Title: Prevalence of anti-rubella, anti-measles and anti-mumps IgG antibodies in neonates and pregnant women in Catalonia (Spain) in 2013. Susceptibility to measles increased from 2003 to 2013.

Authors: Pedro Plans,[1,7] Fernando de Ory,[2,7] Magda Campins,[3] Elena Álvarez,[4] Toni Payà,[5] Eulalia Guisasola,[2,7] Carme Compte,[4] Kilian Vellbé,[5] Consol Sánchez,[6] María José Lozano,[6] Iris Aran,[5] Alexandra Bonmatí,[4] Ramon Carreras,[5] Mireia Jané,[1,7] Lluís Cabero[6]

From: 1. Public Health Agency of Catalonia; 2. Centro Nacional de Microbiología, Instituto de Salud Carlos III, Madrid; 3. Preventive Medicine and Epidemiology Service, Hospital Vall d'Hebron of Barcelona; 4. Obstetrics Service, Hospital Josep Trueta of Girona; 5. Ginaecology and Obstetrics Service, Hospital del Mar of Barcelona; 6. Obstetrics Service, Hospital Vall d'Hebron of Barcelona; 7. CIBER of Epidemiology and Public Health (CIBERESP), Instituto de Salud Carlos III, Madrid, Spain.

Corresponding author: Dr. Pedro Plans
                    Public Health Agency of Catalonia
                    Department of Health of Catalonia
                    Roc Boronat 83-95
                    008005 Barcelona
                    Spain
                    Email: pedro.plans@gencat.cat

ABSTRACT

Nonimmune neonates and nonimmune pregnant women are at risk of developing rubella, measles and mumps infections, including congenital rubella syndrome. We describe the seroepidemiology of measles, mumps and rubella in neonates and pregnant women in Catalonia (Spain). Anti-rubella, anti-measles and anti-mumps serum IgG titers were assessed using ELISA tests in 353 cord blood samples from neonates of a representative sample of pregnant women obtained in 2013. The prevalence of protective antibody titers in neonates was 96% for rubella IgG (≥ 8 IU/ml), 90% for measles IgG (>300 IU/ml), and 84% for mumps IgG (>460 EU/ml). Slightly lower prevalences of protective IgG titers, as estimated from the cord blood titers, were found in pregnant women: 95% for rubella IgG, 89% for measles IgG and 81% for mumps. The anti-measles and anti-mumps IgG titers and the prevalences of protective IgG titers against measles and mumps increased significantly ($p<0.001$) with maternal age. The prevalence of protective anti-measles IgG titers decreased by 7% (OR=0.15, $p<0.001$), the prevalence of protective anti-rubella IgG titers increased by 3% (OR=1.80, $p<0.05$), and the MMR vaccination coverage (during childhood) in pregnant women increased by 54% (OR=2.09, $p<0.001$) from 2003 to 2013. We recommend to develop an MMR prevention programme in women of childbearing age based on mass MMR vaccination or MMR screening and vaccination of susceptible women to increase immunity levels against measles, mumps and rubella.

INTRODUCTION

Nonimmune neonates and nonimmune pregnant women are at risk of developing rubella, measles and mumps infections, including congenital rubella syndrome [1−3]. In Catalonia and Spain, current preventive strategy against these diseases is based on the high MMR vaccination coverage during childhood (>90%) and the intensive epidemiological surveillance activities [4]. Children are vaccinated with two doses of measles, mumps and rubella (MMR) vaccine, given at 15 months and 4 years of age [4]. Rubella vaccination of girls aged 11 years began in 1978, and MMR vaccination of children at 12 months began in 1980. In 1988, a second dose of MMR vaccine was added at 11 years of age for all children to replace the rubella vaccine administered to girls. In 1998, administration of the second dose of MMR vaccine was shifted to 4 years of age to ensure that more than 95% of children <10 years of age were immune to measles [4].

In 2010, the European Region of the World Health Organization renewed their commitment to the elimination of measles and rubella and the prevention of congenital rubella by the year 2015, and reduction of mumps incidence [5−7]. Since 1985, great efforts have been made in Catalonia, Spain and other European countries to eliminate measles and rubella and reduce mumps incidence, but cases and outbreaks of measles, mumps and rubella are still occurring [8−10]. In 2013, 36,321 cases of measles, 28,813 cases of mumps and 964 cases of rubella were reported in Europe [9]. Indigenous measles virus transmission was interrupted in Catalonia in 2000, as well as in nine other regions of Spain in 2005 [10], but measles re-emerged in Catalonia in 2006 and 132 cases were reported in Spain in 2013 [9,10]. Several reasons could explain the

persistence of measles, mumps and rubella in Catalonia, Spain and other European countries, including the failure to complete measles, mumps and rubella (MMR) vaccination in some areas or population groups [11,12]; the mobility of people carrying measles, rubella and mumps infections; and the lack of necessary prevalence of protected individuals (91%) required to block transmission of measles, mumps and rubella viruses in the community [4,13].

A seroepidemiological study carried out in Catalonia in 2003 assessed immunity levels against measles and rubella in neonates (cord blood samples), obtaining a prevalence of protective IgG titers of 98% for measles [14] and 93% for rubella [15]. The objectives of this study were: 1) to assess anti-rubella, anti-measles and anti-mumps IgG titers in neonates (cord blood samples) in 2013; 2) to assess the prevalence of protective anti-rubella, anti-measles and anti-mumps IgG titers in neonates and pregnant women; 3) to identify population groups with the higher priority for preventive and epidemiological surveillance activities; and 4) to compare the prevalence of protective anti-measles and anti-rubella IgG titers in neonates and the MMR vaccination coverage in pregnant women in 2003 and 2013.

METHODS

Sample selection

The serological study was carried out in cord blood samples of neonates from a representative sample of pregnant women obtained in Catalonia in 2013. Sampling was carried out in two stages. In the first stage, hospitals were selected. In the second stage, pregnant women who were attended for delivery between January and April of 2013 were asked to participate in the study. All pregnant women were elligible for the study, except those meeting any of the following exclusion criteria: administration of immunosuppresants or other immunomodifying drugs within the six months preceding childbirth, severe concomitant diseases (neoplasia, kidney or liver disease, immunosuppresion, malabsortion syndrome), family history of immunodeficiency, and administration of immunoglobulins or any blood product within the six months preceding childbirth. The sample size, calculated taking into account an alpha error of 5%, a prevalence of 50%, a precision of 6.2% and a design effect of 1.5, was 375. In each hospital, selected pregnant women were informed of the objectives of the study and asked to participate. The Research Ethics Board (REB) of the Vall d'Hebron hospital, Josep Trueta hospital and Mar hospital reviewed and approved the objectives and methodology of the study. Written informed consent was obtained from all participants to participate in the study, obtain umbilical cord blood samples, collect socio-demographic information and assess anti-rubella, anti-measles and anti-mumps IgG titers.

Questionnaire

All participants completed a questionnaire to collect sociodemographic and vaccination information. The sociodemographic variables included: age, place of birth, place of residence, education and social class. The place of residence was classified into urban (>10,000 inhabitants) and rural (<10,000 inhabitants) habitat. The variable immigration was defined according to the place of birth. Immigrants were considered as women who had not been born in Catalonia or another region of Spain. The educational level was classified into lower than Primary education and Primary or higher education. The socioeconomic level was determined by the occupation, classifying all participants in three socio-economic groups (I-III, IV-V and VI) according to the English classification [16]. The MMR and rubella monovalent vaccination information was used to assess the vaccination coverage. The MMR vaccination was considered correct in pregnant women when they had received two doses of MMR vaccine at 12-15 months and 4 years, or one dose of MMR vaccine in those aged ≥35 years (vaccinated before 1988).

Serological analysis

Blood samples were obtained from the umbilical cord at childbirth. Immunoglobulin G (IgG) titers against rubella, measles and mumps were measured using enzyme-linked immunosorbent assays (ELISA; Siemens Healthcare Diagnostics, Germany) according to the manufacturer's instructions. The lowest level of detection were 4 IU/ml for anti-rubella IgG, 150 IU/ml for anti-measles IgG and 230 EU/ml for anti-mumps IgG. In this study, serum samples with anti-rubella IgG ≥8 IU/ml, anti-measles IgG >300 IU/ml and anti-mumps IgG >460 EU/ml were considered positive, and serum samples with anti-rubella IgG <8 IU/ml, anti-measles IgG ≤300 IU/ml and anti-mumps IgG ≤460 EU/ml were considered negative [17,18]. Serum samples with equivocal serologic results for

rubella (4−8 IU/ml), measles (150−300 IU/ml) and mumps (230−460 EU/ml) were retested, considering them as negative when in the second assessment titers were <8 IU/ml for rubella IgG, ≤300 IU/ml for measles IgG and ≤460 EU/ml for mumps IgG. Neonates with titers ≥8 IU/ml for rubella IgG, >300 IU/ml for measles IgG and >460 EU/ml for mumps IgG were considered to be protected [17].

The prevalence of protective anti-rubella, anti-measles and anti-mumps IgG titers in pregnant women was determined from IgG titers in cord blood samples by taking into account the following cord-maternal ratios (titer in cord blood/titer in pregnant women): 1:0.83 for rubella antibodies [19], 1:0.89 for measles antibodies [19−21] and 1:0.77 for mumps antibodies [19]. The cord-maternal ratio for measles IgG antibodies in pregnant women assumed in this study was the average ratio obtained from three seroprevalence studies conducted in developed countries [19−21].

Statistical analysis

Statistical analysis of the results was carried out using IBM-SPSS version 18 software (IBM-SPSS, Chicago, IL, USA). Geometric mean anti-rubella, anti-measles and anti-mumps IgG titers in neonates, and the prevalence of protective anti-rubella, anti-measles and anti-mumps IgG titers in neonates and pregnant women were determined in different sociodemographic groups. Ninety five percent confidence intervals (CIs) were calculated for means and prevalences using the parametric method and the exact binomial method, respectively. The t-test was used to compare mean IgG titers, considering a $p < 0.05$ as statistically significant. Correlation between anti-rubella, anti-measles and anti-mumps IgG titers and study variables were assessed using the Person's

correlation coefficient, considering a p<0.05 as statistically significant. Multiple linear regression ecuations to explain anti-rubella, anti-measles and anti-mumps log IgG titers were developed including all study variables (age, habitat of residence, immigration, social clas and educational level) in the models. The Chi-square test and odds ratio (OR) were used to compare prevalences and percentages of vaccination coverage in different sociodemografic groups, considering a p<0.05 as statistically significant. Multiple logistic regression analysis was used to adjust significant odds ratios obtained in the univariate analysis, including all study variables in the models.

The prevalence of protective anti-measles and anti-rubella IgG titers found in neonates was compared to the prevalences found in the seroprevalence study conducted in 2003,[14,15] considering the same cut-off levels for positivity: >300 IU/ml for measles IgG and ≥8 IU/ml for rubella IgG. The MMR vaccination coverage in pregnant women during childhood (2 doses in pregnant women aged <35 years and 1 dose in those aged ≥35 years) obtained in this study was compared to the vaccination coverage for 1 dose of MMR vaccine obtained in the study conducted in 2003. The chi-square test and odds ratio (OR) were used to compare prevalences of protective antibody titers and percentages of vaccination coverage in 2013 and 2003, considering a p<0.05 as statistically significant. The age-standardized prevalences in 2003 and 2013 were calculated using the Catalan population (pregnant women) in 2012 [22] as the standard population. Thus, the prevalences in 2003 and 2013 were obtained by weighting the proportion for different age groups, taking into account the distribution of the Catalan population.

RESULTS

The total number of umbilical cord blood samples included in the study was 353 (94% participation rate). The distribution of the sample of pregnant women, according to sociodemographic variables, was similar to the distribution in the population of pregnant Catalan women [22], although pregnant women 14–24 years old and those living in urban locations were overrepresented in the sample.

Table 1 presents the geometric mean titers (GMC) and the prevalence of protective IgG titers in neonates for rubella, measles and mumps antibodies. The GMT was 5.3 IU/ml for anti-rubella IgG, 25.3 IU/ml for anti-measles IgG and 28.9 EU/ml for anti-mumps IgG. Anti-rubella, anti-measles and anti-mumps titers in neonates increased with maternal age, with significant correlation coefficients of 0.247 ($p = 0.001$) for anti-measles IgG and 0.16 ($p=0.002$) for anti-mumps IgGs. Three simple linear regression equations were used to explain anti-measles, anti-mumps and anti-rubella IgG titers in neonates, depending on maternal age: log anti-measles IgG (IU/ml) = 2.247 + 0.026 age; log anti-mumps IgG (EU/ml) = 2.697 + 0.016 age; and log anti-rubella IgG (IU/ml) = 1.493 + 0.006 age. Multiple linear regression analysis showed that anti-measles and anti-mumps IgG titers in neonates were associated with maternal age independently of other maternal sociodemographic variables, with a $p<0.001$ for measles and a $p<0.005$ for mumps IgG antibodies.

The prevalence of protective IgG titers in neonates was 96.3% for rubella, 90.4% for measles and 84.1% for mumps (Table 1). The prevalence of anti-measles and anti-mumps protective IgG titers increased significantly ($p<0.001$) with maternal age.

Multiple logistic regression analysis showed that the prevalence of anti-measles and anti-mumps protective IgG titers was associated (p<0.001) with maternal age independently of other studied maternal sociodemographic variables. In all, 274 neonates (77.6%) had protective IgG titers against rubella, measles and mumps; 58 (16.4%) had protective titers against two diseases; 18 (5.1%) had protective titers against one disease; and 3 neonates (0.8%) were unprotected against rubella, measles and mumps.

Table 2 presents the prevalence of pregnant women with protective IgG titers against rubella, measles and mumps. The overall prevalence of protected women was 95.5% for rubella, 88.7% for measles and 81% for mumps. In all, 257 women (72.8%) had protective IgG titers against rubella, measles and mumps; 72 (20.4%) had protective titers against two diseases; 21 (5.9%) had protective titers against one disease; and 3 women (0.8%) were unprotected against rubella, measles and mumps. The prevalence of protective IgG titers against rubella, measles and mumps was slightly lower than in neonates, but the differences were not statistically significant. The prevalence of protective IgG titers against measles and mumps increased significantly (p<0.001) with maternal age. Three simple linear regression equations were used to explain antibody IgG titers in pregnant women, depending on age: log anti-measles IgG (IU/ml) = 2.396 + 0.026 age; log anti-mumps IgG (EU/ml) = 2.584 + 0.016 age; and log anti-rubella IgG (IU/ml) = 1.412 + 0.006 age. Multiple linear regression analysis showed that maternal age was associated with anti-measles IgG and anti-mumps IgG in pregnant women independently of other sociodemographic variables.

Table 3 presents MMR and rubella vaccination coverage in pregnant women (during

childhood) and shows that 51% of women were vaccinated with the MMR vaccine and 12% with the rubella vaccine. Overall, 62% of the women had been vaccinated with the MMR vaccine or the rubella vaccine. MMR vaccination coverage increased with age (p<0.001), while rubella vaccination coverage decreased with age (p<0.001). The percentages of vaccination coverage were higher in autochthonous than immigrant women, with odds ratios of 1.37 for MMR vaccination and 4.67 for rubella vaccination (Table 3).

Table 4 compares the prevalence of protective anti-measles and anti-rubella IgG titers in neonates and MMR vaccination coverage (obtained using a questionnaire) in pregnant women in Catalonia in 2003 and 2013. The prevalence of protective anti-measles IgG titers in neonates decreased by 7% from 2003 to 2013 (p<0.001), and the prevalence of protective anti-rubella IgG titers increased by 3% from 2003 to 2013 (p<0.05). The MMR vaccination rate in pregnant women increased by 54% from 2003 to 2013 (p<0.001). MMR vaccination coverage increased significantly from 2003 to 2013 in both autochthonous and immigrant women. In autochthonous women, MMR vaccination coverage increased from 29.7% in 2003 to 55.7% in 2013 (OR = 2.97; 95% CI: 2.12−4.17, p<0.001). In immigrant women, vaccination coverage increased from 30.9% in 2003 to 39.1% in 2013 (OR = 1.47; 95% CI: 0.85−2-41).

DISCUSSION

The prevalence of protective antibody titers higher than 95% for rubella and lower than 91% for measles and mumps in neonates and pregnant women shows that in 2013, neonates and pregnant women were adequately protected against rubella but not against measles and mumps in Catalonia. Consequently, a new preventive strategy should be developed to reduce the risk of measles and mumps infections in neonates and pregnant women.

The prevalence of protective antibody titers against rubella in neonates and pregnant women was higher than the prevalence of protective antibody titers against measles and mumps. This result could be explained by the higher vaccine-induced immunity provided by MMR vaccines against rubella than against measles and mumps [17,23], and by previous programmes of rubella monovalent vaccinations in Catalonia. Davidkin et al. [23] found that individuals vaccinated with two doses of MMR vaccine in Finland between 1982 and 1989 had a prevalence of protective IgG titers of 100% for rubella antibodies, 95% for measles antibodies and 74% for mumps antibodies.

The geometric mean titer and the prevalence of protective anti-measles IgG titers was higher in the neonates of women aged ≥35 years than in those of women <35 years, as well as being higher in women ≥35 years than in women <35 years. Since immunity to measles had been acquired through measles vaccinations in women aged <35 year but by natural infection in women aged ≥35 years, these results can be explained by the increased immunity against measles viruses in naturally immune women than in vaccinated women [21,24−27]. Leuredian et al. [24] found in the United Kingdom in

2008 that vaccinated women had significantly lower IgG titers than naturally immune women (779 mIU/ml vs. 2,687 mIU/ml, p<0.001) and that the neonates of vaccinated women also had significantly lower IgG titers than the neonates of naturally immune women (698 mIU/ml vs. 2,221 mIU/ml, p<0.001).

Univariate and multivariate linear regression analysis carried out in this study showed a positive correlation between the anti-measles and anti-mumps IgG titers in neonates and pregnant women and maternal age. The study showed on the other hand, a null correlation between anti-rubella IgG titers and maternal age. Seroprevalence studies carried out in other countries found positive correlations between the anti-measles IgG titers in neonates/pregnant women and maternal age [14,28−30]; and positive [28], negative [31−35] or null [36,37] correlations between the anti-rubella IgG titers in neonates/pregnant women and maternal age.

The present study found the prevalence of protective anti-rubella IgG titers to be similar in the neonates of autocthonous and immigrant women (96.9% vs. 95.2%). However, in the study carried out in 2003, the prevalence was higher in the neonates of autocthonous women than in those of immigrant women (94.6% vs. 89.0%, p<0.001) [15]. This change can be explained by the higher MMR vaccination rate in immigrant women in 2013 than in 2003.

This study shows that the susceptibility to measles among neonates increased by 7% from 2003 to 2013. This result can be explained by three factors: 1) greater proportion of neonates of vaccinated women in 2013 than in 2003, 2) waning vaccine-induced immunity for measles antibodies, and 3) lower circulation of wild measles viruses after

13

1980. Several studies have shown that neonates of vaccinated women have lower protective immunity levels against measles than neonates of naturally infected women [21,24−27], and that vaccine-induced measles antibodies wane with time [23]. Consequently, the higher proportion of neonates of vaccinated women and the lower proportion of naturally immunized women in 2013 than in 2003 has generated a lower prevalence of neonates protected against measles in 2013 than in 2003. Our study also shows that the susceptibility to rubella among neonates decreased by 3% from 2003 to 2013. This result indicates that the MMR vaccination programme, developed since 1980, has been able to maintain high anti-rubella immunity levels in pregnant women and neonates since 2003. A possible reason for this is that the MMR vaccine generates high immunity levels against rubella [23], which could be similar to those generated by rubella infections. Davidkin et al. [23] found a prevalence of positive results of 93% for anti-rubella IgG 15 years after the MMR vaccination (2 doses), while the prevalence of positive results was 82% for anti-measles IgG and 40% for anti-mumps IgG.

The overall MMR and rubella vaccination rates found in this study in pregnant women were 51% and 12%, respectively. The MMR vaccination rate increased by 54% from 2003 to 2013 due to higher MMR vaccination rates in both autocthonous and immigrant women in 2013. However, the lower MMR vaccination rate found in 2013 in immigrant women than in autochthonous women suggests that the MMR vaccination status should be reviewed in all immigrant women.

The prevalences of anti-rubella, anti-measles, and anti-mumps protective IgG titers in neonates and pregnant women found in this study were similar to and different from prevalences found in seroprevalence studies carried out in other countries after 2000.

However, it is difficult to compare prevalences obtained in different seroprevalence studies due to differences in sampling methods, populations studied and serological tests used. The prevalence of protective anti-rubella IgG titers found in this study in pregnant women (95%) was similar to the prevalence found in pregnant women in the United States of America (98%) [37], Colombia (93%) [33], Brasil (92%) [34], Iran (96%) [30], Turkey (94−100%) [36,39] and Australia (93%) [31], while it was higher than the prevalence found in Taiwan (89%) [40], Germany (87%) [41], Sudan (72%) [42] and Poland (89%) [35]. The prevalence of protective anti-measles titers found in this study in pregnant women (89%) was similar to the prevalence found in pregnant women or neonates in the United States of America (88%) [37], Argentina (87%) [28], Japan (80−90%) [29], China (90%) [43], while it was higher than the prevalence found in Gerrmany (79%) [41] and Iran (82%) [30]. The prevalence of protective anti-mumps titers found in this study in pregnant women (81%) was similar to the prevalence found in the United States of America (84%) [44].

The prevalence of protective anti-rubella IgG titers found in this study in neonates (96%) was higher than the prevalence found in neonates in Switzerland (91%) [45] and the United Kingdom (92%) [46]. The prevalence of protective anti-measles IgG titers found in this study in neonates (90%) was similar to the prevalence found in neonates in Switzerland (91%) [45] and it was higher than the prevalence found in the United Kingdom (80%) [24], the Netherlands (83%) [46] and Israel (50−81%) [21.24]. The prevalence of protective anti-mumps IgG titers found in this study neonates (84%) was similar to the prevalence found in neonates in the Netherlands (83%) [46] and it was higher than the prevalence found in Switzerland (62%) [45].

This study has several limitations. First, neonates and pregnant women who had anti-rubella, anti-measles anti-mumps titers ≥8 IU/ml, >300 IU/ml and >460 EU/ml, respectively, were considered to be protected against these diseases. Although using lower cut-offs titers should result in higher prevalences of protective titers, these cut-off points are the most accurate ones for deciding immune protection against rubella, measles and mumps [10,17]. Second, the prevalences protective IgG titers in pregnant women were determined by assuming cord-maternal ratios of 1:0.83, 1:0.89 and 1:0.77 for rubella, measles and mumps antibody titers, respectively. Lower cord-maternal ratios would result in lower prevalences of protective IgG titers in pregnant women. However, the cord-maternal ratios assumed in this study can be considered adequate for estimating the prevalence of protective IgG titers in pregnant women for two reasons: seroprevalence studies have found strong correlations between IgG titers in cord blood samples and pregnant women [23−26], and the transplacental transport of antibodies is much lower in neonates of women with high antibody titers [21,38]. Third, the MMR and rubella vaccination rates that were obtained for pregnant in 2013 could be lower than the actual vaccination rate because of recall bias. However, alternative vaccination information was not available for the sample of pregnant women that was studied. Four, the MMR vaccination rate in pregnant women in 2013 was compared to the measles vaccination in 2003.

This study shows that the current preventive strategy against measles, rubella and mumps, which is based on high MMR vaccination coverage during childhood, can be considered to be adequate for preventing rubella and congenital rubella infections. However, this strategy is not effective enough in achieving and maintaining high anti-measles and anti-mumps immunity levels in neonates and pregnant women, and the risk

of measles and mumps infections could be higher in the future because of the decline in the MMR vaccine-induced antibody levels [23,25,47,48]. Neonates and pregnant women are vulnerable to measles and mumps infections for the following reasons: 1) the neonates loss their measles and mumps antibodies before receiving the first dose of the MMR vaccine [19,43]; 2) the prevalence of protective anti-measles and anti-mumps IgG titers found in this study was lower than the critical prevalence necessary to block transmission of measles and mumps viruses in the community (91%) [4]; 3) measles and mumps can be transmitted from imported cases to susceptible neonates and pregnant women [2,3,12,17]; 4) measles related complications are frequent in neonates [7].

Therefore, it is necessary to develop new preventive strategies to increase immunity levels against measles and mumps in pregnant women and neonates, including: 1) MMR screening and vaccination of susceptible women of chilbearing; 2) MMR vaccination (catch-up) of women of childbearing age who have no documentation of completed vaccination, unless they have laboratory evidence of immunity to measles, mumps and rubella, or documentation of provider-diagnosed measles, mumps and rubella; and 3) promotion of MMR vaccination during childhood. Women aged <35 years and immigrant women should be the priority groups for these preventive programmes. The mass MMR vaccination strategy is the most cost-effective immunization strategy since screening costs are higher than vaccination costs [49]. However, MMR screening and vaccination will be the preferred option for women of childbearing age who are willing to avoid MMR vaccination. The preventive strategy based on immunizing women of childbearing age has been used successfully to reduce the incidence of pertussis in pregnant women and neonates in the United Kingdom [50].

Periodic seroprevalence studies should be carried out in Catalonia, as well as in other regions and countries of Europe, to assess the impact of MMR vaccination programmes and to identify the population groups that should have higher priority for preventive and epidemiological surveillance activities [4].

In conclusion, susceptibility to measles increased and susceptibility to rubella decreased from 2003 to 2013. We recommend to develop an MMR prevention programme in women of childbearing age based on mass MMR vaccination or MMR screening and vaccination of susceptible women to increase immunity levels against measles, mumps and rubella.

Acknowledgments

Conflict of interest

The authors have no financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter discussed in the manuscript.

References

1. Robertson SE, Featherstone DA, Gacic-Dobo M, Hersh BS (2003) Rubella and congenital rubella syndrome: global update. Rev Panam Salud Publica 14:306−315

2. American Academy of Pediatrics (2009) Measles. In: Pickering L, Baker C, Kimberlin D, Long S (eds) Red Book: Report of the Committee on Infectious Diseases. American Academy of Pediatrics, Elk Grove Village (IL), USA, pp 444−455

3. Ornoy A, Tenenbaum A (2006) Pregnancy outcome following infections by coxsackie, echo, measles, mumps, hepatitis, polio and encephalitis viruses. Reproductive Toxicology 21:446–457

4. Plans P (2013) New preventive strategy to eliminate measles, mumps and rubella from Europe based on the serological assessment of herd immunity levels in the population. Eur. J Clin Microbiol Infect Dis 32:961−966. Available on line at: http://link.springer.com/article/10.1007%2Fs10096-013-1836-6

5. World Health Organization (WHO) (2010) Resolution. Renewed commitment to elimination of measles and rubella and prevention of congenital rubella syndrome by 2010 and Sustained support for polio-free status in the WHO European Region. WHO Regional Office for Europe, Moscow, Russia. Available on line at: http://www.euro.who.int/__data/ assets/pdf_file/0016/122236/RC60_eRes12.pdf

6. World Health Organization (WHO) (2003) Strategic plan for measles and congenital rubella infection in the WHO European Region. WHO Regional Office for Europe, Copenhagen, Denmark. Available on line at: http://www.euro.who.int/document/e81567.pdf.

7. WHO Regional Office for Europe (1985) Targets for health for all. World Health Organization, Copenhagen, Denmark

8. European Center for Disease Control (ECDC) (2013) Annual Epidemiological Report on Communicable diseases in Europe 2013. ECDC, Stockholm, Sweden. Available on line at: http://www.ecdc.europa.eu/en/publications/Publications/annual-epidemiological-report-2013.pdf

9. World Health Organization (WHO) (2013) Centralized Information System for Infectious Diseases (CISID). Measles, rubella, mumps−2013. Available on line at: http://data.euro.who.int/cisid (accesed 20 september 2014).

10. Peña-Rey I, Castellanos T, Suárez B, Alcalde E, Martínez de Aragón MV (2006) Evaluación del plan nacional de eliminación del sarampión en España: año 2005. Boletin Epidemiol Semanal 14:121–127

11. Muscat M, Bang H, Wohlfahrt J, Glismann S, Mølbak K; EUVAC.NET Group. (2009) Measles in Europe: an epidemiological assessment. Lancet 373:383–389 doi: 10.1016/S0140-6736(08)61849-8

12. Steffens I, Martin R, Lopalco PL (2010) Spotlight on measles 2010: Measles elimination in Europe – a new commitment to meet the goal by 2015. Euro Surveill 15(50):pii=19749. Available on line at: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19749

13. Plans P, Torner N, Godoy P, Jané M (2014) Lack of herd immunity against measles in individuals aged <35 years could explain re-emergence of measles in Catalonia (Spain). Int J Infect Dis 18:81–83

14. Plans P, Costa J, Domínguez A, Torner N, Borras E, Plasència A (2010) Prevalence of protective measles virus antibody levels in umbilical cord blood samples in Catalonia, Spain. Clin. Vaccine Immunol 17:356–359

15. Domínguez A, Plans P, Espuñes J, Costa J, Torner N, Cardeñosa N, Plasència A, Salleras L (2007) Rubella immune status of indigenous and immigrant pregnant women in Catalonia, Spain. Eur J Public Health 17:1–5

16. Office of Population Census and Surveys (1980) Classification of occupations. Office of Population Census, London

17. Centers for Disease Control (CDC) (2013) Prevention of Measles, Rubella, Congenital Rubella Syndrome, and Mumps, 2013: Summary Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 62(RR04):1–34

18. National Committee for Clinical Laboratory Standards (1997) Detection and quantitation of rubella IgG antibody: evaluation and performance criteria for multiple component test products, specimen handling, and use of test products in the clinical laboratory; approved guideline. National Committee for Clinical Laboratory Standards (NCCLS), Villanova, PA, USA. NCCLS guideline I/LA6-A 17:25

19. Sato H, Albertch P, Reynolds DW, Stagno S, Ennis FA (1979) Transfer of measles, mumps, and rubella antibodies from mother to infant. Its effect on measles, mumps, and rubella immunization. Am J Dis Child 133:1240−1243

20. Hashira S, Okitsu-Negishi S, Yoshino K (2000) Placental transfer of IgG subclasses in a Japanese population. Pediatr Int 42:337–342

21. Linder N, Tallen-Gozani E, Germana B, Duvdevani P, Ferber A, Sirota L (2004) Placental transfer of measles antibodies: effect of gestational age and maternal vaccination status. Vaccine 22:1509–1514

22. Institut d'Estadística de Catalunya (IDESCAT). Dades estadístiques de Catalunya, 2012. http://www.idescat.cat/territ/BasicTerr?TC=6&V0=NC&V1=NC&MN=1&V3=35 &PARENT=1&CTX=F" \l "FROM (accessed 4 september 2014)

23. Davidkin I, Jokinen S, Broman M, Leinikki P, Peltola H (2008) Persistence of measles, mumps, and rubella antibodies in an MMR-vaccinated cohort: a 20-year follow-up. J Infect Dis 197:950–956

24. Leuridan E, Hens N, Hutse V, Ieven M, Aerts M, Van Damme P (2010) Early waning of maternal measles antibodies in era of measles elimination: longitudinal study. Br Med J 340:c1626. Available on line at: http://dx.doi.org/10.1136/bmj.c1626

25. Pabst H, Spady D, Marusyk R, Carson M, Chiu L, Joffres M, Karen G (1992) Reduced measles immuntiy in infants in a well-vaccinated population. Pediatr Inf Dis J 11:525–529

26. Brugha R, Ramsay M, Forsey T, Brown D (1996) A study of maternally derived measles antibody in infants born to naturally infected and vaccinated women. Epidemiol Infect 117:519–24

27. Goncalves G, Cutts FT, Hills M, Rebelo-Andrade H, Trigo FA, Barros H (1999) Transplacental transfer of measles and total IgG. Epidemiol Infect 122:273–279

28. Dayan GH, Panero MS, Urquiza A, Molina M, Prieto S, Perego MC, Scagliotti G, Galimberti D, Carroli G, Wolff C, Bi D, Bellini W, Icanogle J, Reef S (2005) Rubella and measles seroprevalence among women of childbearing age, Argentina, 2002. Epidemiol Infect 133:861–869

29. Shoda A, Hayashi M, Takayama N, Oshima K, Nishikawa M, Okazaki T, Negishi M, Hayashida S, Watanabe H, Inaba N (2011) Maternal screening and postpartum vaccination for measles infection in Japan: a cohort study. Br J Obstet Gynaecol 118:88–92

30. Honarvar B, Moghadami M, Moattari A, Emami A, Odoomi N, Lankarani KB (2013) Seroprevalence of Anti-Rubella and Anti-Measles IgG Antibodies in Pregnant Women in Shiraz, Southern Iran: Outcomes of a Nationwide Measles-Rubella Mass Vaccination Campaign. PLoS ONE 8: e55043. doi:10.1371/journal.pone.0055043

31. Sathanandan D, Gupta L, Liu B, Rutherford A, Lane J (2005) Factors associated with low immunity to rubella infection on antenatal screening. Aust N Z J Obstet Gynaecol 45:435–438

32. Byrne L, Brant L, Reynolds C, Ramsay M (2012) Seroprevalence of low rubella IgG antibody levels among antenatal women in England tested by NHS Blood and Transplant: 2004–2009. Is rubella susceptibility increasing? Vaccine 30:161–167

33. Mora-García GJ, Ramos-Clason E, Mazenett E, Gómez-Camargo D (2011) [The seroprevalence of IgG antibodies against rubella (German measles) in 10−49 year-old women from Cartagena, Colombia]. Rev. Salud Publica (Bogota) 13:288–297

34. Artimos de Oliveira S, Bastos Camacho LA, Uzeda Barreto MC, Coca Velarde LG, Siqueira MM (2011) Serologic status of women in an urban population in Brazil before and after rubella immunization campaign using routine screening data. J Infect Dis 204 (Suppl 2):S664–S668

35. Wysokinska T, Janaszek W, Bucholc B, Gorska P, Gniadek G, Slusarczyk J, Rawicz M (2004) The prevalence of anti-rubella antibodies in women of childbearing age in Poland. Vaccine 22:1899–1902

36. Pehlivan E, Karaoglu L, Ozen M, Gunes G, Tekerekoglu MS, Genc MF, Egri M, Ercan C (2007) Rubella seroprevalence in an unvaccinated pregnant population in Malatya, Turkey. Public Health 121:462–468

37. Kennedy CM, Burns BA, Ault KA (2006) Does rubella immunity predict measles immunity? A serosurvey of pregnant women. Infect Dis Obstet Gynecol 13890. doi: 10.1155/idog/2006/13890

38. Van den Berg JP, Westerbeek EAM, van der Klis FRM, Berbers GAM, van Elburg RM (2011) Transplacental transport of IgG antibodies to preterminfants: A review of the literature. Early Human Development 87:67–72

39. Aksakal FN, Maral I, Cirak MY, Aygun R (2007) Rubella seroprevalence among women of childbearing age residing in a rural region: is there a need for rubella vaccination in Turkey? Jpn J Infect Dis 60:157–60

40. Lin CC, Yang CY, Shih YL, Hsu HW, Yang TH, Cheng YW, Chang CF, Hsieh LC, Chen BH, Lee CH, Huang YL (2011) Rubella seroepidemiology and estimations of the catch-up immunisation rate and persistence of antibody titers in pregnant women in Taiwan. Br J Obstet Gynecol 118:706–712

41. Sauerbrei A, Prager J, Bischoff A, Wutzler P (2004) [Antibodies against vaccinepreventable diseases in pregnant women and their offspring. Measles, mumps, rubella, poliomyelitis, and varicella]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 47:10–15

42. Hamdan HZ, Abdelbagi IE, Nasser NM, Adam I (2011) Seroprevalence of cytomegalovirus and rubella among pregnant women in western Sudan. Virol J 8:217

43. Qian XH, Yang P, Tang SZ (2010) [Measles antibody level of productive women in Hongkou District of Shanghai Municipal]. Zhongguo Yi Miao He Mian Yi 16:146–147

44. Haas D, Flowers C, Cogndon C (2005) Rubella, rubeola and mumps in pregnant women susceptible and strategies for testing and vaccinating. Obstet Gynecol 106:295–300

45. Desgrandchamps D, Schaad UB, Glaus J, Tusch G, Heininger U (2000) [Seroprevalence of IgG antibodies against measles, mumps and rubella in Swiss

children during the first 16 months of life] Schweiz Med Wochenschr 130:1479−1486

46. Van den Berg JP, Westerbeek EAM, Smits GP, van der Klis FRM, Berbers GAM, van Elburg RM (2014) Lower Transplacental Antibody Transport for Measles, Mumps, Rubella and Varicella Zoster in Very Preterm Infants. PLoS ONE 9: e94714. doi:10.1371/journal.pone.009471

47. Waaijenborg S, Hahné SJM, Mollema L, Smits GP, Berbers GAM, van der Klis FRM, de Melker HE, Wallinga J (2013) Waning of Maternal Antibodies Against Measles, Mumps, Rubella, and Varicella in Communities With Contrasting Vaccination Coverage. J Infect Dis doi: 10.1093/infdis/jit143. Available on line at: http://jid.oxfordjournals.org/content/early/2013/04/29/infdis.jit143.full.pdf+html

48. Plans-Rubio P (2014) Is the current prevention strategy based on vaccination coverage and epidemiological surveillance sufficient to achieve measles and rubella elimination in Europe? Expert Rev Anti Infect Ther 12:723−726. Available on line at: http://informahealthcare.com/doi/abs/10.1586/14787210.2014.917047

49. Plans-Rubió P (2004) Critical prevalence of antibodies minimizing vaccination costs for hepatitis A, hepatitis B, varicella, measles and tetanus in adults and adolescents in Catalonia, Spain. Vaccine 22:4002–4013

50. Amirthalingam G, Andrews N, Campbell H, Ribeiro S, Kara E, Donegan K Fry NK, Miller E, Ramsay M (2014) Effectiveness of maternal pertussis vaccination in England: an observational study. Lancet 384:1521−1528 doi:10.1016/S0140-6736(14)60686-3

Table 1. Geometric mean anti-rubella, anti-measles and anti-mumps IgG titers and prevalence of protective IgG titers in neonates (blood cord   samples) by maternal socio-demographic variables and maternal MMR vaccination status. Catalonia (Spain), 2013.

Maternal variable		IgG titers in cord blood samples			Prevalence (%) of protective IgG titers[a]			
		Rubella (IU/ml) Mean (95 % CI)	Measles (IU/ml) Mean (95 % CI)	Mumps (EU/ml) Mean (95 % CI)	Rubella % (95 % CI)	Measles % (95 % CI)	Mumps % (95 % CI)	n
Age	15−24 years	5.2 (4.7−5.7)	22.2 (18.7−26.3)	19.7 (17.0−22.6)	95.1 (86.3−99.0)	82.0 (71.5−92.4)	73.8 (61.9−85.6)	61
	25−29 years	4.9 (4.6−5.4)	24.1 (19.4−25.3)	23.7 (20.5−27.3)	97.5 (91.1−99.7)	87.3 (79.4−95.3)	77.2 (67.3−87.1)	79
	30−34 years	5.4 (5.0−5.7)	24.1 (21.6−27.0)	25.0 (22.6−27.5)†	97.4 (92.6−99.5)	90.4 (84.6−96.2)	89.6 (83.5−95.6)	115
	35−49 years	5.5 (5.0−5.9)	32.4 (29.2−35.9)*	26.5 (24.0−29.4)	94.9 (88.5−98.3)	98.0 (92.8−99.7)	89.8 (83.3−96.3)	98
	Total	5.3 (5.1−5.5)	25.3 (23.7−27.0)	28.9 (27.7−30.1)	96.3 (94.2−98.4)	90.4 (87.1−93.6)	84.1 (86.5−88.1)	353
Habitat	Urban	5.3 (5.0−5.5)	25.4 (23.7−27.1)	24.0 (22.5−25.6)	96.2 (93.9−98.5)	90.5 (87.1−93.9)	83.5 (79.3−87.8)	316
	Rural	5.4 (4.9−5.9)	24.9 (19.9−31.1)	25.1 (21.0−29.9)	97.3 (89.8−99.9)	89.2 (74.6−97.0)	89.2 (74.6−97.0)	37
Place of birth	Spain	5.2 (5.0−5.5)	25.7 (23.7−27.8)	23.4 (21.6−25.3)	96.9 (94.5−99.4)	91.3 (84.4−95.1)	82.1 (76.9−87.3)	229
	Other country	5.4 (5.0−5.8)	24.7 (22.1−27.7)	25.5 (23.2−27.9)	95.2 (91.0−99.3)	88.7 (82.7−94.7)	87.9 (81.8−94.0)	124
Educational level	<Primary	5.4 (5.0−5.8)	24.6 (22.1−27.4)	23.0 (20.6−25.6)	96.4 (91.0−99.0)	91.0 (85.2−96.8)	82.0 (74.4−86.6)	111
	≥Primary	5.3 (5.0−5.5)	25.6 (23.7−27.8)	24.6 (22.9−26.4)	96.3 (93.7−98.9)	90.1 (86.1−94.0)	85.1 (80.4−89.8)	242
Social class	I−III	5.3 (5.0−5.7)	25.2 (22.6−28.3)	27.3 (21.0−26.0)	96.6 (91.5−99.1)	92.3 (87.9−97.6)	82.1 (74.7−89.4)	96
	IV−V	5.3 (4.9−5.8)	23.5 (20.6−26.7)	24.5 (22.8−26.3)	97.5 (84.2−98.0)	89.9 (82.6−97.2)	88.6 (81.0−96.2)	100
	VI	5.3 (4.9−5.6)	26.4 (23.9−29.1)	24.2 (22.1−26.5)	95.5 (92.0−99.1)	89.2 (84.0−94.3)	83.4 (77.3−89.6)	157
MMR vaccination[b]	Yes	5.0 (4.6−5.5)	22.6 (17.8−28.8)	22.7 (20.0−25.7)	95.1 (87.8−98.6)	87.7 (79.9−95.4)	81.5 (72.4−90.6)	81
	No	5.1 (4.6−5.8)	22.2 (19.4−25.3)	21.1 (16.3−27.3)	100 (88.1−100)	75.9 (58.6−93.2)	69.0 (50.4−87.5)	29

*p<0.001 for 35-49 years vs. 15-24 years and 25-29 year; †p<0.001 for 30-34 years vs. 15-24 years

MMR: measles, mumps, rubella; CI: Confidence interval

a. Protective IgG titers: ≥8 IU/ml for anti-rubella IgG, >300 IU/ml for anti-measles IgG, >460 EU/ml for anti-mumps IgG.
b. Analysis for neonates of women aged <30 years. The MMR vaccination (obtained by questionnaire) in pregnant women was considered correct when they had received 2 doses of MMR vaccine at 12-15 months and 4 years.

Table 2. Prevalence of protective anti-rubella, anti-measles and anti-mumps IgG titers in pregnant women, estimated from IgG titers in blood cord samples, by socio-demographic variables. Catalonia (Spain), 2013.

		Prevalence (%) of protective IgG titers[a]			
		Rubella % (95 % CI)	Measles % (95 % CI)	Mumps % (95 % CI)	n
Age	15−24 years	95.1 (86.3−99.0)	80.3 (69.5−91.1)	70.5 (58.2−82.8)	61
	25−29 years	94.9 (87.5−98.6)	86.1 (77.8−94.3)	74.7 (64.4−84.9)	79
	30−34 years	97.4 (92.6−99.5)	88.7 (82.5−94.9)	83.5 (76.3−90.7)	115
	35−49 years	93.9 (88.6−99.1)	95.9 (88.9−98.9)	89.8 (83.3−96.3)	98
	Total	95.5 (93.2−97.8)	88.7 (85.2−92.1)	81.0 (76.8−89.2)	353
Habitat	Urban	95.3 (92.7−97.8)	86.6 (84.9−92.3)	80.7 (76.2−85.2)	316
	Rural	97.3 (85.8−99.9)	89.2 (74.6−97.0)	83.8 (74.6−97.0)	37
Place of birth	Spain	96.5 (93.9−99.1)	89.5 (85.3−93.7)	79.0 (73.5−84.8)	229
	Other country	93.5 (88.8−98.3)	87.1 (80.8−93.4)	84.7 (77.9−91.4)	124
Educational level	<Primary	96.4 (91.0−99.0)	89.2 (83.0−95.6)	79.3 (71.3−87.3)	111
	≥Primary	95.0 (92.1−98.9)	88.4 (84.2−92.7)	81.8 (76.7−86.9)	242
Social class	I−III	96.6 (91.5−99.1)	91.5 (86.0−97.0)	77.8 (69.8−85.7)	96
	IV−V	96.2 (83.9−99.2)	86.1 (77.8−94.3)	87.3 (79.4−95.3)	100
	VI	94.3 (90.3−98.2)	87.9 (82.5−93.3)	80.3 (73.7−86.8)	157
MMR vaccination[b]	Yes	92.6 (86.3−98.4)	85.2 (76.8−93.5)	77.8 (68.1−87.4)	81
	No	100 (88.1−100)	75.9 (58.6−93.2)	65.5 (46.5−84.5)	29

*p<0.001 for 35-49 years vs. 15-24 years and 25-29 years
†p<0.001 for 30-34 years vs. 15-24 year
MMR: measles, mumps, rubella; CI: Confidence interval

    a. Protective IgG titers in pregnant women: ≥8 IU/ml for anti-rubella IgG, >300 IU/ml for anti-measles IgG, and >460 for anti-mumps IgG. IgG titers in pregnant women were estimated from titers in cord blood samples by assuming that in pregnant titers were 17%, 11% and 23% lower than in cord blood samples.
  b. Analysis for pregnant women aged <30 years. MMR vaccination (obtained by questionnaire) was considered correct when women had received 2 doses of MMR vaccine at 12-15 months and 4 years.

Table 3. Vaccination coverage for the measles-mumps-rubella (MMR) vaccine and monovalent rubella vaccine in pregnant women (during childhood) by socio-demographic variables. Catalonia (Spain) in 2013.

Maternal Variable		Total sample			Autochthonous pregnant women			Immigrant pregnant women			Autochthonous versus immigrant pregnant women	
		MMR vaccine	Monovalent Rubella vaccine		MMR vaccine	Monovalent rubella vaccine		MMR vaccine	Monovalent rubella vaccine		MMR vaccine	Monovalent rubella vaccine
		% (95% CI)	% (95% CI)	n	% (95% CI)	% (95% CI)	n	% (95% CI)	% (95% CI)	n	OR (95% CI)	OR (95% CI)
Age	15−29 years	73.6 (60.8−87.1)	0.0 (60.8−87.1)	110	78.6 (67.7−89.2)	0.0 (60.8−87.1)	65	66.7 (51.8−81.5)	0.0 (60.8−87.1)	45	1.82 (0.78−4.24)	−
	30−34 years	61.3 (51.7−70.8)	5.4 (51.7−70.8)	111	69.2 (58.3−80.1)	5.1 (1.4−12.6)	78	42.4 (24.0−60.8)	6.1 (0.7−20.2)	33	3.05 (1.33−7.02)*	0.84 (0.14−4.81)
	35−49 years	18.6 (9.8−27.4)	29.1 (9.8−27.4)	86	20.3 (1.6−14.2)	34.8 (22.8−46.7)	69	11.8 (1.5−31.4)	5.9 (0.1−28.7)	17	1.90 (0.39−9.34)	8.53 (1.06−68.3)**
	Total[a]	50.7 (45.0−56.6)	11.7 (8.0−15.5)	307	56.1 (49.2−62.6)	13.2 (8.4−18.0)	212	48.4 (37.4−59.0)	4.2 (1.2−10.4)	95	1.37 (0.84−2.12)	4.67 (1.46−14.8)*
Habitat	Urban	54.6 (48.5−60.7)	7.7 (48.5−60.7)	271	57.2 (49.7−64.7)	10.6 (5.8−15.3)	180	45.9 (38.6−60.3)	2.2 (0.3−7.7)	91	1.37 (0.82−2.27)	5.25 (1.20−23.0)**
	Rural	47.2 (29.5−64.9)	27.8 (29.5−64.9)	36	50.0 (31.1−68.9)	28.1 (11.0−45.3)	32	25.0 (0.6−80.6)	25.0 (0.6−80.6)	4	3.00 (0.28−32.0)	1.17 (0.11−12.8)
Education	<Primary	47.0 (36.7−57.3)	9.0 (36.7−57.3)	100	51.5 (38.9−64.1)	13.2 (4.4−22.0)	68	37.5 (19.2−55.8)	0.0 (0.0−10.9)	32	1.77 (0.75−4.17)	−
	≥Primary	57.0 (50.0−64.0)	10.6 (50.0−64.0)	207	58.3 (49.9−66.7)	13.2 (7.3−19.1)	144	54.0 (40.9−67.0)	4.8 (1.0−13.3)	63	1.19 (0.66−2.17)	1.17 (0.11−12.8)
Social class	I-III	50.9 (41.1−60.7)	16.4 (41.1−60.7)	110	52.1 (37.2−58.5)	18.1 (9.7−26.4)	94	43.8 (19.7−70.1)	6.3 (0.2−30.2)	16	1.40 (0.48−4.07)	3.31 (0.41−26.8)
	IV-V	53.0 (40.0−65.8)	12.1 (40.0−65.8)	66	53.3 (37.6−69.0)	17.8 (5.5−30.1)	45	52.4 (28.6−76.1)	0.0 (0.0−16.0)	21	1.04 (0.37−2.93)	−
	VI	56.5 (46.7−65.4)	3.8 (46.7−65.4)	131	63.0 (51.2−74.8)	4.1 (0.2−11.5)	73	48.3 (34.5−62.0)	3.4 (0.4−11.9)	58	1.82 (0.91−3.68)	1.20 (0.19−7.43)

* p<0.01 for the vaccination coverage in autochthonous vs. immigrant pregnant women

** p<0.05 for the vaccination coverage in autochthonous vs. immigrant pregnant women

OR: Odds ratio; CI: Confidence interval

a. Age standardized vaccination coverage (reference population: pregnant women in Catalonia in 2012)

Table 4. Prevalence (%) of protective anti-measles and anti-rubella IgG titers in neonates, and MMR vaccination coverage (%) in pregnant women (during childhood) in Catalonia (Spain) in 2003 and 2013

| Maternal age | | Year 2003 | | Year 2013 | | Year 2013 vs. 2003 |
		% (95% CI)	n	% (95% CI)	n	OR (95% CI)[a]
Prevalence of protective anti-measles IgG titers (>300 IU/ml) in neonates						
Age (years)	15−24	96.5 (94.2−98.8)	228	82.0 (71.5−92.4)	61	0.18 (0.07−0.44)*
	25−29	98.2 (96.7−99.6)	379	89.9 (79.4−95.3)	79	0.12 (0.05−0.34)*
	30−34	98.1 (96.8−99.4)	529	90.4 (84.6−96.2)	115	0.18 (0.08−0.43)*
	35−49	99.0 (97.1−99.8)	302	98.0 (92.8−99.7)	98	0.48 (0.07−2.92)
	Total[b]	98.6 (98.0−99.2)	1498	91.5 (88.4−94.5)	353	0.15 (0.09−0.27)*
Prevalence of protective anti-rubella IgG titers (≥8 IU/ml) in neonates						
Age (years)	15−24	89.9 (86.3−93.5)	298	95.1 (86.3−99.0)	61	2.16 (0.67−6.87)
	25−29	93.5 (93.1−97.6)	388	97.5 (91.1−99.7)	79	1.87 (0.47−7.39)
	30−34	94.1 (92.0−96.2)	543	97.4 (92.6−99.5)	115	2.41 (0.77−7.52)
	35−49	93.2 (90.2−96.2)	309	94.9 (88.5−98.3)	98	1.36 (0.51−3.57)
	Total[b]	93.6 (92.3−94.9)	1538	96.4 (94.2−98.8)	353	1.80 (1.01−3.22)**
MMR vaccination coverage in pregnant women (2 doses in 2013; 1 dose in 2003)						
Age (years)	15−29	77.4 (74.1−80.6)	667	73.6 (64.9−82.3)	110	0.82 (0.51−1.30)
	30−34	13.2 (10.2−16.2)	529	61.3 (51.7−70.8)	111	10.34 (6.57−16.35)*
	35−49	15.6 (11.3−19.8)	302	18.6 (9.8−27.4)	86	4.24 (0.67−2.30)
	Total[c]	32.9 (30.5−35.3)	1498	50.7 (45.3−56.1)	165	2.09 (1.66−2.65)*

* p<0.001, **p<0.05
OR: Odds Ratio; CI: Confidence interval
a. The Odds Ratio (OR) compares the prevalence in 2013 versus 2003.
b. Age standardized prevalence (reference population: pregnant women in Catalonia in 2012).
c. Age standardized vaccination coverage (reference population: pregnant women in Catalonia in 2012).