Human Vaccines & Immunotherapeutics

ISSN: 2164-5515 (Print) 2164-554X (Online) Journal homepage: www.tandfonline.com/journals/khvi20

The effectiveness of measles-mumps-rubella (MMR) vaccination in the prevention of pediatric hospitalizations for targeted and untargeted infections: A retrospective cohort study

Giuseppe La Torre, Rosella Saulle, Brigid Unim, Angela Meggiolaro, Angelo Barbato, Alice Mannocci & Antonietta Spadea

To cite this article: Giuseppe La Torre, Rosella Saulle, Brigid Unim, Angela Meggiolaro, Angelo Barbato, Alice Mannocci & Antonietta Spadea (2017) The effectiveness of measles-mumps-rubella (MMR) vaccination in the prevention of pediatric hospitalizations for targeted and untargeted infections: A retrospective cohort study, Human Vaccines & Immunotherapeutics, 13:8, 1879-1883, DOI: 10.1080/21645515.2017.1330733

To link to this article: https://doi.org/10.1080/21645515.2017.1330733

Published online: 26 Jun 2017.

Submit your article to this journal

Article views: 3371

View related articles

View Crossmark data

Citing articles: 9 View citing articles

Full Terms & Conditions of access and use can be found at
https://www.tandfonline.com/action/journalInformation?journalCode=khvi20

HUMAN VACCINES & IMMUNOTHERAPEUTICS
2017, VOL. 13, NO. 8, 1879–1883
https://doi.org/10.1080/21645515.2017.1330733

Taylor & Francis
Taylor & Francis Group

SHORT REPORT

Check for updates

The effectiveness of measles-mumps-rubella (MMR) vaccination in the prevention of pediatric hospitalizations for targeted and untargeted infections: A retrospective cohort study

Giuseppe La Torre[a], Rosella Saulle[a], Brigid Unim[a], Angela Meggiolaro[a], Angelo Barbato[b], Alice Mannocci[a], and Antonietta Spadea[b]

[a]Department of Public Health and Infectious Diseases, "Sapienza" University of Rome, Rome, Italy; [b]RM/1 Local Health Unit, Rome, Italy

ABSTRACT

Objectives: To evaluate the effectiveness of the measles-mumps-rubella (MMR) vaccine in reducing hospitalizations for infectious disease, targeted and not targeted, as well as from respiratory diseases in children in Rome.

Methods: The cohort was recomposed through record linkage of 2 archives (vaccination register and hospital discharge records.

Results: The analysis included 11,004 children. 20.9% did not receive the MMR vaccination, 49% and 30.1% received one and 2 doses. There were no hospitalizations for rubella, 2 for mumps, and 12 for measles. The vaccine was highly protective against measles and mumps hospitalizations (HR = 0.10; 95% CI: 0.03.0.34). Regarding all infectious diseases there were 414 hospitalizations, and the vaccine was protective (HR = 0.29; 95% CI: 0.25 to 0.34). Concerning respiratory diseases, there were 809 admissions (7.4%), and the vaccine was highly protective (HR: 0.18; 95% CI: 0.07 to 0.48).

Conclusions: MMR vaccination is effective for the primary prevention of target and not targeted infectious diseases and may also limit hospitalizations for respiratory diseases.

ARTICLE HISTORY
Received 28 March 2017
Revised 4 May 2017
Accepted 11 May 2017

KEYWORDS
hospital discharge; measles; mumps; respiratory diseases; rubella; vaccine

Introduction

Childhood vaccinations recommended around the world are based on the scientific principle of their preventive and protective effect. An appropriate well-planned vaccination card, based on scientific evidence, could bring great benefit by reducing morbidity and mortality in high and low income countries.[1]

Vaccines may have a 'non-specific' protective effect on morbidity and mortality due to diseases not susceptible to vaccination, as demonstrated by different types of studies, both observational and clinical trials performed in low income countries,[2-8] for example as in the case of the beneficial effects of non-specific measles and tuberculosis vaccines (BCG); on the contrary, the inactivated vaccines, such as those against diphtheria and tetanus,[9] polio[10] and hepatitis B,[11] have been associated with different mortality rates between man and women.

Measles, mumps, and rubella are typical childhood infectious diseases, highly contagious, and yet despite this generally have a good prognosis, though they may lead to serious complications and cause an avoidable burden on the health care system.[12]

The measles infection causes immune depression for about 6 weeks.[13] The complications (otitis, pneumonia, bronchitis) that occur in approximately 30% of cases, may arise especially in this period of time. One particularly feared and dangerous complication can be post-infectious encephalitis, while a particularly serious long-term consequence is represented by subacute sclerosing panencephalitis (SSPE), often fatal.[12]

The best known complications of mumps infection instead are: meningitis, orchitis, and pancreatitis. There have been rare cases of unilateral deafness. Orchitis occurs in about 25% of men infected after puberty and, in the case of bilateral orchitis, may result in infertility. This complication tends to occur during the first few days of infection, causing swelling, pain and fever.[14]

Complications of postnatal rubella are rare, but become more common with advancing age. Rubella infection which is transmitted to the fetus through the placenta is certainly the most critical. The danger of provoking birth defects is higher if the infection is contracted by the mother during the first trimester of pregnancy: inner ear deafness and cataracts are the most common defects. Other possible fetal complications may include: developmental disorders, locomotor disorders, encephalitis and low birth weight.[15]

The likelihood of complications and sequelae of measles, mumps, rubella and other infections, increases with the age.[12] On the contrary, the likelihood of adverse events and other complications as a result of MMR vaccination are very rare. They may occur especially in individuals with hypersensitivity to certain vaccine components, technical problems or incorrect administration.[12] On the other hand, there is evidence that MMR vaccination is not only effective, but also cost saving, from both direct cost and societal perspectives.[12,16-17]

CONTACT Prof. Giuseppe La Torre giuseppe.latorre@uniroma1.it Department of Public Health and Infectious Diseases; "Sapienza" University of Rome Italy; Piazzale Aldo Moro 5 – 00185 Rome, Italy.

© 2017 Taylor & Francis

Due to the median coverage of the vaccination, Italy is still one of the European countries with a high number of measles cases per million person[18] placing it far from the desired elimination level, In Italy, the MMR vaccine is recommended by the Ministry of Health. According to the national calendar of vaccinations which are actively offered to the entire population, the anti MMR vaccine is given in 2 doses: at 13th -15th month, 5–6 y (and eventually at 11–18 years)[18]

A recent research, conducted in a cohort of Danish children, revealed that administration of live MMR vaccine versus inactivated DTaP-IPV-Hib, is associated with a lower rate of hospital admissions for generic type infections.[19]

This retrospective cohort study aims to evaluate the impact of MMR vaccination on hospitalization for infectious events and respiratory pathologies (including asthma), and focuses on the pediatric population in the areas of competence of the local health unit ASL Rome1, for a follow up of 2 y. Therefore, it intends to evaluate the effectiveness of the MMR vaccine in reducing hospitalizations from any target infectious disease, and from respiratory diseases and refers to children born in the period ranged between 2008 -2010, who subsequently underwent vaccination in 2009–2011 and resident in the territories of the ASL Rome1.

Results

The study involved the analysis of 11,004 children (5535 males, 5469 females) of mainly Italian nationality (89.1%), resident in the territory of ASL Rome 1.

2302 of these children (20.9%) did not receive the MMR vaccination, 5392 (49%) received one dose and 3310 (30.1%) received 2 doses of this vaccine.

With regard to the target diseases of vaccination, over the period studied, no hospitalizations occurred for Rubella, 2 hospitalizations were seen for Mumps (1 among vaccinated and 1 among unvaccinated children) and 12 occurred for Measles, of which 9 (0.4%) among not vaccinated group, 3 (0.1%) among those vaccinated with one dose, and none among those who received 2 doses of vaccine ($p < 0.001$) (Table 1). Overall, the vaccine was highly protective against measles (HR = 0.09; 95%CI: 0.01- 0,32) or measles and mumps hospitalizations (HR: 0.10; 95% CI: 0.03 to 0.34) (Table 2).

As for all infectious diseases, the target and non-target of vaccination, 414 hospitalizations were noted, of which 262 (11.4%) among those non-vaccinated, 82 (1.5%) among those who had received one dose of vaccine and 70 between those who had received 2 doses ($p < 0.001$) (Table 3). Overall, the vaccine was highly protective against hospitalizations for all infectious diseases (HR:0.29; 95% CI: 0.25 to 0.34).

With regard to respiratory disease, there were 809 admissions (7.4%), of which 424 (18.4%) among those who had not been vaccinated, 202 (3.7%) among children vaccinated having received just the first dose and 183 (5.5%) among children vaccinated with 2 doses ($p < 0.001$) (Table 4). Overall, the vaccine was highly protective against hospitalizations for respiratory diseases, with an HR of 0.18 (95% CI: 0.:07 to 00.48).

Discussion

In our study it resulted that receiving the live MMR vaccine is associated with a lower rate of hospital admissions for any target infectious disease, and for respiratory diseases in children.

As far as concerns the target infectious diseases, no hospitalization was recorded for rubella, while the MMR vaccine was effective in preventing hospitalization for measles and mumps. It is interesting to note that data from this research suggest that the effect of MMR vaccination is mainly due to the measles component, and not to all 3 components of MMR vaccine.

The association was particularly strong for lower respiratory tract infections (HR of 0.18; 95% CI: 0:07 to 00:48) and resulted highly protective against hospitalizations for all infectious diseases (HR: 0.29; 95% CI: 0:25 to 00:34).

Vaccination remains one of the safest and effective interventions available in public health for the primary prevention of infectious diseases, resulting in a medical practice that induces both direct and indirect immunity in individuals vaccinated (herd immunity).[12,20]

The immunological mechanism underlying this effect is not yet entirely understood, but may involve genetic modulation systems; many studies are being performed to investigate the protective effects of non-specific vaccines in low-income countries with a high prevalence of infectious diseases.[12,20]

The mechanisms of immunization induced by the MMR vaccine and the long persistence of B-cell antigen-specific memory (MBCS) in children and young adults still remain unclear.[21-22]

Genetic polymorphisms may be significantly associated with the variability of response mechanisms to infection and vaccination. In particular, the genetic polymorphisms of various families of genes with known immune function, including HLA genes, cytokine and the cytokine receptors, genes that control the innate and humoral immunity, are significantly associated with changes in the immune response to therubella vaccine.[23]

On the contrary, the determinants of immunity induced by the mumps vaccine have not yet been completely clarified.[24]

The variability of the immune response modulated by the human leukocyte antigen gene (HLA) and by genes for cytokines, appears to be an important factor in the protection

Table 1. Hospitalizations for measles and mumps, all infectious diseases and respiratory diseases for all MMR vaccine doses.

Vaccine	Measles N (%)	Mumps N (%)	Measles and Mumps N (%)	All infectious diseases N (%)	All respiratory diseases N (%)
No dose	9 (0.4)	1 (0.04)	10 (0.4)	262 (11.4)	424 (18.4)
1 dose	3 (0.06)	1 (0.01)	4 (0.1)	82 (1.5)	202 (3.7)
2 doses	0 (0)	0 (0)	0 (0)	70 (2.1)	183 (5.5)
Total	12 (0.1)	2 (0.01)	14 (0.1)	414 (3.8)	809 (7.4)
p	*<0.001*	*Ns*	*<0.001*	*<0.001*	*<0.001*

Table 2. Cox regression model results relating to the correlation between MMR vaccine and Measles and Mumps, all infectious diseases and all respiratory diseases.

Vaccine	Measles	Measles and Mumps	All infectious diseases	All respiratory diseases
	HR (95%CI)	HR (95%CI)	HR (95%CI)	HR (95%CI)
No (*reference*)	1	1	1	1
Yes	0.09 (0.01 – 0.32)	0.10 (0.03 – 0.34)	0.29 (0.25 – 0.34).	0.18 (0.07 – 0.48).

against measles; understanding the genetic factors that influence changes in the secretion of cytokines after vaccination against measles would allow a better understanding of the factors that influence the cell-mediated and humoral immunity during this infection.[25]

A recent study reported that receiving the live MMR vaccine after the inactivated DTaPIPV- Hib vaccine was associated with a lower rate of hospital admissions for any infection.[19] On the contrary, children who received DTaP-IPVHib after MMR had a significantly higher rate of infectious disease admission. However vaccinations were registered by general practitioners to obtain reimbursement, therefore there might have been some underreporting.[19]

Table 3. Description of the hospitalization for infectious diseases (by ICD code) in children not vaccinated, vaccinated with one and 2 doses.

ICD code	0 dose	1 dose	2 doses
Typhoid or Paratyphoid fever 002	1	0	0
Other salmonella infections 003	5	2	2
Shigellosis 004	1	0	0
Other protozoal intestinal diseases 007	1	0	0
Intestinal infections due to other organisms 008	52	22	10
Ill-defined intestinal infections 009	63	20	15
Tuberculosis of other organs 017	1	1	0
Whooping cough 033	9	3	2
Streptococcal sore throat and scarlet fever 034	6	1	0
Meningococcal infection 036	1	0	1
Septicemia 038	4	4	2
Actinomycotic infections 039	1	0	0
Bacterial infection in conditions classified elsewhere and of unspecified site 041	24	1	2
Human immunodeficiency virus [HIV] disease 042	2	0	0
Meningitis due to enterovirus 047	1	0	0
Chickenpox 052	5	3	3
Herpes simplex 054	4	0	0
Measles 055	9	3	0
Other viral exanthemata 057	9	2	4
Viral hepatitis 070	0	0	1
Mumps 072	1	1	0
Infectious mononucleosis 075	11	4	5
Other diseases of conjunctiva due to viruses and chlamydiae 077	0	0	4
Other diseases due to viruses and chlamydiae 078	16	1	5
Viral and chlamydial infection in conditions classified elsewhere and of unspecified site 079	18	4	8
Leishmaniasis 085	1	1	0
Relapsing fever 087	11	5	6
Congenital syphilis 090	1	0	0
Other cestode infection 123	1	0	0
Other and unspecified helminthiases 128	1	0	0
Intestinal parasitism, unspecified 129	1	0	0
Other and unspecified infectious and parasitic diseases 136	1	1	0
Late effects of other infectious and parasitic diseases 139	0	3	0
TOTAL	262	82	70

This study has some limitation that must be acknowledged. First of all, we were not able to have data on family income or at least parents' educational level that could have an impact on vaccination attitude. But there is evidence that in Italy socio-economic factors are not associated with low likelihood of getting vaccinated against MMR.[25,26]

Moreover, at the moment of the research, no data on other vaccinations were available, so that we were not able to adjust the analysis for possible confounders. Finally, we choose the starting point of the follow-up of the non-vaccinated children at the median month when they should have been vaccinated. This choice was taken to have the same probability of follow-up of the vaccinated children. However, same results were found, without taking into consideration the follow-up period, using a logistic regression approach and not a Cox proportional hazard model,

In conclusion, even if the study is not novel in the international panorama, we believe it adds some new insight, in

Table 4. Description of the hospitalization for respiratory (by ICD code) in children not vaccinated, vaccinated with one and 2 doses.

ICD code	0 dose	1 dose	2 doses
Acute nasopharyngitis 460	0	3	1
Acute sinusitis 461	0	2	0
Acute pharyngitis 462	15	1	4
Acute tonsillitis 463	9	1	1
Acute laryngitis and tracheitis 464	11	3	5
Acute upper respiratory infections of multiple or unspecified sites 465	12	5	3
Acute bronchitis and bronchiolitis 466	61	38	16
Chronic pharyngitis and nasopharyngitis 472	3	3	4
Chronic sinusitis 473	0	0	2
Chronic disease of tonsils and adenoids 474	102	38	64
Peritonsillar abscess 475	0	0	1
Allergic rhinitis 477	11	5	3
Other diseases of upper respiratory tract 478	16	6	12
Viral pneumonia 480	3	0	1
Pneumococcal pneumonia 481	0	1	1
Other bacterial pneumonia 482	7	4	2
Pneumonia due to other specified organism 483	4	1	1
Pneumonia in infectious diseases classified elsewhere 484	0	1	1
Bronchopneumonia, organism unspecified 485	13	13	4
Pneumonia, organism unspecified 486	67	18	20
Influenza 487	6	1	1
Bronchitis, not specified as acute or chronic 490	0	1	0
Chronic bronchitis 491	4	0	0
Asthma 493	54	30	18
Bronchiectasis 494	0	0	2
Chronic airway obstruction, not elsewhere classified 496	0	1	0
Pneumonitis due to solids and liquids 507	0	1	0
Pleurisy 511	7	1	0
Pneumothorax and air leak 512	1	0	0
Other diseases of lung 518	15	16	11
Other diseases of respiratory system 519	3	8	5
TOTAL	424	202	183

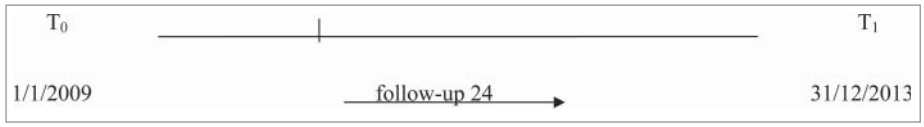

Figure 1. Period of the study follow-up T_0 T_1 1/1/2009 follow-up 24 31/12/2013.

particular for what concerns the protective effect of MMR vaccination against hospitalizations for respiratory diseases in children This result could be a very good argument to reduce the barriers against this vaccination among parents. However, the findings require replication in a larger sample and possibly in a prospective cohort study of high quality, controlling for other types of variables in hospitalized children rather than in a retrospective cohort.

Materials and methods

Study design and setting

The population eligible for enrollment in this retrospective cohort study is represented by children resident in the ASL Rome1, who were present in vaccination registers and had been vaccinated (or not) in the period between 2009–2011 for the MMR. The follow-up started as follows: a) for vaccinated children at the time of vaccination and ending after 24 months; b) for unvaccinated children, the start of the follow-up was considered as the median month when children should have received the vaccine for their birth cohort and ending after 24 months (Fig. 1). In this sample T0 and T1 represent the starting and ending points of study.

For each component of the cohort the status of MMR vaccination was ascertained in the register of ASL, a database that included the names of children vaccinated both at immunization clinics of the ASL and with family pediatricians.

Database

The effectiveness of MMR vaccine in reducing hospitalizations for any infection was assessed by analyzing 2 distinct databases:

a) the vaccination records of the database of the ASL RM-A, from which relevant data were extracted, such as date of birth; MMR vaccination (yes vs no); MMR dose (only for vaccinated); Personal Tax code.
b) the hospital discharge diagnosis which contained the following ICD-9 codes (International Classification of Diseases), in primary or secondary diagnosis:
   - 001 to 139 for infectious and parasitic diseases;
   - from 460 to 519 for respiratory diseases.

The cohort was recomposed through record linkage of the 2 archives, registration and vaccination of hospital discharge records (HDR), using personal tax codes as a common identification in both archives.

Outcome measures and exposure

All children included in the cohort were divided into 2 groups, exposed and unexposed, considering *"exposure"* as the administration of the MMR vaccine and *"outcome"* as the hospitalization for any infectious disease related to the vaccine (measles, mumps and rubella) and all respiratory diseases in the considered time-window.

Statistical analysis

A descriptive analysis was conducted to represent the main characteristics of the sample. A univariate analysis, to evaluate the possible associations between the number of doses of vaccination and the 3 different outcomes considered was also performed. Finally, Cox regression models were constructed to assess the association between the vaccination status and outcomes The results are presented as Hazard ratios (HR) and 95% confidence intervals (95% CI). The models were adjusted considering age and gender as possible confounders.

The statistical analysis was performed using SPSS version 23 for Windows, with the level of significance set at $p < 0.05$.

Disclosure of potential conflicts of interest

None of the authors have any competing interests.

Authorship

G.L.T. A.B. and A.S. designed the study, and together with R.S wrote the protocol and oversaw all aspects of the study. U.B. and A.M. collected data from the sample; G.L.T. conducted and performed the statistical analysis; G.L.T., R.S., U.B., A.M. wrote the manuscript in all his sections. A.S. and A.B contributed to the discussion. All authors contributed to and have approved the final manuscript.

References

[1] Aaby P, Whittle H, Benn CS. Vaccine programmes must consider their effect on general resistance. BMJ 2012;344:e3769; PMID:22700785; https://doi.org/10.1136/bmj.e3769
[2] Benn CS, Netea MG, Selin LK, Aaby P. A small jab—a big effect: non-specific immunomodulation by vaccines. Trends Immunol 2013;34 (9):431-9; PMID:23680130; https://doi.org/10.1016/j.it.2013.04.004
[3] Aaby P, Samb B, Simondon F, Seck AM, KnudsenK, Whittle H. Non-specific beneficial effect of measles immunization: analysis of mortality studies from developing countries. BMJ 1995; 311(7003):481-5; PMID:7647643; https://doi.org/10.1136/bmj.311.7003.481
[4] Aaby P, Martins CL, Garly ML, Balé C, Andersen A, Rodrigues A, Ravn H, Lisse IM, Benn CS, Whittle HC. Non-specific effects of standard measles vaccine at 4.5 and 9 months of age on childhood mortality: randomized controlled trial. BMJ 2010; 341:c6495; PMID:21118875; https://doi.org/10.1136/bmj.c6495
[5] Aaby P, Roth A, Ravn H, Napirna BM, Rodrigues A, Lisse IM, Stensballe L, Diness BR, Lausch KR, Lund N, et al. Randomized trial of BCG vaccination at birth to low-birth-weight children: beneficial nonspecific effects in the neonatal period? J Infect Dis 2011; 204 (2):245-52; PMID:21673035; https://doi.org/10.1093/infdis/jir240
[6] Biering-Sørensen S, Aaby P, Napirna BM, Roth A, Ravn H, Rodrigues A, Whittle H, Benn CS. Small randomized trial among low-birth-weight children receiving bacillus Calmette-Guérin vaccination at first

health center contact. Pediatr Infect Dis J 2012; 31(3):306-8; PMID:22189537; https://doi.org/10.1097/INF.0b013e3182458289

[7] Roth AE, Benn CS, Ravn H, Rodrigues A, Lisse IM, Yazdanbakhsh M, Whittle H, Aaby P. Effect of revaccination with BCG in early childhood on mortality: randomized trial in Guinea-Bissau. BMJ 2010; 340:c671; PMID:20231251; https://doi.org/10.1136/bmj.c671

[8] Shann F. The non-specific effects of vaccines. Arch Dis Child 2010; 95 (9):662-667; PMID:20716675; https://doi.org/10.1136/adc.2009.157537

[9] Aaby P, Benn C, Nielsen J, Lisse IM, Rodrigues A, Ravn H. Testing the hypothesis that diphtheria-tetanus-pertussis vaccine has negative non-specific and sex-differential effects on child survival in high-mortality countries. BMJ Open 2012; 2(3):e000707; PMID:22619263; https://doi.org/10.1136/bmjopen-2011-000707

[10] Aaby P, Garly ML, Nielsen J, Ravn H, Martins C, Balé C, Rodrigues A, Benn CS, Lisse IM. Increased female-male mortality ratio associated with inactivated polio and diphtheria-tetanus-pertussis vaccines: observations from vaccination trials in Guinea-Bissau. Pediatr Infect Dis J 2007; 26(3):247-252; PMID:17484223; https://doi.org/10.1097/01.inf.0000256735.05098.01

[11] Garly ML, Jensen H, Martins CL, Balé C, Baldé MA, Lisse IM, Aaby P. Hepatitis B vaccination associated with higher female than male mortality in Guinea-Bissau: an observational study. Pediatr Infect Dis J 2004; 23(12):1086-1092; PMID:15626943

[12] Rosian-Schikuta I, Fröschl B, Habl C, Stürzlinger H. The Measles-Mumps-Rubella Vaccination from a health political and economical point of view. GMS Health Technol Assess 2007; 3:Doc12.

[13] Griffin DE. Measles virus-induced suppression of immune responses. Immunol Rev 2010; 236:176-89; https://doi.org/10.1111/j.1600-065X.2010.00925.x

[14] Centers for Disease Control and Prevention. Mumps. In: Epidemiology and Prevention of Vaccine-Preventable Diseases, 13th Edition. April 2015, 247-60.

[15] Centers for Disease Control and Prevention. Rubella. In: Epidemiology and Prevention of Vaccine-Preventable Diseases, 13th Edition. April 2015, 325-40.

[16] Zhou F, Shefer A, Wenger J, Messonnier M, Wang LY, Lopez A, Moore M, Murphy TV, Cortese M, Rodewald L. Economic evaluation of the routine childhood immunization program in the United States, 2009. Pediatrics 2014; 133(4):577-85; PMID:24590750; https://doi.org/10.1542/peds.2013-0698

[17] Rivière M, Tretiak R, Levinton C, Fitzsimon C, Leclerc C. Economic benefits of a routine second dose of combined measles, mumps and rubella vaccine in Canada. Can J Infect Dis 1997; 8(5):257-64; https://doi.org/10.1155/1997/215175

[18] Ministero della Salute. Piano Nazionale Prevenzione Vaccinale (PNPV) 2012–2014.

[19] Sørup S, Benn CS, Poulsen A, Krause TG, Aaby P, Ravn H. Live Vaccine Against Measles, Mumps, and Rubella and the Risk of Hospital Admissions for Nontargeted Infections. JAMA 2014; 311(8):826-835; PMID:24570246; https://doi.org/10.1001/jama.2014.470

[20] Plans-Rubió P. Evaluation of the establishment of herd immunity in the population by means of serological surveys and vaccination coverage. Hum Vaccin Immunother 2012; 8: 184—188; PMID:22426372; https://doi.org/10.4161/hv.18444

[21] Kakoulidou M, Ingelman-Sundberg H, Johansson E, Cagigi A, Farouk SE, Nilsson A, Johansen K. Kinetics of antibody and memory B cell responses after MMR immunization in children and young adults. Vaccine 2013; 31(4):711-7; https://doi.org/10.1016/j.vaccine.2012.11.031

[22] Kennedy RB, Ovsyanniko IG, Haralambieva IH, Lambert ND, Pankratz VS, Poland GA. Genetic polymorphisms associated with rubella virus-specific cellular immunity following MMR vaccination. Human Genetics 2014; 133(11):1407-17; https://doi.org/10.1007/s00439-014-1471-z

[23] Kyaw MH, Rue AM, Klahn J, Obrecht LA, Krohn T, Rowland J, Rubin S, Safranek Thomas J, Bellini WJ, Dayan GH. Long-Term Persistence of Mumps Antibody after Receipt of 2 Measles-Mumps-Rubella (MMR) Vaccinations and Antibody Response after a Third MMR Vaccination among a University Population. J Infect Dis 2008; 197(12):1662-8; https://doi.org/10.1086/588197

[24] Ovsyannikova IG, Ryan JE, Vierkant RA, Pankratz VS, Jacobson RM, Poland GA. Immunologic significance of HLA class I genes in measles virus-specific IFN-gamma and IL-4 cytokine immune responses. Immunogenetics 2005; 57(11):828-36; https://doi.org/10.1007/s00251-005-0061-6

[25] Restivo V, Napoli G, Marsala MG, Bonanno V, Sciuto V, Amodio E, Calamusa G, Vitale F, Firenze A. Factors associated with poor adherence to MMR vaccination in parents who follow vaccination schedule. Hum VaccinImmunother 2014; 11(1).

[26] Impicciatore P, Bosetti C, Schiavio S, Pandolfini C, Bonati M. Mothers as active partners in the prevention of childhood diseases: maternal factors related to immunization status of preschool children in Italy. Prev Med 2000; 31(1):49-55; https://doi.org/10.1006/pmed.2000.0677