

MONITORING THE EFFECT OF VACCINATION ON MUMPS CASES COMPLICATIONS IN THE CZECH REPUBLIC - SURVEILLANCE DATA 2013-2022

SPREMLJANJE UČINKA CEPLJENJA NA ZAPLETE PRI PRIMERIH MUMPSA NA ČEŠKEM - NADZORNI PODATKI 2013-2022

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ABSTRACT

Introduction: Mumps data were analysed to assess the effect of vaccination on mumps complications and hospitalisation.

Keywords:

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Mumps complications
Orchitis
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Vaccination
Vaccine effectiveness

Methods: The mumps cases reported to the Czech nationwide surveillance system from 2013 to 2022 were analysed using logistic regression with an odds ratio (aOR) adjusted for age, sex, year of onset and administrative region to measure the association between vaccination and complications or hospitalisation. Adjusted vaccine effectiveness (aVE) was calculated: $aVE = (1 - aOR) \times 100$.

Results: A total of 11,913 mumps cases were reported, of which 6,885 (58%) were male. The median age of the study participants was 16 (range: 0-89 years). No complications occurred in 91% of patients. Mumps orchitis occurred in 633 (9%) male cases. A total of 946 (8%) patients required hospitalisation. The highest proportion of complications and hospitalisations was in the age group 35-44 years. Two doses of vaccine reduced statistically significantly the risk of any complications and of hospitalisation compared with unvaccinated patients: aOR 0.48 (95% CI: 0.37, 0.62), aVE of 52% (95% CI: 38, 63); and aOR 0.43 (95% CI: 0.33, 0.56), aVE of 57% (95% CI: 44, 67), respectively. Two doses showed statistically significant aVE 50% (95% CI: 32, 64) against orchitis, and 59% (95% CI: 23, 79) against meningitis. Among the two-dose recipients, the proportion of complications increased gradually with the time from the second dose.

Conclusions: Our findings demonstrated a protective effect of two-dose vaccination against mumps complications and hospitalisation for mumps. We recommend continuing routine childhood mumps vaccination and maintaining high MMR coverage in Czechia.

IZVLEČEK

Uvod: Analizirali smo podatke o mumpsu, da bi ocenili učinek cepljenja na zaplete in hospitalizacijo zaradi mumpsa.

Ključne besede:

mumps
zapleti
hospitalizacija
cepljenje
učinkovitost cepljenja

Metode: Primere mumpsa, ki so bili v obdobju 2013-2022 prijavljeni v državni sistem nadzora na Češkem, smo analizirali z logistično regresijo z razmerjem obetov (aOR), prilagojeno glede na starost, spol, leto začetka in upravno regijo, da bi ugotovili povezavo med cepljenjem in zapleti ali hospitalizacijo. Izračunali smo prilagojeno učinkovitost cepiva (aVE): $aVE = (1 - aOR) \times 100$.

Rezultati: Skupaj je bilo prijavljenih 11.913 primerov mumpsa, od tega 6885 (58 %) pri moških. Povprečna starost udeležencev v študiji je bila 16 let (razpon: 0-89 let). Pri 91 % bolnikov ni prišlo do zapletov. Mumps orchitis se je pojavil pri 633 (9 %) moških. Skupaj je 946 (8 %) bolnikov potrebovalo hospitalizacijo. Največji delež zapletov in hospitalizacij je bil v starostni skupini 35-44 let. Dva odmerka cepiva sta statistično pomembno zmanjšala tveganje za nastanek morebitnih zapletov in hospitalizacijo v primerjavi z necepljenimi bolniki: aOR 0,48 (95 % IZ: 0,37, 0,62), aVE 52 % (95 % IZ: 38, 63) in aOR 0,43 (95 % IZ: 0,33, 0,56), aVE 57 % (95 % IZ: 44, 67). Dva odmerka sta pokazala statistično pomembno aVE 50 % (95 % IZ: 32, 64) v primerjavi z orchitisom in 59 % (95 % IZ: 23, 79) v primerjavi z meningitisom. Delež zapletov med prejemniki dveh odmerkov se je postopoma povečeval s časom od drugega odmerka.

Zaključki: Naše ugotovitve so pokazale zaščitni učinek cepljenja proti zapletom in hospitalizaciji zaradi mumpsa. Priporočamo nadaljevanje rutinskega cepljenja otrok proti mumpsu in ohranjanje visoke stopnje precepljenosti s cepivom OMR na Češkem.

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1 INTRODUCTION

Mumps is a viral respiratory infection caused by an RNA virus of the family *Paramyxoviridae*, genus *Rubulavirus* (1). The disease starts with nonspecific prodromal symptoms: malaise, fever, myalgia, headache and anorexia (1). The common course of the disease is acute parotitis in up to 70% of cases. The following complications may occur: orchitis (the most frequent complication), oophoritis, meningitis, encephalitis, pancreatitis, myocarditis, deafness and so forth (1). Asymptomatic and subclinical mumps infections can account for up to 20% of all infections (2). The incubation period is 16-19 days (range 12-25 days) (1). Mumps is transmitted by droplet spread and by direct contact with the saliva of an infected person (1).

It belongs to notifiable diseases only in some countries. The global annual number of reported cases in the years 1999-2022 ranged from 169,799 in 2019 to a maximum of 726,638 in 2011, based on the World Health Organization (WHO) Global Health Observatory data repository (3).

The incidence of mumps per 100,000 population reported in the European Union/European Economic Area (EU/EEA) in 2013-2021 decreased from 5.9 in 2013 to 0.4 cases in 2021. The most recent EU/EEA data available before the COVID-19 pandemic in 2018 show an incidence of 2.6 cases/100,000 population, and a higher proportion of cases occurred in males in all age groups. Hospitalisations and complications due to mumps in 2018 were rare (4.5% and 6.5%, respectively), with no deaths reported. The Czech Republic (CZ) belonged to those EU/EEA countries with the highest notification rate in 2018 (5.1 cases/100,000 population). In 2021, 1,567 cases of mumps were reported by 27 EU/EEA Member States, with an overall notification rate of 0.4 cases/100,000 population. This was significantly lower than the notification rates reported during the previous four years (range 1.7-4.2). In 2022, 27 EU/EEA countries reported 2,593 mumps cases, with an overall notification rate of 0.7 cases/100,000 population (4).

1.1 Surveillance of mumps in CZ

According to Czech national legislation, mumps is a mandatorily notifiable disease (5). The current mumps surveillance system in CZ is comprehensive, nationwide, case-based and harmonised with the EU case definition 2008 requirements. General practitioners and physicians from hospitals report cases to the Regional Public Health Authority (RPHA). The RPHA collects information on individual mumps cases, performs epidemiological investigation and uploads the data to the electronic nationwide infectious disease notification system. The National Institute of Public Health (NIPH) collaborates on data validation and analyses and reports them to the European Surveillance System and WHO database.

Mumps belongs to vaccine preventable diseases. A two-dose mandatory vaccination programme covered by public health insurance began in the former Czechoslovakia in 1987 with a bivalent measles-mumps vaccine. The first dose was given at 15 months of age, the second dose 6-10 months after the first dose. In 1995, the trivalent measles-mumps-rubella (MMR) vaccine was introduced nationwide. Since January 2018, the first dose of MMR vaccine has been administered at 13-18 months of age and second dose at 5-6 years of age (6).

The vaccination coverage (VC) has been evaluated annually by administrative surveys. The VC data from a 2019 survey showed that for children born in 2016 and 2017, one-dose MMR VC was 96.55% and 94.41%, respectively. Coverage with the second dose was not available in CZ in 2019 (7). The latest available one-dose MMR VC figure (for 2022) for children aged 2 years born in 2020 in CZ was 87.0%, based on data from health insurance companies (8).

The aim of the study was to assess the effect of vaccination on mumps complications and the need for hospitalisation based on mumps cases reported to the nationwide surveillance system in 2013-2022. Furthermore, the intention was to evaluate the effect of the time interval from the administration of the second dose of vaccine on the development of complications.

2 METHODS

2.1 Study population and data sources

Pseudonymised data were retrieved from the Czech electronic nationwide infectious disease surveillance systems EpiDat (until 2017) and ISIN (from 2018). The surveillance system contains mumps data reported as confirmed cases (meeting the laboratory criteria), probable cases (meeting the clinical criteria with an epidemiological link) and possible mumps cases (meeting the clinical criteria). All reported mumps cases were included in this study regardless of their case classification (confirmed, probable and possible case). All cases were checked for duplicity and data integrity.

A case was defined as any patient with clinical presentation of mumps reported to the surveillance system under the code "B26" of the 10th Revision of International Classification of Diseases in the ten-year period 2013-2022 according to the date of disease reporting. A case was defined as vaccinated if the patient received at least one dose of mumps vaccine more than 25 days before the symptoms onset, which we decided based on the incubation period and at least partial onset of immunity after vaccination.

Incidence was calculated based on mid-year population data published by the Czech Statistical Office (9, 10).

2.2 Data analysis

Mumps cases were described in terms of age, sex, year of reporting, administrative region (third level of the Nomenclature of Territorial Units for Statistics - "NUTS 3" was used), vaccination history and disease severity by complications and hospitalisation. The vaccination history included vaccination status, number of doses and the date of vaccination. Epidemiological characteristics of the cases were analysed using absolute and relative frequencies. Fisher's exact test was used to examine the significance of the association between the two characteristics.

To assess the effect of vaccination on the occurrence of mumps complications and hospitalisation in those fully vaccinated with two (or three) doses of MMR vaccine, partially vaccinated with one dose of MMR vaccine and unvaccinated mumps cases were compared.

Simple and multiple logistic regression models were used to assess the relationship between vaccination status and selected mumps complications or hospitalisation. They resulted in unadjusted odds ratios (OR) and odds ratios adjusted for age, sex, year of onset and NUTS 3 (aOR). In the case of separation problems related to small numbers of observations in some subcategories, the logistic regression model was fitted using the Firth's bias reduction method (11). The adjusted vaccine effectiveness (aVE) was computed as $aVE = (1 - aOR) \times 100$. Point estimates for odds ratio and vaccine effectiveness were supplemented with 95% confidence intervals (95% CI). Cases with an unknown vaccination status and vaccinated cases with an unknown number of vaccine doses were excluded from the analytical part of the study.

The risk of mumps complications was evaluated using logistic regression in relation to the time between the date of the vaccination with the second dose of MMR vaccine and the onset of disease and age at the second dose. The time interval from the second dose to disease onset was divided into five-year periods.

Findings with p-values less than 0.05 were considered statistically significant. Statistical analyses were performed in STATA, version 17 (StataCorp LLC, College Station, Texas, USA).

3 RESULTS

3.1 Descriptive analysis

Over the ten-year study period the mumps cases in CZ were distributed unevenly (Table 1). The incidence of reported mumps cases per 100,000 population ranged from 0.4 to 54.3. The highest morbidity was reported in 2016, followed by a significant decline in subsequent years. The total of 11,913 mumps cases was reported within the study period. Of these, 6,885 (58%) were males. The mean age at disease onset was 18.3 years, median age 16 years

(range 0-89 years). The age groups 10-14 and 15-19 years were the most affected. Cases were reported from all fourteen CZ regions, with the highest incidence in the South Bohemian Region (Table 1).

In total, 40% of all cases of mumps were laboratory confirmed and 35% were epidemiologically linked to a confirmed case. Possible cases were reported based on typical clinical symptoms in 25% of all cases of mumps. Of the total 11,913 analysed cases, 9,714 (81.5%) were vaccinated, 1,673 (14%) unvaccinated and in 526 (4.4%) cases the status was unknown. Ninety-four percent of those vaccinated were vaccinated with two doses (Table 2).

Ninety-one percent of the cases had no clinical complications. The most frequent complication was orchitis, reported in 633 (9.2%) male patients. Of all the cases, meningitis affected 126 (1.1%), pancreatitis 37 (0.3%) and encephalitis 11 (0.1%). Oophoritis was detected in 8 (0.2%) females. Further, there were 88 (0.7%) other complications and 139 (1.2%) cases had unknown information about mumps complications. Of those with a known hospitalisation status (n=11,844), 946 (7.9%) required hospitalisation (Tables 2 and 3). The proportion of hospitalised patients was significantly higher in males (10.2%) than in females (5.0%), $p < 0.001$. Orchitis was the most common complication in males in age groups 25-34 (31%), 15-19 (25%) and 20-24 (19%) years. The highest proportion of mumps complications and hospitalisations was reported in the age group 35-44 years (22.8% and 19.4%, respectively), followed by the age group 25-34 years (17.5% and 17.0%, respectively). Males accounted for 87.5% of all mumps complications (790/903) and 73.5% of hospitalisations (695/946).

3.2 Effectiveness of MMR vaccination to prevent mumps complications or hospitalisation

Among the mumps cases with complications, 59% reported being vaccinated with two doses of MMR vaccine, while among cases without any complications 85% received two doses of vaccine ($p < 0.001$). Among the hospitalised cases, 62% were vaccinated with two doses, while of those non-hospitalised the rate was 85% ($p < 0.001$). Therefore, two doses of vaccine substantially and significantly ($p < 0.001$) reduced the risk of any complications and the need for hospitalisation compared with unvaccinated patients, resulting in an aOR 0.48 (95% CI: 0.37, 0.62) and an aOR 0.43 (95% CI: 0.33, 0.56), which corresponds to aVE of 52% (95% CI: 38, 63) and 57% (95% CI: 44, 67), respectively. Two doses also showed significant aVE of 50% (95% CI: 32, 64) against orchitis in males, and 59% (95% CI: 23, 79) against meningitis in all cases (Table 4).

Even in single-dose vaccinated cases, a significant reduction in the risk of any complications and the need for hospitalisation was demonstrated, $p < 0.05$.

Table 1. Demographic characteristics of mumps cases, infectious disease surveillance system, Czech Republic, 2013-2022.

	Number of mumps cases (n=11,913)	Proportion (%)	Incidence of mumps cases per 100,000 population and year
Year of onset			
2013	1,553	13.0	14.8
2014	677	5.7	6.4
2015	1,616	13.6	15.3
2016	5,733	48.1	54.3
2017	1,407	11.8	13.3
2018	537	4.5	5.1
2019	191	1.6	1.8
2020	93	0.8	0.9
2021	38	0.3	0.4
2022	68	0.6	0.6
Distribution of cases by administrative region			
Prague	1,041	8.7	8.1
Central Bohemian	853	7.2	6.3
South Bohemian	2,438	20.5	38.1
Plzeň	446	3.7	7.7
Karlovy Vary	274	2.3	9.3
Ústí nad Labem	386	3.2	4.7
Liberec	602	5.1	13.7
Hradec Králové	649	5.4	11.8
Pardubice	821	6.9	15.8
Vysočina	1,642	13.8	32.2
South Moravian	798	6.7	6.7
Olomouc	381	3.2	6.0
Zlín	240	2.0	4.1
Moravian-Silesian	1,342	11.3	11.1
Gender			
Male	6,885	57.8	13.2
Female	5,028	42.2	9.3
Age group (years)			
0	10	0.1	0.9
1-4	269	2.3	6.0
5-9	1,371	11.5	24.1
10-14	3,417	28.7	64.8
15-19	3,142	26.4	65.5
20-24	1,353	11.4	24.8
25-34	1,479	12.4	10.6
35-44	506	4.2	3.0
45-54	214	1.8	1.5
55-64	95	0.8	0.7
65-74	46	0.4	0.4
75+	11	0.1	0.1

Nearly two thirds of the mumps cases complicated with orchitis (409 men) were hospitalised compared with 3% of those hospitalised among the males without mumps complications ($p<0.001$).

Of the 126, 37 and 11 mumps cases with meningitis, pancreatitis and encephalitis, respectively, 97%, 46% and 91% were hospitalised. These proportions were significantly higher in all three situations compared with 3% of hospitalised cases among those with no reported mumps complications, $p<0.001$.

In two-dose vaccine recipients, the proportion of mumps cases with complications increased significantly with the time passed from the second dose of vaccination, $p<0.001$ (Table 5). Each subsequent category of time period is significantly different from the previous one, except for the last category of 25+ years, which shows no significant difference from the category of 20-24 years.

4 DISCUSSION

This study builds on the work of Czech authors confirming the protective effect of MMR vaccination against mumps complications for data covering the period 2007-2012 (12). In our study, teenagers were the most affected age group. This result is in line with studies which have demonstrated that the highest burden of disease is currently among adolescents and young adults (12-15).

Due to the COVID-19 pandemic, it could not be ruled out that some mild mumps cases have not been detected in CZ. Mumps is a respiratory disease, so the implementation of non-pharmaceutical interventions (NPIs) during the COVID-19 pandemic may have influenced and reduced the number of mumps cases reported in CZ; a similar decrease of mumps cases was reported in other countries (4).

Table 2. Vaccination and hospitalisation status of mumps cases, infectious disease surveillance system, Czech Republic, 2013-2022.

	Number of mumps cases	Proportion (%)
Vaccination status (n=11,913)	9,714	81.5
Vaccinated	1,673	14.0
Unvaccinated	526	4.4
Unknown		
Vaccinated by doses (n=9,714)		
1 dose	156	1.6
2 doses	9,134	94.0
3 doses	29	0.3
Unknown number of vaccine doses	395	4.1
Hospitalisation (n=11,913)		
Yes	946	7.9
No	10,898	91.5
Unknown	69	0.6

Several studies confirmed the reduction in the incidence of many communicable diseases, including several vaccine-preventable diseases during the pandemic, most likely due to social distancing, school closures and other NPIs reducing the likelihood of transmission (16-18).

In the last decade, mumps outbreaks were reported in several regions of CZ, with the highest incidence in South Bohemia in 2016 (19). The increase in mumps incidence in the highly vaccinated population in CZ seems to be a consequence of a secondary vaccination failure due to waning immunity over time (20, 21). This view is supported by the fact that in the mumps outbreak in South Bohemia, the age group 15-19 years was the most affected (19-21). The results of the serological surveys from 2013 demonstrated that only 33% of individuals in the age group 15-19 years had mumps antibodies (19, 22). Genotype G, which is predominant in Europe, has also been detected in CZ (20).

The most frequent complication in our study was mumps orchitis, which occurred in 9% of male cases, while in the previous CZ study it was reported in 12% of males. In the current study, a smaller proportion of cases were hospitalised due to the clinical course of the disease (8%) than in the previous CZ study with 12% hospitalised cases (12). We hypothesized that the higher number of hospitalisations in males could be due to the number of reported orchitis cases, which reveals a more severe course of mumps. In a Spanish study, the most frequent complication among hospitalised mumps cases was meningitis (13).

In our study, 19% of the unvaccinated participants had complications, while among one- or two-dose vaccine recipients the rate was about 5%. The reason for that difference is in vaccination status itself.

Table 3. Mumps complications, hospitalisation and vaccination, infectious disease surveillance system, Czech Republic, 2013-2022.

	Mumps vaccination					
	Three doses	Two doses	One dose	Zero doses	Unknown	Total
Total number of cases	29	9,134	156	1,673	921	11,913
Complications						
None	27	8,608	145	1,339	752	10,871
Orchitis ^a	2	312	6	231	82	633
Meningitis	0	69	0	38	19	126
Pancreatitis	0	20	0	13	4	37
Encephalitis	0	3	0	6	2	11
Oophoritis ^b	0	3	0	5	0	8
Other	0	54	1	22	11	88
Unknown	0	65	4	19	51	139
Hospitalisation						
Yes	2	494	8	297	145	946
No	27	8,605	147	1,359	761	10,899
Unknown	0	35	1	17	15	68

Note: ^aonly among males (6,885), ^bonly among females (5,028)

Table 4. Number of cases with mumps complications or hospitalisation by MMR vaccination status and adjusted MMR vaccine effectiveness, Czech Republic, 2013-2022.

Type of complications	Vaccination by number of doses ^b	Number of cases	Number of cases with complications (%)	Unadjusted odds ratio (95% CI)	Adjusted ^c odds ratio (95% CI)	p value	Adjusted ^c vaccine effectiveness % (95% CI)
Any complication	0	1,654	315 (19.0)	Ref	Ref		
	1	152	7 (4.6)	0.21 (0.10, 0.44)	0.42 (0.19, 0.95)	0.036	58 (5, 81)
	2	9,069	461 (5.1)	0.23 (0.20, 0.27)	0.48 (0.37, 0.62)	<0.001	52 (38, 63)
Orchitis ^a	0	967	231 (23.9)	Ref			
	1	92	6 (6.5)	0.22 (0.10, 0.52)	0.57 (0.23, 1.38)	0.213	43 (-38, 77)
	2	5,174	312 (6.0)	0.20 (0.17, 0.25)	0.50 (0.36, 0.68)	<0.001	50 (32, 64)
Meningitis	0	1,654	38 (2.3)	Ref			
	1	152	0 (0.0)	0.14 (0.01, 2.25)	0.18 (0.01, 3.12)	0.240	82 (-212, 99)
	2	9,069	69 (0.8)	0.32 (0.22, 0.48)	0.41 (0.21, 0.77)	0.006	59 (23, 79)
Pancreatitis	0	1,654	13 (0.8)	Ref			
	1	152	0 (0.0)	0.40 (0.02, 6.74)	0.70 (0.03, 14.56)	0.820	30 (-1,356, 97)
	2	9,069	20 (0.2)	0.28 (0.14, 0.55)	0.46 (0.15, 1.44)	0.181	54 (-44, 85)
Hospitalisation	0	1,637	296 (18.1)	Ref			
	1	151	8 (5.3)	0.25 (0.12, 0.52)	0.46 (0.22, 0.97)	0.042	54 (3, 78)
	2	9,034	491 (5.4)	0.26 (0.22, 0.30)	0.43 (0.33, 0.56)	<0.001	57 (44, 67)

Note:

Ref - reference category (unvaccinated)

^a only males, of 6,885 males

^b 29 cases (16 males and 13 females) in three-dose vaccine recipients were not included in the analysis

^c adjusted for age, gender, year of onset and region (NUTS 3)

Table 5. Mumps complications in MMR vaccinated patients by time passed from the second dose, Czech Republic, 2013-2022.

Time from the second dose (in years)	Number of cases	Number of cases with complications	% of mumps cases with complications	Adjusted ^b odds ratio	95% CI	p value
0-4	531	1	0.2	Ref ^a		
5-9	2,283	26	1.1	Ref ^a		
10-14	3,287	151	4.6	5.26	3.45, 8.01	<0.001
15-19	1,981	170	8.6	10.29	6.77, 15.63	<0.001
20-24	734	86	11.7	14.53	9.28, 22.75	<0.001
25+	194	18	9.3	11.30	6.07, 21.06	<0.001
Total	9,010	452	5.0			

Note:

^aRef - reference category 0-9 compounded from two categories: 0-4 and 5-9 years

^bodds ratio adjusted for age at the 2nd dose

Another large retrospective cohort study analysing Korean mumps data reported that only 2% of patients had related complications (less than in our study) and the most reported complication was mumps orchitis among 42% of the males with complications, while meningitis was most frequent among females. The Korean authors concluded that in their study mumps complications were more frequent among males than in females (15) which is in line with our study results, where males accounted for 88% of all the complications.

We found that two doses of vaccine significantly reduced the risk of hospitalisation, corresponding to aVE 57% and the risk of any complication corresponding to aVE 52% in the study period 2013-2022, while in the previous CZ study

the aVE was higher (71% and 68%, respectively) (12). In a large mumps outbreak in the Jerusalem district, authors estimated aVE against complications as 63% and aVE against hospitalisation as 44%, both for two doses of vaccine (23).

Our study results also demonstrated that two doses of vaccine significantly reduced the risk of orchitis and meningitis corresponding to aVE 50% and 59%, respectively. The previous CZ study showed aVE against orchitis of 72% and against meningitis aVE of 64% (12). We used the same methodology as in the previous CZ study, therefore we assume that probably other factors could play a role resulting in a lower aVE in our study, as the proportion of complications was similar in both CZ studies (e.g. the vaccination status by itself, worse quality of the source

data inserted in the notification system). The rate of unknown vaccine status in the two CZ studies (current one and in the years 2007-2012) is not similar. In the current CZ study 4% of mumps cases had unknown vaccination status. In addition, another 4% of cases in the current study had an unknown number of vaccine doses. In a previous CZ study (2007-2012) vaccination status of mumps cases was: 0 doses (17% of cases), 1 dose (<1% of cases), 2 doses (82% of cases) and 3 doses (<1% of cases).

Although mumps incidence was the highest among teenagers, the highest proportion of mumps complications and hospitalisations was reported in the 35-44 years age group. In the Spanish study, hospitalisation and complication rates increased over time in the age group 25-34 years (13).

Among the two-dose recipients, the rate of complications increased from 0 to 12% in the post-vaccination interval categories after the second dose from 0-4 years to 20-24 years, then decreased slightly to 9% at 25+ years. These results of the effect of a time interval after the second dose of the vaccine on the risk of mumps complications are in line with the previous CZ study, when the rate of complications was higher and increased up to 16% (12).

The childhood immunisation programme against MMR in CZ has changed since January 2018, and not enough data for the evaluation of the new schedule was available. As of 31 December 2020, more than 95% of those born in 2017 received at least one dose of the MMR vaccine in different regions. It is important to improve VC with two doses of MMR vaccine, especially in regions with lower VC. The administrative control of vaccination in CZ was cancelled from 1 January 2022 and its results should be replaced by VC estimates obtaining data from health insurance companies (8, 24).

As part of ongoing surveillance, it is necessary to maintain high data quality when entering it in the notification system.

Reporting bias may have been present in our study, especially for the vaccination status variable, which could not be verified as the national vaccination register was launched only in January 2023. In addition, the legislation valid until the end of 2017 did not explicitly state the upper interval at which the first or second dose of MMR vaccine could be administered, therefore it was not possible to distinguish between people vaccinated on or off the immunisation schedule. Therefore, in the analytical study, a person was assessed as vaccinated regardless of the interval between the first and second dose of the immunisation schedule. Since this is a trivalent vaccine, some patients may have been vaccinated for reasons other than MMR vaccination in childhood according to the national schedule (e.g. outbreak of measles in the population, for travel reasons).

Mumps cases are reported through a passive surveillance system, therefore under-reporting cannot be ruled out. Information on hospitalisation is usually recorded at the time of testing and hospitalisations may also have been underreported.

5 CONCLUSIONS

Our findings demonstrated that two doses of vaccine substantially and statistically significantly reduced the risk of any complications and the need for hospitalisation compared with unvaccinated patients. A protective effect of two-dose vaccination against mumps complications in general and against orchitis and meningitis in particular, and against hospitalisation for mumps was confirmed. Teenagers were the most affected age group in terms of incidence, but the highest complications and hospitalisations rates were reported in 35-44 years old. This study showed that the majority of mumps patients did not require hospitalisation. The most frequent complications were orchitis, meningitis, pancreatitis and encephalitis. Among the two-dose recipients, the proportion of complications increased gradually with the time interval after the second dose.

In the future, it will be desirable to evaluate aVE based on a new vaccination register or vaccination data from health insurance companies. To assess the burden of the disease, a seroepidemiological study seems suitable as the last nationwide serological survey of mumps antibodies was performed in 2013. Further monitoring and research are required to evaluate the new MMR vaccination schedule in order to assess if it has been more effective. We recommend continuing routine childhood mumps vaccination and maintaining high MMR coverage in CZ.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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ETHICAL APPROVAL

Ethical approval was not required as in the Czech Republic public health agencies are able to access and use personal identifiable information for communicable disease investigations in the public interest.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study can be obtained upon request from the corresponding author.

AUTHORS CONTRIBUTIONS

All authors listed have contributed to this manuscript and all have read and approved the final version of this manuscript.

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REFERENCES

- Heymann DL. Control of communicable diseases manual. 21st ed. Washington: American Public Health Association; 2022.
- European Centre for Disease Prevention and Control. Facts about mumps [Internet]. 2023 [cited 2024 Feb 16]. Available from: <https://www.ecdc.europa.eu/en/mumps/facts>
- World Health Organization. Global Health Observatory data repository [Internet]. 2024 [cited 2024 Jul 30]. Available from: <https://www.who.int/data/gho/data/indicators/indicator-details/GHO/mumps---number-of-reported-cases>
- European Centre for Disease Prevention and Control. Surveillance and disease data for mumps: Annual epidemiological reports [Internet]. 2021 [cited 2024 Feb 16]. Available from: <https://www.ecdc.europa.eu/en/mumps/surveillance-and-disease-data>
- Ministry of Health of the Czech Republic. Act No. 258/2000 Coll., on the protection of public health and on the amendment with some related Acts. Praha; 2000.
- The National Institute of Public Health. Measles - history of vaccination [Internet]. 2022 [cited 2024 Feb 16]. Available from: <https://szu.cz/tema/a-z-infekce/s/spalnicky/spalnicky-historie-vakcinace/>
- Dlhý J, Kyselý Z, Svrčinová P. Administrative estimate of vaccination coverage in the Czech Republic by 31 December 2019. *Zprávy ČEM*. 2022;31(2):61-75.
- National health information portal. Institute of Health Information and Statistics of the Czech Republic. Central vaccination records: Data summaries. Overview of vaccination coverage of selected vaccines in the Czech Republic [Internet]. 2024 [cited 2024 Jul 30]. Available from: <https://www.nzip.cz/clanek/1703-datove-souhrny-prehled-proockovanosti-vybranych-vakcin-kraje-okresy-cr>.
- Czech Statistical Office. Mid-year population 2013-2017 [Internet]. 2024 [cited 2024 Jul 30]. Available from: https://vdb.czso.cz/vdbvo2/faces/en/index.jsf?page=vystup-objekt-vyhledavani&vyhlText=obyvatelstvo&bkvt=b2J5dmF0ZWxzZHZv&pvo=DEM001D320201&z=T&f=TABULKA&katalog=all&c=v33-3__RP2017&u=v1328__VUZEMI__97__19&str=v1328.
- Czech Statistical Office. Mid-year population 2018-2022 [Internet]. 2024 [cited 2024 Jul 30]. Available from: https://vdb.czso.cz/vdbvo2/faces/en/index.jsf?page=vystup-objekt-vyhledavani&vyhlText=obyvatelstvo&bkvt=b2J5dmF0ZWxzZHZv&pvo=DEM001D320201&z=T&f=TABULKA&katalog=all&c=v33-3__RP2022&u=v1328__VUZEMI__97__19&str=v1328
- Firth D. Bias reduction of maximum likelihood estimates. *Biometrika*. 1993; 80(1):27-38. doi: 10.2307/2336755.
- Orlíková H, Malý M, Lexová P, Šebestová H, Limberková R, Jurzykowska L, et al. Protective effect of vaccination against mumps complications, Czech Republic, 2007-2012. *BMC Public Health*. 2016;16(1):1-10. doi: 10.1186/s12889-016-2958-4.
- López-Perea N, Masa-Calles J, de Mier MDVT, Fernández-García A, Echevarría JE, De Ory F, et al. Shift within age-groups of mumps incidence, hospitalizations and severe complications in a highly vaccinated population. Spain, 1998-2014. *Vaccine*. 2017;35(34):4339-4345. doi: 10.1016/j.vaccine.2017.06.075.
- St-Martin G, Knudsen LK, Engsig FN, Panum I, Andersen PHS, Rønn J, et al. Mumps resurgence in Denmark. *J Clin Virol*. 2014;61(3):435-438. doi: 10.1016/j.jcv.2014.08.013.
- Yoo JW, Tae BS, Chang HK, Song MS, Cheon J, Park JY, et al. Epidemiology of mumps, mumps complications, and mumps orchitis in Korea using the National Health Insurance Service database. *Investig Clin Urol*. 2023;64(4):412-417. doi: 10.4111/icu.20230064.
- Middeldorp M, van Lier A, van der Maas N, Veldhuijzen I, Freudenburg W, van Sorge NM, et al. Short term impact of the COVID-19 pandemic on incidence of vaccine preventable diseases and participation in routine infant vaccinations in the Netherlands in the period March-September 2020. *Vaccine*. 2021;39(7):1039-1043. doi: 10.1016/j.vaccine.2020.12.080.
- Ullrich A, Schranz M, Rexroth U, Hamouda O, Schaade L, Diercke M, et al. Impact of the COVID-19 pandemic and associated non-pharmaceutical interventions on other notifiable infectious diseases in Germany: An analysis of national surveillance data during week 1-2016-week 32-2020. *Lancet Reg Health Eur*. 2021;6. doi: 10.1016/j.lanepe.2021.100103.
- Huh K, Jung J, Hong J, Kim M, Ahn JG, Kim JH, et al. Impact of nonpharmaceutical interventions on the incidence of respiratory infections during the coronavirus disease 2019 (COVID-19) outbreak in Korea: A nationwide surveillance study. *Clin Infect Dis*. 2021;72(7):e184-e191. doi: 10.1093/cid/ciaa1682.
- Kotrbova K, Lunackova J. Major mumps outbreak in the South Bohemian Region, a question for the buster vaccination. *Int J Infect Dis*. 2016;53:146. doi: 10.1016/j.ijid.2016.11.358.
- Havlíčková M, Limberková R, Smíšková D, Herrmannová K, Jiřincová H, Nováková L, et al. Mumps in the Czech Republic in 2013: Clinical characteristics, mumps virus genotyping, and epidemiological links. *Cent Eur J Public Health*. 2016;24(1):22-28. doi: 10.21101/cejph.a4512.

21. Smetana J, Chlibek R, Hanovcova I, Sosovickova R, Smetanova L, Polcarova P, et al. Serological survey of mumps antibodies in adults in the Czech Republic and the need for changes to the vaccination strategy. *Hum Vaccin Immunother.* 2018;14(4):887-893. doi: 10.1080/21645515.2017.1412021.
22. Bílková-Fránková H, Kloudová A, Zelená H. Multipurpose serological survey (measles, mumps, pertussis, viral hepatitis type B) 2013, Czech Republic - final report, annex 1. *Zprávy CEM.* 2014;1-152.
23. Zamir CS, Schroeder HS, Shoob H, Abramson N, Zenter G. Characteristics of a large mumps outbreak: Clinical severity, complications and association with vaccination status of mumps outbreak cases. *Hum Vaccin Immunother.* 2015;11(6):1413-1417. doi: 10.1080/21645515.2015.1021522.
24. Dlhý J, Kyselý Z, Ciupek R. Administrative estimates of vaccination coverage in children, the Czech Republic. *Vaccinology.* 2023;17(2):54-62.