination coverage for the first dose of measles-mumps-rubella vaccine (A) in children aged two years (2009) and (B) in 16 year-olds (2008), by region, Italy



<sup>a</sup> The region did not participate in the survey.

vaccinated with one dose (if recently vaccinated with the second dose) [17].

Imported cases were defined as cases in which the disease resulted from exposure to measles virus outside Italy, as evidenced by at least some of the exposure period (7–18 days before rash onset) occurring outside Italy and rash onset occurring within 18 days of entering Italy.

Biological samples for genotyping were analysed by the national reference laboratory at the National Health Institute in Rome and by regional reference laboratories in Liguria, Veneto and Apulia (samples from Liguria and Piedmont regions were analysed by the Department of Health Sciences of the University of Genoa; samples from Apulia by the Department of Biomedical Sciences and Human Oncology of the University of Bari and samples from Veneto by the reference laboratory in Padua).

Reverse transcription-polymerase chain reaction was used to amplify measles virus sequences from RNA extracted from throat swabs or urine specimens of suspected measles cases. As recommended by the World Health Organization (WHO), strains were genotyped by sequencing the 450 nucleotides that code for the C-terminus of the viral nucleoprotein (N) [18].

Incidence was calculated by using age-specific population data for 2010 obtained from the national Institute of Statistics (ISTAT) [19].

## Results

A total of 2,151 possible, probable or confirmed cases were reported from 15 of the 21 Italian regions, giving a national cumulative incidence in the 15-month

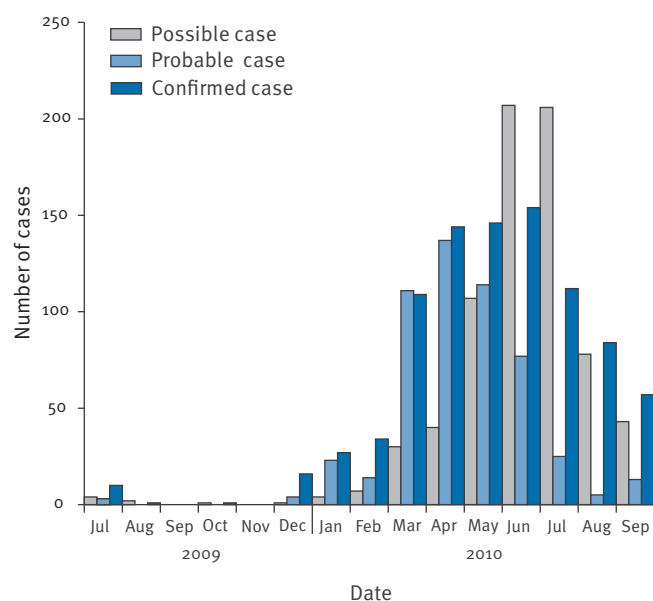
reference period of 3.6 per 100,000 population (population of 60,340,328). Overall, 895 cases (41.6%) were classified as laboratory confirmed, 526 (24.5%) were probable and 730 (33.9%) were possible. Figure 2 shows the number of measles cases reported nationally by month and by type of case from July 2009 to September 2010.

Few cases were reported from July to November 2009. The number of reported cases increased from December 2009 reaching a peak of 438 cases in June 2010 and then decreased in the following months, with 113 cases reported in September 2010.

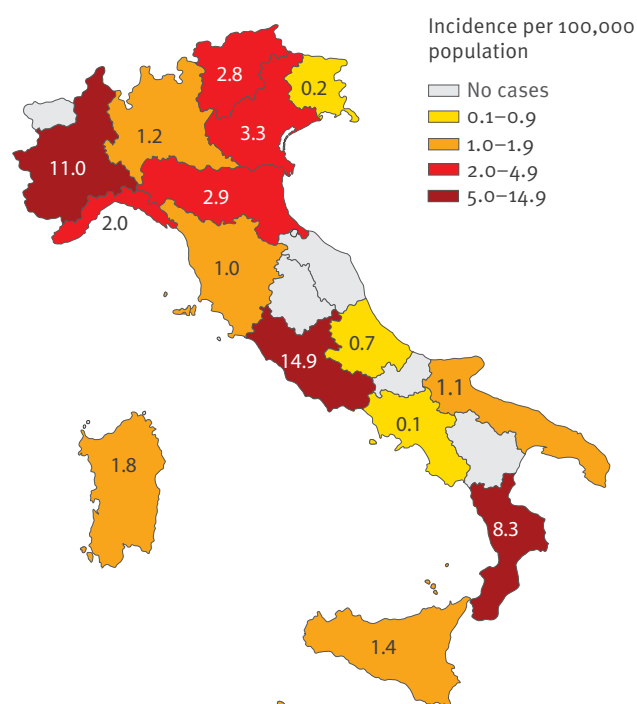
Measles incidence varied between regions, from 0.1 per 100,000 population to 14.9 per 100,000 population (Figure 3). The highest incidence was reported from the Lazio region in central Italy (14.9 per 100,000 population) followed by Piedmont in northern Italy (11.0 per 100,000 population); more than 60% (n=1,324) of cases were reported from these two regions). The Calabria region in southern Italy reported the third highest incidence (n=166; incidence 8.3 per 100,000 population). Five regions (one in the north, two in the centre and two in the south) did not report measles cases during the 15-month period while three regions, two of which were in southern Italy, reported fewer than 12 cases each.

Measles virus transmission occurred in families, schools and healthcare and other community settings. A total of 34 cases in 10 regions were healthcare workers, including physicians, nurses, medical students,

**FIGURE 2**  
Reported measles cases by month and type of case, Italy, July 2009–September 2010 (n=2,151)



**FIGURE 3**  
Reported measles incidence per 100,000 population, by region, Italy, July 2009–September 2010 (n=2,151)



student nurses and other hospital workers. It is not known whether any of the cases in healthcare workers were nosocomial. In addition, two clusters were reported among Roma/Sinti populations in Calabria (10 cases) in May 2010 and in Lombardy (4 cases) in July 2010. One laboratory-confirmed Roma case was reported from the Apulia region in June 2010 and one Roma case, classified as possible, from the Lazio region in August 2010.

A total of 13 cases, all unvaccinated, were likely to have acquired the virus abroad, from Brazil, Canada, Mexico, South Africa, Tanzania and European countries including Croatia, France, Ireland, Spain, Switzerland and the United Kingdom.

### Age and sex distribution of cases

Information on the sex of cases was available for 2,148 cases (99.9%): 1,123 (52.3%) were male. Age was reported for 2,079 cases (96.7%) in 14 regions, one of which reported only two cases. The age distribution of cases and incidence per age group are shown in Table 1.

A total of 1,270 cases (61%) were aged 15–44 years. Overall, the highest incidence was seen in the age group 15–19 years followed by the age group under one year. However, some regional differences were

**TABLE 1**

Age distribution of measles cases and incidence by age group, Italy, July 2009–September 2010 (n=2,079)

| Age group (years) | Number of cases | Incidence per 100,000 population |
|-------------------|-----------------|----------------------------------|
| <1                | 69              | 12.3                             |
| 1–4               | 220             | 9.6                              |
| 5–9               | 155             | 5.5                              |
| 10–14             | 300             | 10.7                             |
| 15–19             | 416             | 14.0                             |
| 20–24             | 292             | 9.4                              |
| 25–44             | 562             | 3.2                              |
| ≥45               | 65              | 0.2                              |
| <b>Total</b>      | <b>2,079</b>    | <b>3.6</b>                       |

**TABLE 2**

Vaccination status of measles cases by age group, Italy, July 2009–September 2010 (n=1,856)

| Vaccination status          | Number (%) of cases by age group in years |                    |                    |                    |                    |                    |                    |                   |                      |
|-----------------------------|---|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|-------------------|----------------------|
|                             | <1  | 1–4                | 5–9                | 10–14              | 15–19              | 20–24              | 25–44              | ≥45               | Total                |
| Unvaccinated                | 68 (98.6)                                 | 161 (78.5)         | 129 (87.8)         | 256 (92.1)         | 333 (92.8)         | 233 (93.6)         | 475 (96.0)         | 54 (100.0)        | 1,709 (92.1)         |
| One dose                    | 1 (1.4)                                   | 41 (20.0)          | 16 (10.9)          | 21 (7.6)           | 22 (6.1)           | 13 (5.2)           | 18 (3.6)           | 0 (0.0)           | 132 (7.1)            |
| Two doses                   | 0 (0.0)                                   | 2 (1.0)            | 2 (1.4)            | 1 (0.4)            | 3 (0.8)            | 2 (0.8)            | 1 (0.2)            | 0 (0.0)           | 11 (0.6)             |
| Unspecified number of doses | 0 (0.0)                                   | 1 (0.5)            | 0 (0.0)            | 0 (0.0)            | 1 (0.3)            | 1 (0.4)            | 1 (0.2)            | 0 (0.0)           | 4 (0.2)              |
| <b>Total</b>                | <b>69 (100.0)</b>                         | <b>205 (100.0)</b> | <b>147 (100.0)</b> | <b>278 (100.0)</b> | <b>359 (100.0)</b> | <b>249 (100.0)</b> | <b>495 (100.0)</b> | <b>54 (100.0)</b> | <b>1,856 (100.0)</b> |

observed. Most notably, adolescents and/or young adults (age groups 10–14 years, 15–19 years and 20–24 years) were the most affected age groups in six regions, while seven regions reported higher incidences either in infants (aged under 1 year) or in children aged 1–4 years, in comparison with older age groups. In six of these seven regions, adolescents (10–14 years) and or adults (15–44 years) were nevertheless among the three most affected age groups in each region. In the remaining region, the most affected people were those below 10 years of age.

The median age of cases was 18 years (range: 1 month–82 years). The median age varied by region, from 12 years in the Sicily region (southern Italy) to 26 years in the Emilia Romagna and Liguria regions (both in north-eastern Italy).

### Vaccination status of cases

Vaccination status was available for 1,856 cases (86.3%). Overall, 1,709 cases (92.1%) were unvaccinated, 132 (7.1%) had received only one dose of a measles-containing vaccine, 11 (0.6%) were vaccinated with two doses and four (0.2%) had received an unspecified number of doses. Table 2 shows vaccination status by age group. Among unvaccinated cases, 69 were too young to be vaccinated routinely (aged under one year). The percentage of cases vaccinated with one dose was 20% (n=41) among 1–4 year-olds and decreased with increasing age to 3.6% (n=18) in the 25–44-year age group. Of the cases aged over 44 years (n=54), none had been vaccinated.

### Hospitalisations and complications

Information regarding hospital admissions for measles was available for 1,822 cases (84.7%), of whom 652 (35.8%) were hospitalised. Complications occurred in 14% of cases (n=305). Some cases reported more than one complication: a total of 422 complications were reported (Table 3). No deaths were reported.

Diarrhoea was the most frequent complication but more severe complications, such as pneumonia, thrombocytopenia and encephalitis, were also reported. The three reported cases with encephalitis were aged 23, 26 and 38 years. None had been vaccinated against measles

and all were laboratory confirmed. Other reported complications included respiratory complications, vomiting and dehydration, hepatitis, arthralgia and complications in pregnancy. Four women were infected during pregnancy, of whom two had a spontaneous abortion and two a premature delivery. The mean age of cases with complications was 21 years (range: 0–57 years).

The incidence of each complication also varied among the regions (Table 3). Two of the 15 regions with cases did not report complications. However, the number of reported cases in these regions was very small (n=2 and n=8). In the remaining 13 regions, the percentage of cases with at least one complication varied from 7% to 50%.

### Phylogenetic analysis of measles virus

Measles virus from specimens collected from 111 cases in 13 of the 15 affected regions were genotyped: three different genotypes were identified, D4, D8 and B3. D4 genotype sequences were isolated from 87 cases in 11 regions. D8 genotype sequences were isolated from 21 cases in four regions. The B3 virus genotype was isolated from one case reported in May 2010 in the Piedmont region and from three cases reported in August 2010 in the Liguria region.

### Discussion and conclusion

Like other countries in the WHO European Region, Italy did not meet the 2010 elimination target [1]. Progress has been made in the country in improving measles surveillance and case investigation, and the percentage of laboratory-confirmed cases has increased from

30% to 41% since 2008 [13]. However, vaccination coverage levels remain below the recommended 95%.

Measles incidence was found to vary greatly among the regions. Over 60% of cases were reported from only two regions while the rest were reported from 14 regions, some of which reported very few cases. Five regions did not report cases. The observed differences in incidence are not explainable by the current regional MMR vaccination coverage levels: These have become more homogenous across the country in recent years; however, wide regional differences in MMR coverage levels have been recorded in the past, which may have led to a loss of temporal synchronisation of measles outbreaks between regions [20]. In fact, since September 2010 new outbreaks have occurred in regions that reported a low measles incidence in 2009 to 2010.

The observed differences among regions are also likely to be, at least partly, due to under-reporting. Under-reporting of infectious diseases in Italy, especially in southern regions, has been well documented for the statutory notification system [21,22]. The degree of under-reporting to the enhanced measles surveillance system is unknown; however, an evaluation of the performance of the system, including completeness of reporting, is currently under way.

As expected, most reported cases were unvaccinated and, as in previous outbreaks in 2008 [13], adolescents and young adults were particularly affected. The median age of reported measles cases was 17 years in 2008 and has further increased to 18 years in 2009 to 2010. These data indicate that there continue to be large pockets of susceptible individuals especially among adolescents and young adults (mainly those aged 10 to 19 years). Low measles vaccination coverage rates were reported among 16 year-olds in a 2008 survey [11]. Efforts to prevent measles must therefore be aimed at improving MMR vaccine uptake not only in small children, but also in older age groups. In the above-mentioned survey, lack of information on the need to be vaccinated was the most frequently reported reason among adolescents for missed measles vaccination, indicating the need for an effective communication programme addressing underestimation of the risks associated with measles and the safety and side effects of the MMR vaccine [23]. Our analysis also shows a high measles incidence in children under one year of age. There is no policy in Italy to vaccinate children in childcare or nursery settings, before 12 months of age, in non-outbreak settings. However, in outbreak settings, the new national measles elimination plan, approved several months following the described outbreak, recommends vaccinating children from six months of age [24].

Regional differences were observed in age-specific incidence of measles cases. However, in all but one region, adolescents and/or young adults were among

**TABLE 3**  
Number of reported complications and incidence per 1,000 measles cases, Italy, July 2009–September 2010

| Diagnosed complication   | Number of complications | Incidence per 1,000 measles cases <sup>a</sup> (range according to region) |
|--------------------------|-------------------------|--|
| Diarrhoea                | 116                     | 53.9 (20.7–166.7)  |
| Otitis                   | 51                      | 23.7 (0.0–111.1)   |
| Pneumonia                | 48                      | 22.3 (0.0–133.3)   |
| Keratoconjunctivitis     | 49                      | 22.8 (0.0–142.9)   |
| Laryngotracheobronchitis | 32                      | 14.9 (0.0–130.4)   |
| Thrombocytopenia         | 7                       | 3.2 (0.0–111.1)  |
| Encephalitis             | 3                       | 1.4 (0.0–15.9)   |
| Convulsions              | 2                       | 0.9 (0.0–14.5)   |
| Other                    | 114                     | 53.0 (0.0–270.3)   |
| <b>Total</b>             | <b>422<sup>b</sup></b>  | –  |

<sup>a</sup> Calculated using as the denominator the total number of measles cases reported, n=2,151.

<sup>b</sup> A total of 305 cases had complications; some reported more than one complication.

the most affected. The exception is a region situated in northern Italy, where the most affected groups were infants and children aged up to nine years. It is well known that anti-vaccination activists are present in this region [25] and even though the regional coverage rate for the first dose of MMR vaccine (93%) was slightly above the national average in 2009 (90%), the presence of people opposed to vaccines may have led to the build-up of pockets of susceptible children, especially in some areas of the region.

A number of cases were in healthcare workers and transmission occurred in various healthcare settings, including hospitals, emergency rooms and ambulatory-care settings. Healthcare workers should have documented evidence of measles immunity, as they place themselves and patients at risk if they are not vaccinated against measles. Also, effective airborne infection control practices should be implemented in all healthcare settings.

The presence of imported cases highlights the ease with which measles virus can spread across countries with the movement of individuals. Information on the number of chains of transmission that occurred following the importations was not reported.

Many cases with severe complications were reported, especially in the older age groups, and over 650 cases were hospitalised. The percentage of complications seen is in accordance with that reported in the literature [26,27] and clearly reflects the severity of measles. Encephalitis was observed in three cases, seven cases had thrombocytopenia and many cases had pneumonia (in some, it led to respiratory insufficiency). It is also noteworthy that the four measles cases who were pregnant had a spontaneous abortion or premature delivery. Health professionals and the general public should be made aware of the occurrence of these serious complications. In addition, it must not be forgotten that cases of measles, in particular those requiring hospitalisation, impose a substantial economic burden on the healthcare system and society [28] and that MMR vaccination has been shown to be extremely cost saving [29].

Public health control measures during the 2009 to 2010 outbreaks included contact tracing, offering vaccination to susceptible contacts, excluding cases and susceptible contacts from school, and alerting primary care practitioners, paediatricians and hospital emergency rooms. A first dose of MMR vaccine was offered to unvaccinated contacts and a second dose to people vaccinated with one dose. However, in most regions, viral transmission was not effectively interrupted by outbreak control measures indicating that these are probably insufficient and should be further strengthened. A survey conducted to evaluate the degree of implementation of strategies included in the national measles elimination plan showed that the type and extent of public health response measures to measles

cases varied among local health authorities [30]. In particular, only 41% of the authorities reported that they regularly collected biological specimens from suspected measles cases for laboratory confirmation of diagnosis, 76% reported regular active contact tracing and 58% regular vaccination of susceptible contacts.

Phylogenetic analyses revealed circulation of measles virus genotypes D4, D8 and B3 in Italy during the period covered in our analysis. The D4 genotype sequences were all closely related to each other and were indistinguishable from those that had circulated in Italy in 2008 [13] and in 2009 and 2010 in the WHO European Region [5,31,32]. D4 had been the predominant viral genotype circulating in the country in 2008 [13] and probably represents an endemic strain of the virus in Italy. BLAST analysis showed that the D8 genotype sequences were all closely related to each other and to strains that had circulated in 2009 in Europe and India. This genotype was first isolated in Italy in February 2008 [13], while B3 was identified in 2006 to 2007, in an outbreak in Apulia and in the Lazio, South Tyrol and Sardinia regions [33-35]. The B3 genotype recently isolated was indistinguishable from viruses isolated in Africa in 2009 [36]. A detailed evaluation of the molecular characteristics and lineages of circulating measles virus genotypes in Italy and their source is under way. Nevertheless, the data presented here show that a limited number of genotypes are presently circulating in Italy, as occurs in countries with endemic transmission of measles virus, as opposed to countries reaching elimination, in which co-circulation of multiple imported genotypes generally occurs [37].

In conclusion, various challenges to reaching the measles elimination goal exist in Italy. In agreement with the renewed commitment to eliminate measles and rubella and prevent congenital rubella syndrome in the WHO European Region [38], a new measles and congenital rubella elimination plan has been recently approved in Italy [24] with a target date of 2015. The emphasis is on implementing: (i) evidence-based interventions to increase the use of MMR vaccine [39]; (ii) strategies to increase MMR vaccine uptake in adolescents and young adults; and (iii) communication activities on MMR vaccine, such as distributing fact sheets and information brochures and organising continuing medical education activities for health professionals [23]. These and other elimination strategies of the plan, including strengthening epidemiological surveillance, should be implemented fully and appropriately by all regions and local health authorities in order to meet the elimination goal by 2015.

The data presented here highlight the severity of measles and the importance of achieving high vaccination coverage not only in young children but also in adolescents and young adults. The challenges faced by Italy are not unique to the country [40]: in order to achieve measles elimination in Europe by 2015, coordinated efforts by all WHO European Member States are essential.

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