

Factors associated with poor adherence to MMR vaccination in parents who follow vaccination schedule

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Abbreviations: CI_{95%}, 95% confidence interval; IQR, interquartile range; MMR, Measles, Mumps and Rubella; OR, odds ratio; mo, months; y, years

Due to median vaccination coverage far from elimination level, Italy is still an European country with high number of measles cases per million of people. In this study we explored potential socioeconomic, medical and demographic factors which could influence the propensity of family members for measles vaccination schedule.

A cross-sectional study was performed through a questionnaire administered to the parents of children who received the first dose of MMR vaccine in two different vaccination centers in the Palermo area from November 2012 to May 2013.

Overall, the role played by internet (OR 19.8 $P = 0.001$) and the large number of children in a family (OR 7.3 $P \leq 0.001$) were the factors more associated to be unvaccinated, whereas the birth order of the child (OR 0.3 $P < 0.05$ for the oldest children vs. the closer young one) and reporting a lack of MMR vaccination as a "personal decision" (OR 0.19 $P \leq 0.01$) inversely correlated with the risk of quitting vaccination.

These findings can be useful for a better knowledge of disaffection to vaccination practice in local settings and could contribute to improve and maintain timely uptake, suggesting approaches to optimize the uptake of MMR tailored to the needs of local populations.

Introduction

The dramatic reduction of the incidence of vaccine-preventable diseases during the last decades, contributed to the public perception that the severity of the disease and susceptibility to it have decreased.¹ Recent parental concerns about perceived vaccine safety issues, such as a purposed association between vaccines and autism, although not supported by a credible body of scientific evidence, have led increasing numbers of parents to refuse or delay vaccination for their children.^{2–4}

The introduction of measles vaccination in Europe in the 1960s and 1970s significantly changed the epidemiology of measles. While some European countries virtually eliminated measles within a few years after introducing measles vaccination, other countries who failed to achieve the high vaccination coverage required for elimination noticed only limited impact on incidence, experiencing how rapidly evolving outbreaks over 6–8 mo in the pre-vaccine era have been replaced by comparatively slowly propagating outbreaks over longer periods, several years sometimes.⁵

In Italy, measles vaccination was first introduced in 1976 and, to date, is included in the national immunization program in association with Mump and Rubella as MMR associated vaccine. MMR vaccine is provided free of charge between the 13th and 15th mo of age, as first dose, and between 5th and 6th y, as second dose, by local vaccination centers, because it was included in the list of "essential health interventions".⁶ However, the uptake of measles vaccine still remain relatively low in Italy with irregular levels across regions.

In Sicily also, due to non-satisfactory vaccine coverage, in 2010 and 2011 a prolonged outbreak accounting for more than 2000 cases affecting essentially peoples of two age classes: 1–4 and 15–20 y old was registered.⁷ In those years, vaccination coverage for the first dose of MMR was 85.3% and 86.8%, respectively.⁸

The aim of the study is to evaluate the refuse level of first MMR dose, a better knowledge of the social-demographic characteristics associated with refused vaccination, and the reasons reported by parents for their child's immunization status.

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Materials and Methods

A cross-sectional study was performed in two vaccination centers of Palermo area from November 2012 to May 2013. The user base population of the centers analyzed is about 1180 children per birth cohort, thus representing about 24% of the target population per year. The population of study included parents who accepted/refused the first dose of MMR vaccination for children among the thirteenth and the twentieth month of birth. A total of 489 parents in the two centers satisfied the study criteria although 46 were not included because they refused to undergo interview. Overall, 443 parents were interviewed. Of these, 356 (80.4%) were mothers with a mean age of 32.8 y (95% CI: 32.3–33.3) and 87 (19.6%) were fathers with a mean age of 36.2 y (95% CI: 35.6–36.8). All enrolled individuals were given a telephonic questionnaire, by two standardized physician interviewer, that investigated demographic and socio-economic factors of parents and medical characteristics of parent's children. At least five attempts to contact families of selected children were made, before excluding them. Informed consent was obtained according to Italian law, and confidentiality of responses was assured. The questionnaire was pre-tested on a convenience sample of parents to ensure clarity of interpretation and ease of completion to improve validity of responses.

Measures

Measures were reported by the main respondent (mother and father) during interviews. The outcome measure was represented by MMR vaccine status at age 13–15 mo and was obtained from the database of the vaccination centers. Children's parents were classified as unimmunized (received no combined MMR) and partially vaccinated (received one combined MMR). Our criteria for refusing vaccination allowed for a 5-mo grace period for receipt of MMR, and a parent who has decided to vaccinate his/her children within 5 mo of becoming age-eligible was considered to be vaccinated.

The covariates were indicators of doubt about vaccines. We explored parent's socio-demographic and economic characteristics (age, country of origin, educational level, economic referred level and unemployed status in the last 2 y) as well as their knowledge about MMR vaccination (rules for administration of MMR vaccine, reason to vaccinate/not vaccinate for MMR, informative sources about MMR and role of websites and pediatrician towards MMR). Furthermore, children's demographic and medical factors were also investigated (sex, age, birth order, previous hospital admission, chronic disease, adverse reaction to former vaccination, chronic drugs use).

Parents' educational level was classified according to the Italian law: primary school (5 y of education), secondary school (3 y of education), high school (5 y of education) and degree (5 y of education). Parents' economic level reported was scored on a 10-point Likert scale with options ranging from "1" (low level) to "10" (high level). In Sicily, like other Italian regions, the MMR vaccine is highly recommended by the Ministry of Health and administrated free of charge between the thirteenth and fifteenth month of life.⁶ Hence, the degree of knowledge of parents about the rules for administration of MMR vaccine were also evaluated.

Furthermore, were also investigated reasons for scarce adherence to first dose of MMR classifying according to Millennium Cohort Study as "practical" (such as missing an appointment), "medical" (eg, child had chronic illness), "conscious decision" (including fear and links with autism) or "other" (which included "I don't know").⁹ Sample size was calculated with the use of software Epi Info to find the factors associated with parent's decision not to vaccinate their children for MMR. All the other socio-demographic, economic and medical variables, except the continuous ones, were in "yes/no" format.

Statistical analysis

The level of significance chosen for all analyzes was 0.05 two-tailed. For categorical variables absolute and relative frequencies were calculated, while continuous variables not normally distributed were represented as median (interquartile range, IQR). The normal distribution was assessed with the Shapiro–Wilk test. Differences in socio-demographic, economic and medical characteristic were tested using Student *t* test for continuous variables normally distributed, Wilcoxon-Mann-Whitney test on the equality medians for continuous variables non normally distributed and χ^2 tests for categorical variables. The odds ratio (OR) and 95% confidence interval ($CI_{95\%}$) were also calculated.

Furthermore a bivariable logistic regression analysis was performed to examine the association of MMR refusal and socio-demographic, economic and medical characteristics. All variables that were found to be statistically significant on bivariable analysis were included in a multivariable logistic regression model. The goodness of fit was calculated for each model and the model with the lowest log-likelihood ratio test was considered to have the best predictive ability. The adjusted OR (adj-OR) with $CI_{95\%}$ was also calculated for variables that are not distributed in the final model. Data analysis was performed with the software Stata/MP 11.2.

Results

In **Table 1** are depicted the socio-demographic characteristics of the 443 parents finally enrolled into the study. Overall, 66 (14.9%) refused the first dose of MMR and 377 (85.1%) decided to take the first dose of MMR for their children.

The mothers of unvaccinated were more frequently Italian (95.5% vs. 89.9% $P < 0.001$) and had more children (2 vs. 1 $P < 0.001$) than mothers of vaccinated children. Parents of unvaccinated children have taken their decision to refuse MMR vaccine often with the second born (50.0% vs. 39.5%) rather than with the first one (25.8% vs. 49.8%) compared with the choices of vaccinated children's parents ($P = 0.002$).

About medical characteristics, the parents of unvaccinated compared with those of vaccinated children had: increased consumption of drugs for children's chronic diseases (18.2% vs. 8.3% $P = 0.016$) and higher prevalence of children's chronic diseases (25.8% vs. 10.6% $P = 0.001$).

The parents of unvaccinated children less frequently thought that the vaccination was mandatory (39.4% vs. 63.7% $P < 0.001$), they used most frequently as sources of information on

Table 1. Socio-demographic, economic and medical factors of parents and their children

Factors		Total N (%)	No- MMR vaccinated N (%)	MMR vaccinated N (%)	P value
Total		443 (100.0)	66 (14.9)	377 (85.1)	
Mother's country of origin?	Italian	402 (90.7)	63 (95.5)	339 (89.9)	0.019
	Foreign	30 (6.8)	0 (0.0)	30 (8.0)	
	Not responding	11 (2.5)	3 (4.5)	8 (2.1)	
Mother's age?(years)		33 (29–37)	34 (30–38)	33 (29–36)	0.418
Mother's study title?	Degree	114 (25.7)	15 (22.7)	99 (26.2)	0.940
	High school	170 (38.4)	25 (37.9)	145 (38.5)	
	Secondary school	132 (29.8)	19 (28.9)	113 (30.0)	
	Primary school	16 (3.6)	3 (4.5)	13 (3.4)	
	Nothing	0 (0.0)	0 (0.0)	0 (0.0)	
	Not responding	11 (2.5)	4 (6.0)	7 (1.9)	
Mother's age at first child? (years)		29 (24–33)	27 (22–33)	29 (24–32.5)	0.057
Number of mother's children's?		2 (1–2)	2 (2–3)	1 (1–2)	< 0.001
Father's country of origin?	Italian	390 (88.1)	42 (63.6)	348 (92.3)	0.112
	Foreign	21 (4.7)	0 (0.0)	21 (5.6)	
	Not responding	32 (7.2)	24 (36.4)	8 (2.1)	
Father's age? (years)		36 (32–40)	37 (33–43)	36 (32–40)	0.675
Father's study title?	Degree	93 (21.0)	12 (18.2)	81 (21.5)	0.410
	High school	177 (39.9)	21 (31.8)	156 (41.4)	
	Secondary school	136 (30.8)	23 (34.8)	113 (30.0)	
	Primary school	20 (4.5)	5 (7.6)	15 (4.0)	
	Nothing	2 (0.4)	0 (0.0)	2 (0.5)	
	Not responding	15 (3.4)	5 (7.6)	10 (2.6)	
You or your husband have been unemployed or downgraded in work over the past 2 y?	Yes	134 (30.2)	16 (24.2)	118 (31.3)	0.285
	No	283 (63.9)	45 (68.2)	238 (63.1)	
	Not responding	26 (5.9)	5 (7.6)	21 (5.6)	
What is the economic level of your family (from 1 to 10)?		6 (6–7)	6 (5–7)	6 (6–7)	0.078
Was the child ever hospitalized?	Yes	96 (21.7)	20 (30.3)	76 (20.2)	0.091
	No	327 (73.8)	45 (68.2)	282 (74.8)	
	Not responding	20 (4.5)	1 (1.5)	19 (5.0)	
Has child ever taken drugs chronically?	Yes	43 (9.7)	12 (18.2)	31 (8.3)	0.016
	No	380 (85.8)	53 (80.3)	327 (86.7)	
	Not responding	20 (4.5)	1 (1.5)	19 (5.0)	
Has child ever had a chronic disease?	Yes	57 (12.9)	17 (25.8)	40 (10.6)	0.001
	No	363 (81.9)	48 (72.7)	315 (83.6)	
	Not responding	23 (5.2)	1 (1.5)	22 (5.8)	
Has the child ever had adverse reactions to vaccines?	Nothing	222 (50.2)	36 (54.6)	186 (49.3)	0.428
	Mild	73 (16.4)	12 (18.2)	61 (16.2)	
	Severe	99 (22.3)	16 (24.2)	83 (22.0)	
	Not responding	49 (11.1)	2 (3.0)	47 (12.5)	

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Table 1. Socio-demographic, economic and medical factors of parents and their children (continued)

Factors		Total N (%)	No- MMR vaccinated N (%)	MMR vaccinated N (%)	P value
What are the rules of MMR administration?	Mandatory	266 (60.0)	26 (39.4)	240 (63.7)	< 0.001
	Recommended	111 (25.1)	33 (50.0)	78 (20.7)	
	Other	32 (7.2)	5 (7.6)	27 (7.2)	
	Not responding	34 (7.7)	2 (3.0)	32 (8.4)	
Informative source on MMR vaccine:					
Physicians	Yes	293 (66.1)	39 (60.6)	254 (67.9)	0.190
	No	150 (33.9)	27 (39.4)	123 (32.1)	
Family/friends	Yes	111 (25.1)	9 (13.6)	102 (27.1)	0.020
	No	332 (74.9)	57 (86.4)	275 (72.9)	
Websites	Yes	51 (11.5)	16 (24.2)	35 (9.3)	< 0.001
	No	392 (88.5)	50 (75.8)	342 (90.7)	
Other mass media	Yes	54 (12.2)	16 (24.2)	38 (10.1)	0.010
	No	389 (87.8)	50 (75.8)	339 (89.9)	
Other	Yes	25 (5.6)	6 (9.1)	19 (5.0)	0.007
	No	418 (94.4)	60 (90.1)	358 (95.0)	
What was the role of the websites on the decision to vaccinate your child for MMR?	Positive	53 (12.0)	2 (3.0)	51 (13.5)	< 0.001
	Negative	41 (9.2)	21 (31.8)	20 (5.3)	
	None	338 (76.3)	42 (63.7)	296 (78.5)	
	Not responding	11 (2.5)	1 (1.5)	10 (2.7)	
What was the role of paediatrician on the decision to vaccinate your child for MMR?	Positive	370 (83.5)	53 (80.4)	317 (84.1)	0.044
	Negative	9 (2.0)	4 (6.0)	5 (1.3)	
	None	52 (11.7)	8 (12.1)	44 (11.7)	
	Not responding	12 (2.7)	1 (1.5)	11 (2.9)	
What are the reasons not to get vaccinated for MMR?	Practical	161 (36.3)	28 (42.4)	133 (35.3)	< 0.001
	Medical	140 (31.6)	33 (50.0)	107 (28.4)	
	Conscious decision	93 (21.0)	3 (4.6)	90 (23.8)	
	Other	7 (1.6)	0 (0.0)	7 (1.9)	
	Not responding	42 (9.5)	2 (3.0)	40 (10.6)	
What are the reasons to get vaccinated for MMR?	Practical	261 (58.9)	28 (42.5)	233 (61.8)	< 0.001
	Medical	108 (24.4)	25 (37.9)	83 (22.0)	
	Conscious decision	36 (8.1)	5 (7.6)	31 (8.2)	
	Other	4 (0.9)	4 (6.0)	0 (0.0)	
	Not responding	34 (7.7)	4 (6.0)	30 (8.0)	
Children sex	Male	214 (48.3)	31 (47.0)	183 (48.5)	0.891
	Female	221 (49.9)	31 (47.0)	190 (50.4)	
	Not responding	8 (1.8)	4 (6.0)	4 (1.1)	
Age (months)		15 (12–18)	16 (13–20)	14 (12–17)	0.054
Birth order	First	205 (46.4)	17 (25.8)	188 (49.8)	0.002
	Second	182 (41.2)	33 (50.0)	149 (39.5)	
	Third	34 (7.7)	10 (15.2)	24 (6.4)	
	Fourth	10 (2.3)	2 (3.0)	8 (2.1)	
	Fifth	2 (0.1)	1 (1.5)	1 (0.3)	
	Not responding	10 (2.3)	3 (4.5)	7 (1.9)	

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MMR vaccination websites (24.2% vs. 9.3% $P < 0.001$) and other mass media (24.2% vs. 10.1% $P = 0.01$) and less commonly family/friends (13.6 vs. 27.1% $P = 0.02$) compared with parents of vaccinated children. Furthermore, the parents of unvaccinated children more frequently reported that the websites (31.8% vs. 5.3% $P < 0.001$) and the pediatricians (6.0% vs. 1.3% $P = 0.044$) had a negative role on their decision.

Unvaccinated parents compared with those vaccinated reported most commonly medical reasons as reason for refusing MMR vaccine (50.0% vs. 28.4% $P < 0.001$) but less practical (42.4% vs. 53.3% $P < 0.001$) and conscious decision (4.6% vs. 23.8% $P < 0.001$), hence as motivation to be vaccinated reported less frequently medical reasons (42.5% vs. 61.8% $P < 0.001$).

Table 2 shows the results of the multivariable analysis of the relationship between the parents who refused MMR and the variables that were significant in bivariable analysis. A significant direct relationship was found between the rejection of MMR and the negative role played by websites on the decision to vaccinate their children (Adjusted OR 19.78, $P = 0.001$) and the same was “having a greater number of children” (Adjusted OR 7.31 $P < 0.001$). A significant inverse relationship was found between parents who refused MMR and birth order of their children (Adjusted OR 0.35, $P = 0.038$) and conscious decision as reason for not to get vaccinated (Adjusted OR 0.19, $P = 0.01$).

Discussions

The Italian Plan for Elimination of Measles and Congenital Rubella (PNEMoRC 2010–2015) has sets the adoption of ordinary and extraordinary actions for the achievement, by 2015, of a vaccination coverage $>95\%$ for the first dose of MMR within 24 mo of life.¹⁰ Several factors have been identified as determinants of potential deficient immunization rates in infancy and childhood. The effect of some factors could depends on country-specific circumstances; for example, on parent’s attitudes and beliefs regarding vaccination. This study has investigated the phenomenon of refusal of MMR vaccination in a sample population of the greatest city in Sicily and which reasons lead parents to not vaccinate for first dose MMR.

About 15 percent of the sample analyzed decided not to vaccinate their child for first shot of MMR. This data highlights a sub-optimal vaccine uptake in Sicily respect to national and international vaccination coverage.^{8,11} This vaccination coverage can lead, in the future, to experience slowly propagating outbreaks with longer intervals and consequently with an effect on the age distribution of cases during outbreaks.⁵ These information must be known and periodically reviewed in order to achieve adequate vaccination coverage in hard to reach groups.

In particular this study suggests that the factor more affecting the refusal of MMR was the negative role played by websites on parents’ decision to vaccinate their children. To date about 80% of users access the network to inquire about health issues, of these one-fifth

seek data on vaccines, and 70% admit to be conditioned.¹² It was observed that a single access to an anti-vaccination site for just 5–10 min, increase the perception of the risks associated with the use of vaccines and decrease the perception of risks from non-use of vaccines.¹³ Moreover it was found that the adverse publicity has a gradual build-up and prolonged effect, rather than an instant impact on the decision to vaccinate for MMR.¹⁴

Additionally, to have a mother with a greater number of children was shown to be an important negative predictor for MMR in toddlers in the current study. Number of siblings was also previously founded to predict a child’s immunization status in a study conducted on either mandatory or state-funded routine vaccines.¹⁵ The importance of ensuring that infants from larger families complete their primary immunizations on time should be made clear in immunization publicity because these unvaccinated children of larger families are at increased risk of exposure to infection from younger siblings.

A condition founded to be associated with the probability of rejecting MMR was a lower birth order of the children. This result contrasts with those of previous studies.¹⁶ These can be explained because parents acquire adequate knowledge on vaccination with younger children after experienced a wrong treatment of measles that was learned from the pre-vaccine era.¹⁷

Finally conscious decision was another factor that reduce the probability to refuse MMR. In the case of MMR a full information can lead to a reduction of missed vaccination in particular in hard to reach parents. This fact was also confirmed in a study where parents who refused combined vaccines acting on the uncertainty and the lack of clear information.^{18,19}

The main limitation of the study appears to be the only setting of Palermo area and small number of cases. However, this study can provide an initial data that have to be extend to the national setting through the conduction of a multicenter survey.

Nonetheless, this paper provides important information on the barriers experienced by families during times of no outbreak to improve and sustain the current MMR program. Furthermore in this study, the distinction between compulsory and optional vaccinations (a distinguishing aspect of childhood immunization policy in Italy) was also taken into account. Indeed the immunization status of children was extracted from the medical records of involved vaccination centers. These determine better reproducibility of the study compared with others.²⁰

Identifying populations at risk of underimmunization is essential to planning effective interventions for increasing vaccine coverage. Among the tools realized in Italy to counteract misinformation on vaccine there is the project “VaccinarSI”,

Table 2. Multivariable logistic regression of factors directly and inversely associated with parents who refused MMR

Factors	AdjOR	CI _{95%}	
		Lower	Upper
Negative role of websites on the decision to vaccinate for MMR (vs no role)	19.78	3.32	117.82
Number of mother’s children (per unit increase)	7.31	2.89	19.87
Birth order (older child vs. the close young one)	0.35	0.13	0.94
Conscious decision like reason not to get vaccinated for MMR (vs practical reason)	0.19	0.05	0.67

promoted by the Italian Society of Hygiene. The project has the aim to reply the lack of information on the web and at the same time, to show the validity of the vaccinations. The portal also provides scientific data developed in a clear and simple way, and accompanied by verifiable sources.²¹ It would also be necessary to conduct a Health Technology Assessment on the abolition of mandatory vaccination in Italy.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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