

# Mumps outbreak in the former Yugoslav Republic of Macedonia, January 2008 – June 2009: epidemiology and control measures

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Mumps is a mandatorily notifiable disease in the former Yugoslav Republic of Macedonia. Routine vaccination with one dose of measles-mumps-rubella (MMR) vaccine at the age of 13 months started in 1983 and a two-dose vaccination schedule, with the second dose at the age of seven years, was implemented in 1997. The previous mumps outbreak in the country was reported in 1996, with 4,321 registered cases. In October 2007, an increase in mumps notifications was observed. Between January 2008 and June 2009, the Institute of Public Health received 16,352 notifications of mumps cases through the routine surveillance system. Young people aged 15–19 years ( $n=7,876$ , 48.2%) were most affected; more males (61.2%,  $n=10,013$ ) were reported than females. Of the cases whose vaccination status was checked ( $n=14,178$ , 86.7%), 19.5% had not been vaccinated, 37% had been vaccinated with one MMR dose, 34.4% had received two doses, 0.6% had been vaccinated during catch-up vaccination (with MMR vaccine for people aged 15–26 years) and for 8.5% there were no records of vaccination. For 13.3% ( $n=2,174$ ) of reported cases, their vaccination status was not checked. In February 2009, biological specimens (serum, saliva and urine) from 20 cases aged 15–19 years were sent to the National Institute for Public Health and the Environment (RIVM) in the Netherlands for genotyping. Of the 20, nine had been vaccinated with two doses of MMR vaccine, five with one dose, one had not been vaccinated and five had no records of vaccination). Mumps viral RNA was detected in samples from 17 patients: the sequence of the amplified small hydrophobic gene from all 17 showed that the mumps virus was genotype G5.

## Introduction

Mumps, caused by a paramyxovirus, is generally a mild disease with fever, headache and swelling of the salivary glands (parotitis). It is spread directly from infected to susceptible people by respiratory droplets. The infection can be asymptomatic in up to 20% of cases; 40–50% of cases can have nonspecific or

primarily respiratory symptoms [1]. Parotitis occurs in 30–40% of infected people [1], but complications such as meningitis (in up to 15% of cases), encephalitis or orchitis may occur [2]. Permanent sequelae occur in about 25% of encephalitis cases, with an overall mortality of 1 per 10,000 cases [2]. In children, deafness caused by mumps affects approximately 5 per 100,000 cases [1,2]. Mumps infection during the first 12 weeks of pregnancy is associated with a 25% incidence of spontaneous abortion, although malformations following mumps virus infection during pregnancy have not been found [1].

Mumps is a mandatorily notifiable disease in the former Yugoslav Republic of Macedonia. Routine vaccination with one dose of measles-mumps-rubella (MMR) vaccine at the age of 13 months started in 1983 and a two-dose vaccination schedule, with the second dose at the age of seven years (or the year the child first starts school), was implemented in 1997. In 1969 to 1982, before mandatory mumps vaccination was introduced, the number of mumps cases in the country ranged from 2,143 (in 1969) to 8,436 (in 1979) (Figure 1). After the introduction in 1983 of mandatory single-dose MMR vaccination, the incidence of mumps decreased until 1996, with notifications falling from a high of 5,161 (in 1986) to 1,016 (in 1988). Until the outbreak described here, the last reported outbreak occurred in 1996, with 4,321 cases.

From 1997, when vaccination with a second dose of MMR vaccine was introduced in the country, the number of reported mumps cases decreased substantially, with a mean of 218 notifications per year during 1997 to 2006. The number of notifications fell from a high of 441 (in 2001) to 49 (in 2006).

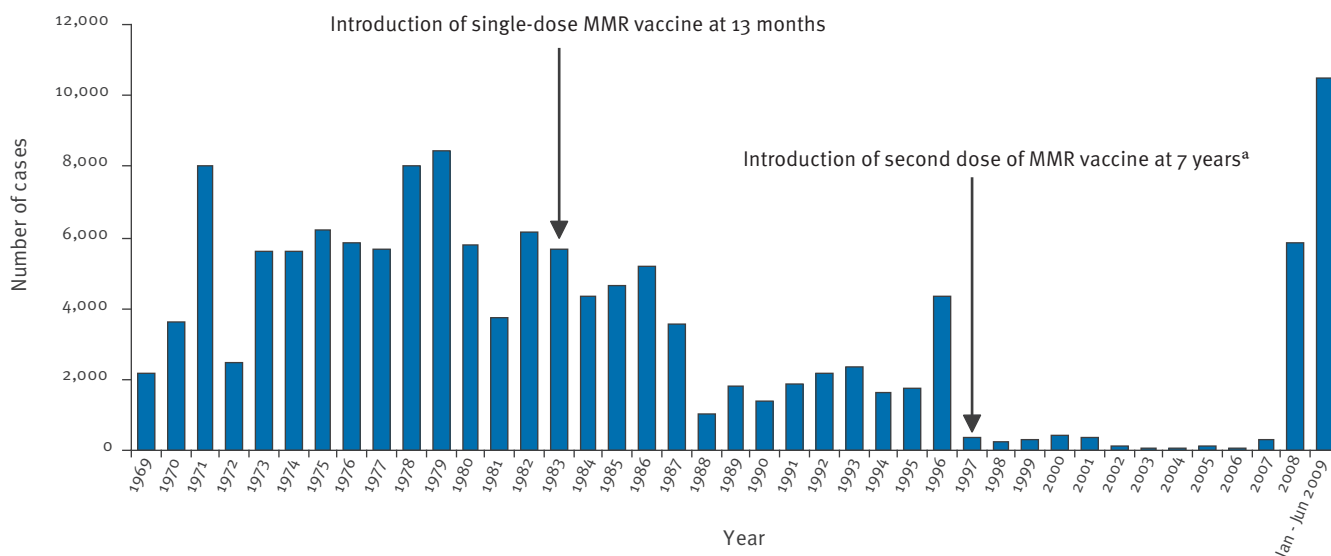
During 1969 to 1983, 94.8% of mumps cases were in children aged 0–14 years. The most affected age group was 0–6 years, comprising 49.5% of all cases, followed by the 7–9 years age group (28.8%) and 10–14 years

age group (16.5%). After the introduction of a single dose of MMR vaccine, during 1984 to 1996 the age distribution of cases shifted to slightly older age groups: the age group 0–6 years accounted for 28.4% of notified cases, 7–9 years for 25.8%, 10–14 years for 30.6% and 15–19 years for 12%. In the previously reported outbreak in 1996, 52.6% of notified mumps cases were aged 15–19 years.

In October 2007, the number of reported mumps cases began to increase (n=25). The number rose substantially in 2008 (with 5,865 cases that year) and continued to increase until February 2009 (in January – February 2009, there had been 4,561 cases). The number of reported cases then began to fall. In this report, we analyse the outbreak from January 2008 to June 2009 (during which time 16,352 cases had been reported).

**FIGURE 1**

Annual notification of mumps cases, former Yugoslav Republic of Macedonia, January 1969 – June 2009 (n=137,993)

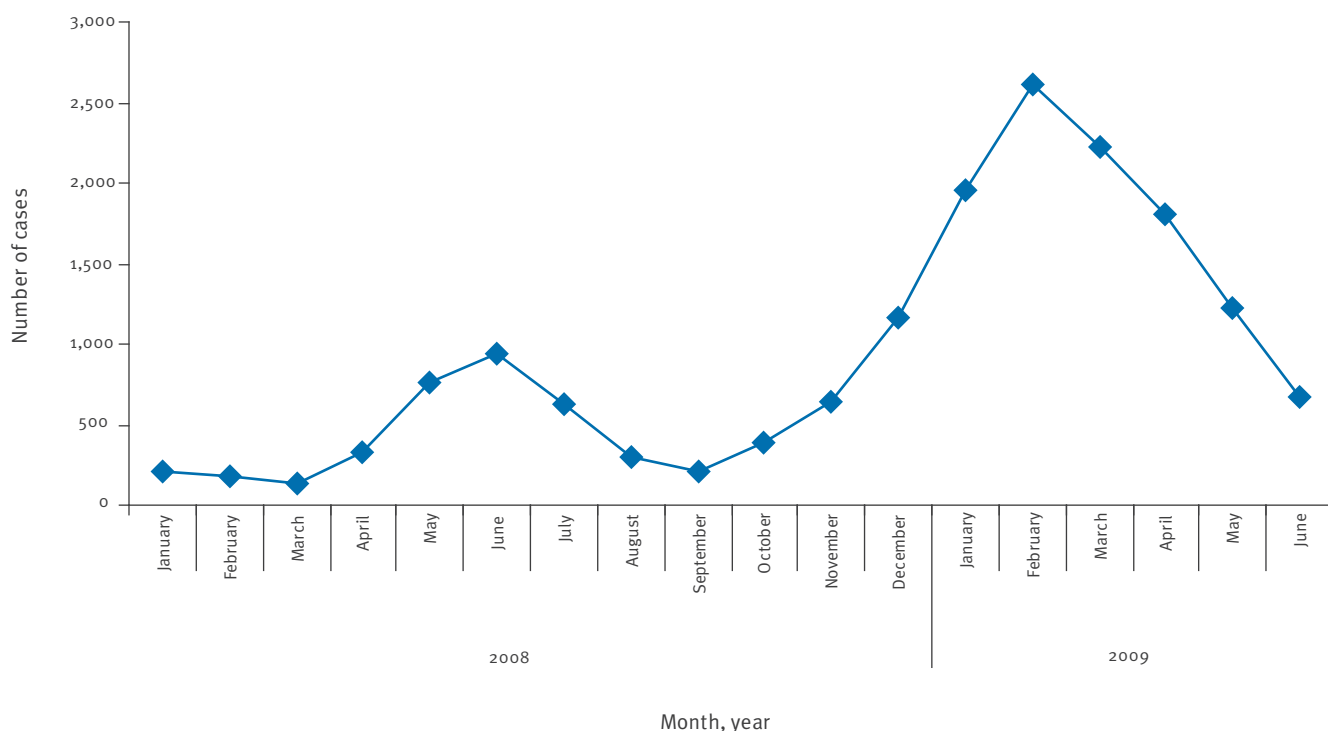


Jan: January; Jun: June; MMR: measles-mumps-rubella.

<sup>a</sup> Or the year the child starts school.

**FIGURE 2**

Monthly notification of mumps cases, former Yugoslav Republic of Macedonia, January 2008 – June 2009 (n=16,352)



## Methods

### Mumps surveillance in the former Yugoslav Republic of Macedonia

Notifications from general practitioners and hospital clinicians are collected by public health centres. The country's surveillance system for communicable diseases requires each of the 10 regional public health centres to notify the national Institute of Public Health of mumps cases that meet the clinical classification, are laboratory confirmed or are epidemiologically linked with a laboratory-confirmed case. The Institute of Public Health then enters the details into a national database.

As a result of the increased number of reported mumps cases, the Ministry of Health issued an order in December 2007 for enhanced mumps surveillance in the country, as recommended by the Commission for Communicable Diseases. Enhanced surveillance included strengthening the control of mumps case reporting (by increasing the number of visits of the Health Inspectorate to general practitioners to ensure timely and complete reporting) and field visits of

epidemiologists to find and vaccinate susceptible children (i.e. those who had not been vaccinated with MMR vaccine or had been partially vaccinated or those who had no record of MMR vaccination and had no medical record of previous mumps infection). School absence, was also monitored. In addition, on entry into primary or secondary school, children had to have proof of MMR vaccination, or medical proof of previous mumps infection.

In January 2008, as part of the country's enhanced surveillance of mumps, the Institute of Public Health recommended that epidemiologists and public health workers from the public health centres examine the vaccination records of each notified mumps case. These records were the cases' personal vaccination cards and vaccination registers, both of which were kept at the vaccination sites.

In addition to regular notification, from January 2008 to September 2009, public health centres also reported mumps cases on separate forms, which were then sent

**TABLE 1**

Notified mumps cases and incidence by health region, former Yugoslav Republic of Macedonia, January 2008 – June 2009 (n=16,352)

Health region	2008		2009	
	Incidence/100,000 population	Number of notified cases	Incidence/100,000 population	Number of notified cases
Bitola	167	313	177	331
Kocani	646	728	473	533
Ohrid	10	15	53	82
Prilep	223	262	1,016	1,193
Kumanovo	318	553	416	723
Skopje	112	659	626	3,698
Stip	606	608	660	662
Strumica	1,267	1,332	472	496
Tetovo	6	20	578	1,799
Veles	728	1,375	513	970
<b>Total</b>	<b>287</b>	<b>5,865</b>	<b>514</b>	<b>10,487</b>

**TABLE 2**

Mumps cases by age group and sex, former Yugoslav Republic of Macedonia, January 2008 – June 2009 (n=16,352)

Age (years)	Number of cases (%)	Cumulative incidence/ 100,000 population	Sex	
			Male	Female
0–4	283 (1.7)	231	170	113
5–9	805 (4.9)	562	493	312
10–14	3,080 (18.8)	1,921	1,869	1,211
15–19	7,876 (48.2)	4,761	4,764	3,112
20–24	2,220 (13.6)	1,371	1,460	760
25–34	1,381 (8.4)	458	891	490
35–44	392 (2.4)	132	192	200
45–54	220 (1.3)	81	128	92
55–64	60 (0.4)	32	25	35
≥65	35 (0.2)	16	21	14
<b>Total</b>	<b>16,352 (100)</b>	<b>809</b>	<b>10,013</b>	<b>6,339</b>

to the Epidemiology Department at the Institute of Public Health as aggregate weekly numbers, showing year of birth and vaccination status.

Data on cases notified through the regular surveillance system and enhanced surveillance of mumps cases were analysed using Microsoft Excel and SPSS v16.

Coverage data for MMR vaccination were obtained from the archives of the Institute of Public Health and from annual coverage reports from the Department for Monitoring of Immunization at the Institute of Public Health. The data come from vaccination sites on the number of children eligible for vaccination and the number vaccinated in the calendar year. The information collected by the public health centres is sent to the Institute of Public Health, where national, regional and subregional coverage is then estimated for each vaccine in the calendar year, for inclusion in a national database.

## Results

In October 2007, a substantial rise in the number of mumps notifications was seen, compared with the means for the previous five years. A total of 284 cases were registered in 2007; 71.8% of these (n=204) were registered in the last three months of the year. The first cases reported were young Roma adolescents and, in November 2007, cases were reported among young adults in the general population by the regional public health centres in Bitola and Prilep, where the first two local outbreaks were reported. The cases reported in 2007 were not included in our analysis, as we had very limited information on their vaccination status.

In 2008, a total of 12 local outbreaks were reported from six health regions, with a total of 5,865 cases. The peak of the first wave of the outbreak was observed in June 2008 (n=942). The number of notifications then started to decrease in July and August 2008, possibly because of schools' summer vacation. With the start of the following school year, the number of mumps notifications started to rise again, with a mean monthly increase of 66.8% until February 2009, when the highest number of monthly notifications was received (n=2,602).

By the end of June 2009, nine of the 10 regional public health centres had reported outbreaks, with a total of 10,487 cases – exceeding previous annual numbers of mumps cases in the country (Figure 1).

From March to June 2009, the number of new notifications decreased each month: 2,231 in March, 1,802 in April, 1,223 in May and 670 in June (Figure 2).

## Geographical distribution of mumps cases

Of the mumps cases reported between January 2008 and June 2009, 89.5% (n=14,635) were from urban areas and 10.5% (n=1,717) from rural regions. In 2008, the highest mumps incidence (1,267 per 100,000

population) was registered in the health region of Strumica in the east and central part of the country, followed by Veles (728 per 100,000 population), Kocani (646 per 100,000 population) and Stip (606 per 100,000 population). In 2009, the epidemic shifted to the north-west of the country, with the highest incidence registered in Prilep (1,016 per 100,000 population), Stip (659 per 100,000 population), Skopje, the capital city (626 per 100,000 population) and Tetovo (578 per 100,000 population) (Table 1).

## Age and sex distribution of mumps cases

Some 61.2% (n=10,013) of all notified mumps cases in the January 2008 to June 2009 outbreak were male; 38.8% (n=6,339) were female (Table 2). Their ages ranged from 0 to 89 years (mean: 18 years; median: 17 years). The most affected age group (15–19 years) accounted for 48.2% of all mumps cases in the outbreak and had the highest cumulative incidence (4,761 per 100,000 population). Patients aged 10–14 years accounted for 18.8% of cases, with a cumulative incidence of 1,921 per 100,000 population and the 20–24 years age group had 13.6% of cases, with a cumulative incidence of 1371 per 100,000 population (Table 2).

## Vaccination status of mumps cases

From regional and local public health centres, the Institute of Public Health received information on vaccination status for 86.7% (n=14,178) of all notified mumps cases (n=16,352). Of cases whose vaccination status had been checked, 19.5% (n=2,764) had not been vaccinated, 37.0% (n=5,243) had been vaccinated with one dose of MMR or other mumps-containing vaccine, 34.4% (n=4,880) had been fully vaccinated with two doses of MMR or other mumps-containing vaccine, 0.6% (n=85) had been vaccinated with MMR in the catch-up vaccination for 15–26-year-olds and there were no vaccination records for 8.5% (n=1,206) (Table 3). For 13.3% (n=2,174) of all notified cases, the Institute of Public Health did not receive any information regarding vaccination status.

Of the cases who had been eligible for two-dose MMR vaccination (i.e. those born from 1990 to 2001) and whose vaccination status had been checked (n=9,693), 7% (n=680) had not been vaccinated, 35.2% (n=3,411) had been vaccinated with one dose of MMR or other mumps-containing vaccine, 48.9% (n=4,745) had been vaccinated with two doses of MMR or other mumps-containing vaccine, 0.8% (n=75) were vaccinated in the MMR catch-up vaccination and for 7.8% (n=761) there were no data on vaccination status (Table 3).

Of the cases with checked vaccination status, 44.7% (n=3,157) of those born from 1990 to 1994 (i.e. aged 15–19 years) received both doses and 39.2% (n=2,764) received only one dose, while of cases born from 1995 to 1999 (i.e. aged 10–14 years), 62.2% (n=1,481) received both doses and 23.1% (n=550) received one dose. Of the cases born from 1982 to 1989 – who had

been eligible for only one dose of MMR vaccine – 53.3% (n=1,413) had been vaccinated (Table 3).

The January 2008 to June 2009 outbreak started and incidence was highest among people born in 1991 to 1994: of the cases whose vaccination status was checked (n=14,178), 45.6% (n=6,466) were born in this period; people born in 1992 alone accounted for 15.6% (n=2,216) (Table 3). The lowest coverage with MMR or

other mumps-containing vaccine (35.1%) was registered in 1993 (i.e. coverage of people born in 1992) and in 1992 (52.9% coverage, of people born in 1991), as a result of vaccine shortages.

As a result of shortage of MMR vaccine in 1993, monovalent measles vaccine was used in most of the country; only in some parts were a bivalent measles–mumps vaccine or monovalent mumps and measles

**TABLE 3**

Vaccination status of mumps cases<sup>a</sup> with checked vaccination records by year of birth, former Yugoslav Republic of Macedonia, January 2008 – June 2009 (n=14,178)

Year of birth	Number of cases vaccinated with two doses of MMR vaccine <sup>b, c</sup>	Number of cases vaccinated with one dose of MMR vaccine <sup>b</sup>	Number of cases vaccinated in catch-up MMR vaccination	Number of cases not vaccinated	Number of cases with no vaccination records	Total (%)
≤1978	0	7	0	864	29	900 (6.3)
1979	1	2	0	91	5	99 (0.7)
1980	1	4	0	125	9	139 (1.0)
1981	3	12	0	134	7	156 (1.1)
1982	2	70	0	74	21	167 (1.2)
1983	6	73	1	65	28	173 (1.2)
1984	10	121	0	76	41	248 (1.7)
1985	11	165	0	86	50	312 (2.2)
1986	9	173	0	77	40	299 (2.1)
1987	12	223	0	113	54	402 (2.8)
1988	21	299	0	124	63	507 (3.6)
1989	50	289	9	133	62	543 (3.8)
1990	131	285	3	101	69	589 (4.2)
1991	550	710	19	120	116	1,515 (10.7)
1992	846	1,025	35	158	152	2,216 (15.6)
1993	858	491	14	104	130	1,597 (11.3)
1994	772	253	3	40	70	1,138 (8.0)
1995	553	167	0	49	61	830 (5.9)
1996	359	145	0	31	56	591 (4.2)
1997	252	104	1	29	28	414 (2.9)
1998	182	76	0	14	34	306 (2.2)
1999	135	58	0	22	26	241 (1.7)
2000	70	44	0	12	9	135 (1.0)
2001	37	53	0	21	10	121 (0.9)
2002	6	109	0	20	13	148 (1.0)
2003	1	96	0	14	10	121 (0.9)
2004	1	77	0	12	9	99 (0.7)
2005	1	55	0	12	1	69 (0.5)
2006	0	37	0	11	3	51 (0.4)
2007	0	19	0	20	0	39 (0.3)
2008	0	1	0	12	0	13 (0.1)
Total (%)	<b>4,880</b> (34.42)	<b>5,243</b> (36.98)	<b>85</b> (0.60)	<b>2,764</b> (19.49)	<b>1,206</b> (8.51)	<b>14,178 (100.0)</b>

MMR: measles-mumps-rubella.

<sup>a</sup> Only mumps cases for which the Institute of Public Health received information regarding vaccination status.

<sup>b</sup> Or other mumps-containing vaccine.

<sup>c</sup> Some of the cases born in 1979 to 1989 are reported to have received two doses since in some parts of the country, single dose MMR vaccination started before 1983 and introduction of a second dose started before 1997. Some of the cases born in 2002, started school earlier than usual (at the age of six years), and so were vaccinated with two doses. Some cases born in 2003 to 2005 are reported to have received two doses of MMR vaccine: the reason for this is unknown.

vaccines used. Children who did not receive MMR vaccine in 1992 were scheduled for vaccination (and thus eligible) in 1993, so the denominator was much higher than usual. In order to estimate the coverage of vaccination with a mumps-containing vaccine in 1993, we took as denominator all children eligible for MMR vaccine (including those not vaccinated in 1992 and scheduled for vaccination in 1993) and as nominator only those who had received a mumps-containing vaccine. This calculation leads to a very low vaccination coverage of 35.1%.

Coverage of MMR or other mumps-containing vaccine was also low (75.6%) in 1994 (in people born in 1993) and in 1996 (in people born in 1995), with coverage of 88% (Figure 3). However, the number of mumps cases was also high in people born in 1995–1999 ( $n=2,382$  with checked vaccination status), despite high vaccination coverage (mean for the first dose: 95.0%; mean for the second dose: 95.5%).

During the field visits conducted in the affected regions in 2008 and 2009, the team from the Institute of Public Health identified some oversights in immunisation records from the years in which there had been a shortage of MMR vaccine (1992–1997). It was

recorded on some cases' vaccination cards that they had received MMR vaccine when in fact they had not. In the vaccination card, the date of vaccination and vaccine serial number are recorded (in the MMR field of the card). However, in some cases, the serial number corresponded to a monovalent measles vaccine or a bivalent measles–mumps vaccine. The extent of these oversights is hard to quantify, but it is possible that, for people born in 1991 to 1996, the proportion of mumps cases vaccinated with one or two doses of MMR or other mumps-containing vaccine could be smaller than reported and could therefore lead to overestimates of the proportion of cases vaccinated against mumps.

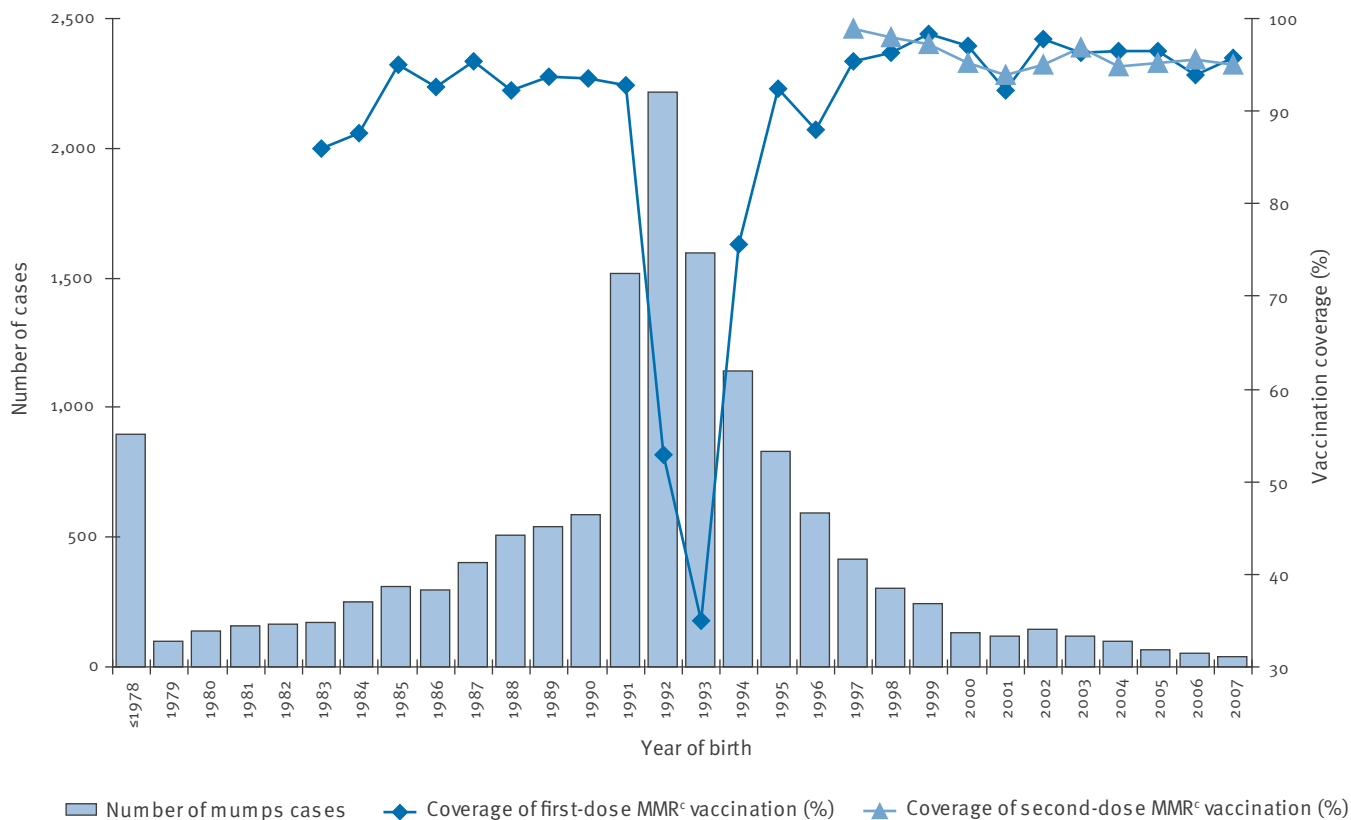
### Catch-up MMR vaccination

The Ministry of Health ordered that from December 2007 susceptible children aged up to 14 years should be found and vaccinated with two doses of MMR vaccine in accordance with the country's immunisation requirements. As part of the anti-epidemic measures, children entering primary or secondary school had to have evidence of vaccination against mumps or medical records of past mumps infection.

In March 2008, the Institute of Public Health recommended MMR catch-up vaccination to the Committee

**FIGURE 3**

Vaccination coverage<sup>a</sup> and number of mumps cases<sup>b</sup>, former Yugoslav Republic of Macedonia, January 2008 – June 2009 ( $n=14,178$ )



MMR: measles-mumps-rubella.

<sup>a</sup> Vaccination coverage is presented by calendar year. For example, coverage with the first MMR dose in 1993 refers to the 1992 birth cohort, etc.; coverage with the second MMR dose in 2008 refers to the 2001 birth cohort, etc.

<sup>b</sup> Only mumps cases for which the Institute of Public Health received information regarding vaccination status.

for Communicable Diseases at the Ministry of Health. In February 2009, the Ministry of Health ordered mandatory additional, catch-up vaccination of susceptible people (those unvaccinated, vaccinated with one dose of a mumps-containing vaccine, or with no record of vaccination) aged 15–19 years. In March 2009, non-mandatory MMR vaccination was offered free of charge to people aged 20–26 years.

During 2 February to 31 May 2009, 58,351 people were vaccinated with MMR through this catch-up vaccination; 90.5% of them (n=52,795) were aged 15–19 years (Table 4).

After the start of the catch-up vaccination, the number of new mumps notifications started to decrease especially among people in the 15–19 years and 20–29 years age groups. However, mumps incidence among children aged 10–14 years remained at same level until June 2009, when the number of mumps notification in

this age group decreased by 34.3% compared with the previous month (Figure 4).

### Clinical complications in mumps cases

In January to June 2009, clinical complications from mumps infection were reported in 6.1% (n=641) of all registered cases. Of these, 39% (n=250) had manifestations of orchitis, 4.7% (n=30) were diagnosed with meningitis, pancreatitis occurred in 0.8% (n=5), while 55.5% (n=356) were hospitalised due to more severe manifestation of mumps infection.

### Mumps virus genotype

In February 2009, 68 biological specimens (serum, saliva and urine) from 20 mumps cases aged 15–19 years were sent to the National Institute for Public Health and the Environment, (RIVM) in the Netherlands for genotyping. Of these, 45% nine had received two doses of MMR vaccine, five had one dose, one had not been vaccinated and for five, there were no records of vaccination. Mumps viral RNA was detected in the specimens from 17 cases. Sequencing of the amplified small hydrophobic gene showed that all 17 viral isolates were genotype G5.

### Discussion

As in many other European countries [3-7], the former Yugoslav Republic of Macedonia has experienced an increase in mumps notifications, particularly among young age groups (15–26 years). The first such increase was registered in October 2007 and continued in 2008 and 2009. In the first six months of 2009, mumps incidence was highest in people aged 15–19 years (birth cohort 1990–1994), accounting for almost half of the cases notified during the outbreak.

**TABLE 4**

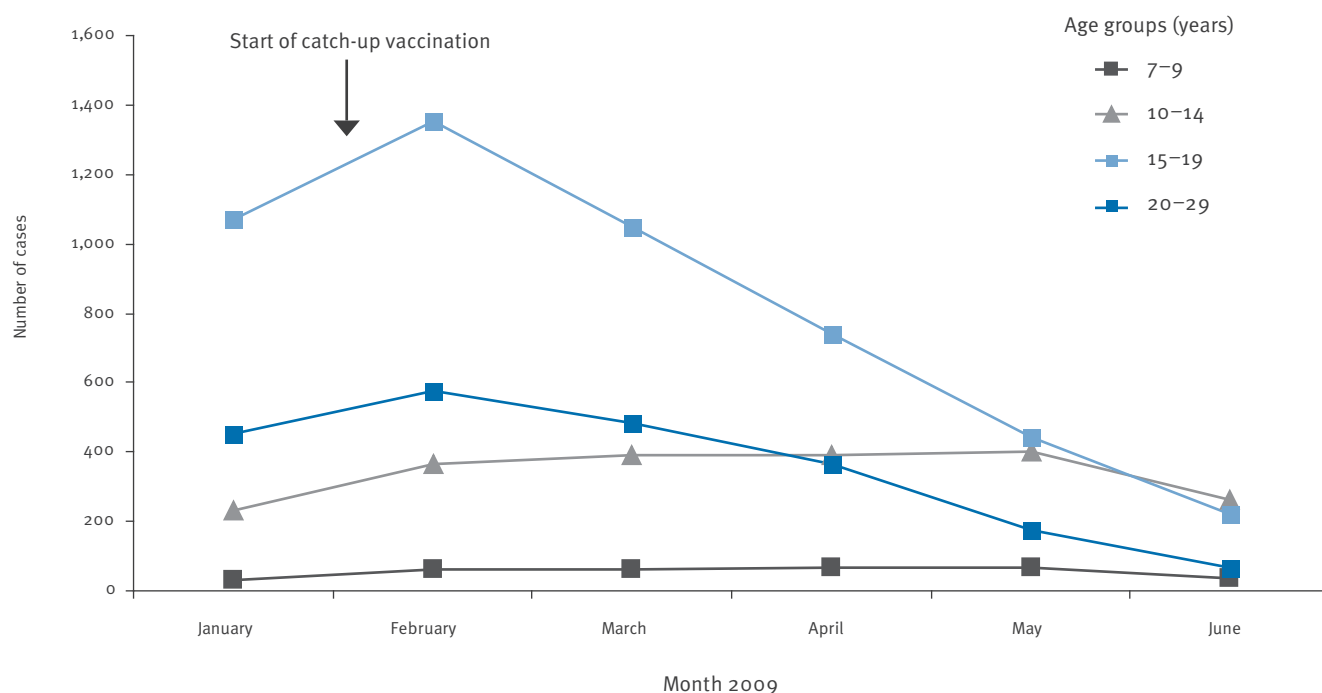
Number of people vaccinated in the catch-up MMR vaccination by age group, former Yugoslav Republic of Macedonia, 2 February – 30 May 2009 (n=58,351)

Age group (years)	Number of people vaccinated
8–9	508
10–14	2,071
15–19	52,795
20–26	2,977
<b>Total</b>	<b>86,592</b>

MMR: measles-mumps-rubella.

**FIGURE 4**

Monthly number of mumps cases by age group, former Yugoslav Republic of Macedonia, January – June 2009 (n=10,487)



Several factors may have contributed to the clustering of cases in this age group. The first is the low vaccination coverage in this cohort (mean: 69.8% for the first dose of MMR or other mumps-containing vaccine).

Another factor might be extended close contacts between young adults (in classrooms and dormitories, etc.), which could facilitate the transmission of mumps, which is spread by direct contact or airborne droplets [10]. Late implementation of the catch-up MMR vaccination for people aged 15–26 years may also have contributed to case clustering.

Waning immunity [8, 9] cannot be excluded. In the cases aged 15–19 years (born 1990–1994) – the most affected age group – the time from the last dose of mumps-containing vaccine to infection was 8–12 years. Waning immunity might also be relevant in cases born between 1982 and 1989, who had been eligible for only one dose of MMR vaccine. For these people, the time from the last dose of MMR vaccine was 19–26 years. Additionally, in this group, 53.3% (n=1,413) (of cases with checked vaccination status) had been vaccinated, but as demonstrated elsewhere [10], protection after one dose of MMR vaccine varies from 65% to 90%.

In the epidemic, 18.8% (n=3,080) of cases were people aged 10–14 years (birth cohort 1995–1999). Of those with checked vaccination status, 1,481 (62.2%) had been vaccinated with two doses of MMR vaccine. The reasons for the outbreak in this age group are unknown.

Possible failures in the vaccine cold chain could also have contributed to lower vaccine efficacy in the affected age groups eligible for one or two doses of MMR vaccine.

### Virus genotype

Viral isolates from 17 cases were shown to be genotype G5: viruses of this genotype had been responsible for mumps outbreaks in the United Kingdom (in 2003–2008), United States, Canada (in 2005–2006) and Moldova (in 2008) [4].

### Type of mumps vaccine

Data on the vaccine types used during 1982 to 1999 were incomplete, making it impossible to correlate the vaccine type and number of cases. Before 2000, each public health centre was responsible for the procurement of vaccines. However, records of the manufacturers and vaccine types used during 1982 to 1999 were incomplete. Only three public health centres could show records of the vaccine type used: an MMR vaccine manufactured by the Institute of Immunology in Zagreb, Croatia. From 1992, due to conflicts in the Balkans, vaccines were largely supplied through humanitarian aid; however, records on vaccine types used were again partial. From 2000, the Ministry of Health became responsible for the procurement and

distribution of vaccines to all public health centres in the country.

### Conclusion

What remains to be explained is the high incidence of cases in people aged 10–14 years (born from 1995 to 1999), despite high coverage of two-dose MMR vaccination, especially as the time to their second dose of MMR vaccine would have been no longer than seven years. Further studies are needed to measure seroconversion rates after MMR vaccination among different age groups, as are other studies to analyse possible vaccination failure.

In order to prevent future outbreaks of vaccine-preventable diseases, high vaccine coverage must be maintained and timely catch-up vaccination carried out if gaps in vaccination coverage are identified.

In order to improve surveillance of communicable diseases, especially vaccine-preventable diseases, in the former Yugoslav Republic of Macedonia, further training of health workers regarding recording and reporting of vaccinations is necessary. In addition, data on communicable diseases and vaccination history should be recorded electronically.

### Acknowledgements

We would like to express our gratitude to the epidemiologists and other health workers from the public health centres and vaccination sites for their dedicated work during this outbreak and for collecting data on the mumps cases. The contribution of biologist Elizabeta Janceska to the laboratory work is acknowledged.

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