

COMMUNICATIONS C9  
Thursday 15 October  
h. 8.30  
Brown Room 1

## Assessment of the effectiveness of the universal varicella vaccination program in Toscana (Italy), in the period 2010-2013

### Valutazione dell'efficacia del programma di vaccinazione universale antivaricella in Toscana (Italia), nel periodo 2010-2013

Luca Pieri,<sup>1</sup> Barbara Rita Porchia,<sup>1</sup> Francesca Pieralli,<sup>1</sup> Ornella Varone,<sup>1</sup> Giuditta Niccolai,<sup>1</sup> Annalisa Roselli,<sup>2</sup> Sara Boccalini,<sup>3</sup> Paolo Bonanni,<sup>3</sup> Angela Bechini,<sup>3</sup> and the Working Group of Tuscan LHU's \*

<sup>1</sup>Scuola specializzazione in Igiene e medicina preventiva, Università di Firenze, Italy; <sup>2</sup>Dip. Prevenzione, ASL 4 Prato, Italy; <sup>3</sup>Dip. Scienze della salute, Università di Firenze, Italy

**Corresponding author:** Luca Pieri; e-mail: pieriluca@gmail.com

#### Abstract

**Objective.** To assess the effectiveness of the varicella vaccination program in Toscana after one dose of vaccine, in the birth cohorts 2008-2011.

**Design.** Varicella vaccine effectiveness (VE) was calculated using the "screening method", based on vaccine coverage (VC) at 24 months and proportion of vaccinated subjects among varicella notified cases (PVC), verified through the Local Health Units' (LHUs) immunization registries. Breakthrough varicella (BV) was defined as a case of varicella occurring in a child vaccinated  $\geq 42$  days before the date of disease onset.

**Setting and participants.** The study was conducted in the 12 Tuscan LHUs and included all varicella cases notified in 2010-2013 in children of the birth cohorts 2008-2011.

**Main outcome measures.** BV cases; VE after one dose of varicella vaccine; time interval between varicella vaccination and symptom onset.

**Results.** VC was 79.8%, VE reached 90.8% (95%CI 89.5%-92.0%) and the proportion of BV among notified cases was 26.6%. The median time interval between vaccination and symptom onset was 25 months.

**Conclusions.** The very low rate of BV cases among vaccinated children confirms the high effectiveness even of a single dose of varicella vaccine and does not support a change of the current immunization schedule.

(*Epidemiol Prev* 2015; 39(4) Suppl 1: 119-123)

**Key words:** varicella, vaccine effectiveness, screening method, breakthrough varicella, Toscana

#### Riassunto

**Obiettivo.** Valutare l'efficacia del programma di vaccinazione antivaricella in Toscana, dopo una singola dose di vaccino, per le coorti di nascita 2008-2011.

**Disegno.** Per calcolare l'efficacia vaccinale (EV) è stato applicato il "metodo di screening" utilizzando i dati di copertura vaccinale a 24 mesi e la proporzione dei casi vaccinati (*varicella breakthrough*, VB), verificati attraverso le anagrafi vaccinali delle ASL. Sono stati classificati come VB i casi con sintomi insorti dopo almeno 42 giorni dalla prima dose di vaccino.

**Setting e partecipanti.** Lo studio include i casi di varicella notificati nel periodo 2010-2013, per le coorti di nascita 2008-2011, nelle 12 ASL della Toscana.

**Principali misure di outcome.** Casi VB; EV dopo singola dose di vaccino; intervallo di tempo tra vaccinazione e inizio sintomi.

**Risultati.** La CV è stata del 79,8%, l'EV è risultata pari al 90,8% (IC95% 89,5%-92,0%) e la percentuale dei casi VB sul totale delle notifiche è stata del 26,6%. L'intervallo mediano tra la vaccinazione e la comparsa dei sintomi è stato di 25 mesi.

**Conclusioni.** La bassissima percentuale di casi VB sul totale dei vaccinati conferma l'elevata efficacia sul campo anche di una sola dose di vaccino anti-varicella e non depone per una modifica della attuale schedula vaccinale.

(*Epidemiol Prev* 2015; 39(4) Suppl 1: 119-123)

**Parole chiave:** varicella, efficacia vaccinale, metodo di screening, fallimenti vaccinali, Toscana.

## INTRODUCTION

Varicella is an acute contagious viral disease, caused by the varicella zoster virus (VZV), which is spread by air droplets or by contact with vesicle liquid. Varicella has a worldwide distribution, affects mostly children and, despite being generally a mild disease, may be fatal, especially in neonates and immunocompromised people.<sup>1</sup>

A live attenuated varicella vaccine has been available since 1974, and in 1996 universal one-dose routine vaccination was introduced in United States.<sup>2,3</sup> This led to a drastic reduction of varicella incidence. Nevertheless, the observation of "breakthrough" varicella (BV) cases (cases of varicella occurring 42 days or more after vaccination following exposure to wild-type virus), even in communities with a high vaccination coverage, with a relative shift of the disease onset towards older ages, led the Advisory Committee on Immunization Practices (ACIP) to recommend a second dose of the vaccine for children aged 4-6 years in 2007.<sup>4</sup>

In Europe, six countries endorsed Universal Varicella Vaccination (UVV) for children at the national level (Cyprus, Germany, Greece, Latvia, Luxemburg and Austria) and two countries at the regional level (Spain, Italy).<sup>5</sup> A two-dose schedule, with an interval of 1 to 6 years, is used for administration of Measles-Mumps-Rubella (MMR) vaccines in most countries in Europe.<sup>6</sup>

In Italy, UVV was introduced in 2003 and has been limited to those regions able to guarantee high level (over 80%) of vaccination coverage (VC), in order to avoid a possible shift of infection towards adulthood.<sup>7</sup>

A two-dose regimen for varicella vaccination is recommended and has been now implemented for at least 2 years in eight Italian regions (Puglia, Basilicata, Calabria, Friuli-Venezia Giulia, Sardegna, Sicilia, Veneto, and Toscana) with different schedules. A general reduction of incidence and hospitalization rates for varicella was observed between 2003-2012. Moreover, immunization coverage with first dose at 24 months of age was high in the eight regions (84%-95%) in 2012.<sup>7</sup> Since 2015, other regions have included UVV in their immunization program. Toscana had 3,750,511 inhabitants in 2014, of whom 191,356 (5,1%) were under 5 years.<sup>8</sup> The Tuscan health system is organized in 12 LHUs (Local Health Units). Each LHU ensures the essential levels of assistance, including routine vaccination programs; all vaccine doses administered are registered in a computerized vaccination registry.

Tuscany was one of the first Italian regions to introduce a program of universal vaccination against varicella with a combined measles, mumps, rubella, and varicella (MMRV) vaccine, in July 2008. The schedule calls for the first dose of vaccine at the age of 13-15 months and a second dose at the age of 5-6 years.<sup>9</sup> The aim of this study is to assess the effectiveness of the varicella vaccination program in Toscana in preventing varicella cases, in subjects belonging to the birth cohorts 2008-2011.

## MATERIALS AND METHODS

Varicella is subject to mandatory notification in Italy. All notifications are routinely collected at the regional level and repor-

ted in the Italian Computerized Surveillance System for Communicable Diseases (SIMI). In SIMI, patient information such as date of birth, gender, date of symptom onset, date of notification, place of residence, and vaccination status are available.<sup>10</sup> In order to assess whether surveillance data collected in Toscana permitted a rapid "screening" analysis, a pilot study was performed in 2014 in two Tuscan LHU (Firenze and Prato),<sup>11</sup> and subsequently extended to all LHUs during 2015.

Immunization coverage at 24 months of age for varicella-containing vaccines in the years 2010-2013 were obtained from official regional data. Notification data were retrieved from SIMI and the vaccination status was double checked into each LHU immunization registry.

The current study was conducted in the 12 Tuscan LHUs and included all varicella cases notified between 1 January 2010 and 31 December 2013 in children born between 1 January 2008 and 31 December 2011. In the current analysis, only birth cohorts for whom vaccination coverage data at 24 months were available (2008-2011) were included.

Varicella vaccine effectiveness for at least one dose of vaccine was calculated using the screening method proposed by Farrington.<sup>12</sup> Such method is based on the known relationship between the proportion of vaccinated population (PPV=vaccination coverage), vaccine effectiveness (VE) and proportion of vaccinated subjects among disease cases (PCV); identifying two of those parameters it is possible to calculate the third. Therefore, reliable values of VC and PCV are essential in order to obtain a good estimate of vaccine effectiveness.<sup>13</sup>

VE is then given by the following formula:

$$VE = 1 - [(PCV / 1-PCV) (1-PPV / PPV)]$$

Moreover, 95% confidence intervals were calculated by birth cohort, expressing VE with the following equation:<sup>14</sup>

$$VE = 1 - (\text{incidence rate}_{\text{vaccinated}} / \text{incidence rate}_{\text{unvaccinated}})$$

The ratio between the incidence rates among vaccinated and unvaccinated individuals corresponds to a relative risk.

Data collection was performed from February 2015 to May 2015 and consisted of three phases:

- extraction of all varicella notifications collected in SIMI between 2010 and 2013;
- selection of cases that occurred in children born in the birth cohorts 2008-2011;
- assessment of their vaccination status using the LHU immunization registries.

Exclusion criteria were: place of residence outside Toscana, wrong date of birth, data missing in the immunization registry. The case definition for breakthrough varicella (BV) adopted in this study was a case of varicella occurring in a child vaccinated  $\geq 42$  days before the date of disease onset.

The time interval between date of vaccination and date of symptom onset was calculated for all BV cases and expressed in months of 30 days. The median of the time interval, the 25th, and the 75th percentiles were also calculated.

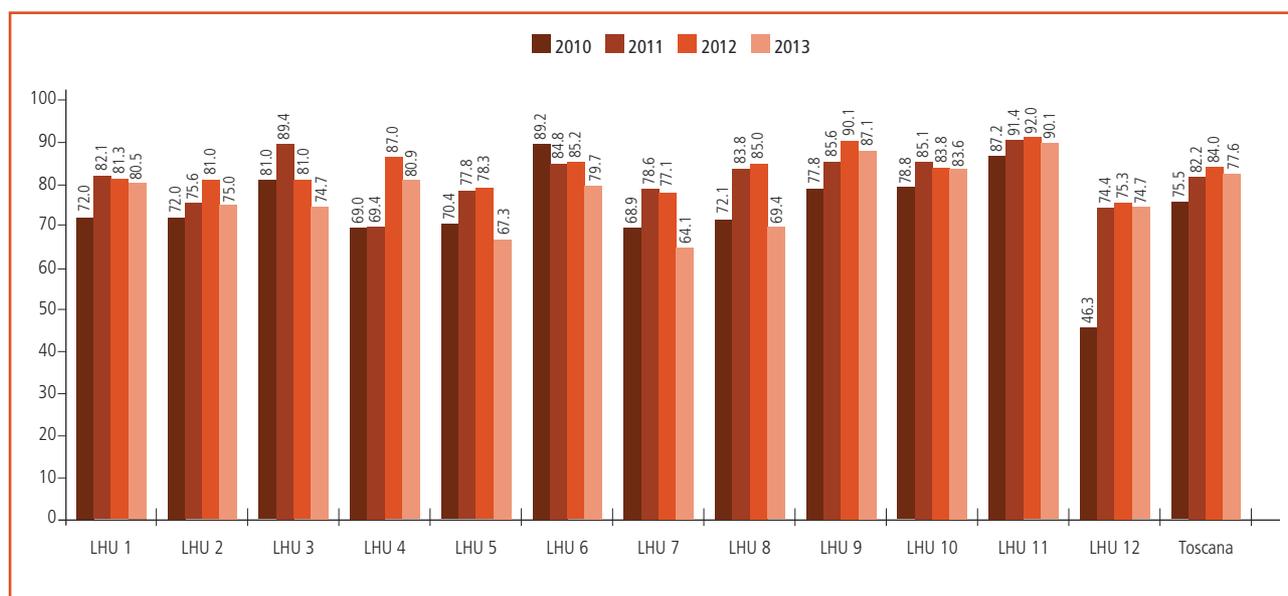


Figure 1. Varicella vaccination coverage (%) at 24 months of age in Toscana and in the 12 LHUs, in the period 2010-2013.

Figura 1. Copertura vaccinale (%) a 24 mesi in Toscana e nelle 12 ASL, nel periodo 2010-2013.

## RESULTS

In Toscana, immunization coverage at 24 months of age for varicella vaccination in the years 2010-2012 (birth cohorts 2008-2010) rose from 75.4% to 84%, while in the 2011 birth cohort, recorded in 2013, it decreased to 77.6%.

Vaccination coverage data show a wide variability among all LHUs, with a range from 46.3% (LHU 12) to 89.2% (LHU 6) in the 2008 birth cohort, and from 64.1% (LHU 7) to 90.1% (LHU 11) in the 2011 birth cohort. In 2013, a lower level of VC was observed in all LHUs compared to 2012 (figure 1).

The proportion of BV among notified cases showed a wide variability in the 12 LHUs. In LHU 2, no BV case was registered, while in two LHUs (LHU 1 and LHU 6) the percentage reached 40% (table 1). Overall, the percentage of vaccinated subjects experiencing BV in the birth cohorts 2008-2011 was only 0.3% at the regional level (table 1).

Between 2010 and 2013, 103,738 out of 130,012 children born between 2008 and 2011 and resident in Toscana had received at least one dose of varicella vaccine (average VC of 79.8%). In the same period 1,080 cases of varicella were diagnosed in chil-

dren of the same birth cohorts, 287 (26.6%) of these cases had previously been vaccinated (varicella breakthrough cases). Therefore, effectiveness after one dose of varicella vaccine, calculated with the screening method, was 90.8% (95%CI 89.5-92.0) with a range from 77.8% to 98.6% (table 2).

In breakthrough varicella cases, analyzing the time interval between vaccination and symptom onset, a median value of 25 months was calculated for the whole population. In particular, 64 BV cases occurred 15 months after vaccination (25th percentile) and 246 cases after 35 months (75th percentile).

## DISCUSSION

The present study was performed to assess the effectiveness of the varicella vaccination program in Toscana using the screening method, as already done in Navarre (Spain) and Puglia (Italy). Both studies reported a high VE value of 96.8% and 98.8% respectively.<sup>15,16</sup>

The effectiveness of a single dose of vaccine against the disease of any severity reported by varicella surveillance in the United States and international case-control studies outside of outbreak

	VC (%)	Vaccinated	Notified cases	BV cases	PCV (%)	BV/vaccinated (%)
LHU 1	78.7	4,880	15	6	40.0	0.1
LHU 2	75.8	5,966	13	0	0.0	0.0
LHU 3	83.6	8,667	52	12	23.1	0.1
LHU 4	76.2	7,481	40	4	10.0	0.1
LHU 5	73.5	9,211	226	58	25.7	0.6
LHU 6	84.8	9,548	120	48	40.0	0.5
LHU 7	72.3	6,892	89	27	30.3	0.4
LHU 8	77.6	9,277	98	25	25.5	0.3
LHU 9	85.0	6,036	94	28	29.8	0.5
LHU 10	82.8	23,832	191	51	26.7	0.2
LHU 11	90.2	8,409	114	26	22.8	0.3
LHU 12	67.2	3,539	28	2	7.1	0.1

Table 1. Vaccination coverage at 24 months of age for varicella in the birth cohorts 2008-2011, breakthrough varicella (BV) cases and proportion of cases notified in vaccinated subjects (PCV), rate of BV cases among all vaccinated subjects, by LHU in Toscana (Italy), 2010-2013.

Tabella 1. Copertura vaccinale per varicella nelle coorti di nascita 2008-2011, casi di "varicella breakthrough" (BV) e proporzione di casi notificati in vaccinati (PCV), proporzione di casi BV sul totale dei vaccinati (BV/vaccinated), per ASL in Toscana (Italia), 2010-2013.

Birth year	Population			Varicella cases			Vaccine effectiveness (%) (95%CI)	
	N	vaccinated		N	vaccinated			
		n	%		n	%		
2008	33,541	25,310	75.5	459	186	40.5	77.8	(73.3 - 81.6)
2009	32,797	26,964	82.2	292	63	21.6	94.0	(92.1 - 95.5)
2010	32,464	27,259	84.0	218	33	15.1	96.6	(95.1 - 97.6)
2011	31,210	24,205	77.6	111	5	4.5	98.6	(96.7 - 99.4)
<b>2008-2011</b>	<b>130,012</b>	<b>103,738</b>	<b>79.8</b>	<b>1,080</b>	<b>287</b>	<b>26.6</b>	<b>90.8</b>	<b>(89.5 - 92.0)</b>

**Table 2.** Estimated vaccine effectiveness (%) of varicella vaccination program by birth cohort (2008-2011), in Toscana (Italy), 2010-2013.

**Tabella 2.** Stima dell'efficacia vaccinale (%) del programma di vaccinazione antivariella per coorte di nascita (2008-2011), in Toscana (Italia), 2010-2013.

periods falls in the range between 71% and 87%.<sup>17</sup> Results of the current study show a cumulative VE of 90.8% in the birth cohorts targeted by the UVV, in line with other studies. Vaccine effectiveness registered a progressive increase from the 2008 to the 2011 birth cohort. This result could be explained by the herd immunity effect and the reduced probability to become infected with VZV, even in case of primary vaccination failure. As a matter of fact, our data do not allow us to establish whether possible changes in accuracy occurred in the assessment of the vaccination status among the birth cohorts, in order to justify the lower value of VE registered in the 2008 birth cohort compared to the other cohorts.

In Toscana, VC at 24 months was high since the first years of UVV introduction; in fact in the 2008 birth cohort, the oldest one considered in our study, VC was over 75%, a successful result for the regional health services. This result is explained by the use of the combined MMRV vaccine, taking advantage of high vaccination coverage for MMR in Toscana after the implementation of the Regional Plan for measles and congenital rubella elimination (i.e., 92% of VC in 2010).<sup>18</sup>

Although there is no doubt in adopting a two-dose schedule for varicella vaccination, as recommended by all international societies (AAP, ACIP, STIKO), on the basis of the US experience,<sup>4,19,20</sup> a lively debate is still undergoing about the best distance between the two doses.

Our findings on the median time interval between vaccination and symptom onset (25 months) suggest that a shorter interval between the two doses of varicella vaccine might be preferable to reduce breakthrough varicella cases. According to our results, a second dose of varicella vaccine given at 3 years of age would have prevented about half of BV cases in our birth cohorts. Nevertheless, in the Tuscan context, considering the low proportion of BV cases among all vaccinated children of the analyzed cohorts and the high varicella VC obtained up to now, shortening the time interval between the two doses of vaccine would not be convenient and should be carefully considered to avoid any potential disruption to a well-established vaccination schedule.<sup>17</sup> Moreover, further studies on primary and secondary vaccine failure should be wisely evaluated prior to suggesting a possible change in the regional recommended schedule. Finally, no consistent trend between breakthrough varicella rate and time since vaccination resulted from our findings.

A limitation of the present study may be related to the reliability

of the input data used to calculate VE. In particular, during our data collection, mismatches between the official regional data system (SIMI) and the vaccination registries of the LHUs were found.

Regarding SIMI, a certain proportion of notified cases in the regional database recorded uncertain or missing fields in reporting vaccination status and date of birth. In order to attain reliable surveillance data, a better implementation of the infectious disease information system would be advisable. For instance, an alert system to avoid empty and misreported fields should be provided.

Moreover, in view of further studies on the impact of the Tuscan vaccination program, it might be useful to adopt a unique regional vaccination registry to reduce the current heterogeneity of local vaccination registries. As a matter of fact, currently the 12 LHUs of Toscana have different computerized vaccination registries available.

Another critical issue was the unavailability of data related to VC at 24 months of age for the first birth cohort target of the UVV (children born in 2007) and consequently the need to exclude it from this study. This was due to the fact that in 2009 VC data for varicella were collected together with those for MMR. The regional data collection form for varicella VC data was implemented in 2010, and varicella vaccination coverage data have therefore been available since that year.

Moreover, at the time of data collection, the unavailability of notification data for the year 2014 and the consequent choice to limit the study period to 2013 could have resulted in an overestimate of VE, mostly for the youngest birth cohort of 2011. The strengths of the study consisted in the voluntary contribution of all 12 Tuscan LHUs to provide data required for the analysis. In particular, this allowed us to obtain results which are representative of the whole regional population. Furthermore, the collaboration between the University of Florence, the healthcare personnel of the 12 LHUs and the regional public health sector contributed to providing a good opportunity to perform supplementary studies on the same topic.

Further development of this study is needed to extend the observation period including 2014 data and to assess the effectiveness of the varicella vaccination program in Tuscany in preventing severe varicella cases, in particular those requiring hospitalization.

**Conflicts of interest:** none declared

### Acknowledgements

The authors would like to thank Michela Baccini, Department of Statistics (University of Florence), for her assistance in the analysis of data, and Emanuela Balocchini, Lucia Pecori, and Sara Gallicchio, Sector of Prevention and Safety in Living and Working Environments, Food and Veterinary - General Direction Rights of citizenship and social cohesion (Toscana Region), for their support in the realization of the study.

**\*Working Group of Tuscan LHU's:** Alessandra Bagnoli,<sup>9</sup> Alessandro Barcioli,<sup>12</sup> Simonetta Baretta,<sup>12</sup> Franco Barghini,<sup>14</sup> Luca Carneglia,<sup>7</sup> Sergio Coccioli,<sup>5</sup> Emanuela De Franco,<sup>7</sup> Alberto Del Forno,<sup>7</sup> Maria Di Cunto,<sup>11</sup> Antonella Di Vito,<sup>5</sup> Anna Cristina Epifani,<sup>2</sup> Paolo Filidei,<sup>13</sup> Nicoletta Gal-

letti,<sup>7</sup> Giovanna Giuffreda,<sup>6</sup> Antonio Lombardi,<sup>8</sup> Rosa Luzzoli,<sup>4</sup> Cinzia Macchi,<sup>7</sup> Paola Marchini,<sup>4</sup> Moreno Marcucci,<sup>5</sup> Gloria Marinari,<sup>8</sup> Maria Teresa Maurello,<sup>10</sup> Franca Mazzoli,<sup>6</sup> Gabriele Mazzoni,<sup>13</sup> Astrid Mercione,<sup>9</sup> Luana Paliaga,<sup>2</sup> Stefano Pieroni,<sup>14</sup> Lucia Righeschi,<sup>10</sup> Elisabetta Raso,<sup>6</sup> Luigi Ricci,<sup>2</sup> Maria Grazia Santini,<sup>12</sup> Elisabetta Sensoli,<sup>6</sup> Alberto Silva,<sup>13</sup> Ersilia Sini-sgalli,<sup>1</sup> Laura Storiotti,<sup>14</sup> Alberto Tomasi,<sup>5</sup> Fabrizia Verdelli<sup>10</sup>

<sup>1</sup>Scuola specializzazione in Igiene e medicina preventiva, Università di Firenze, Italy; <sup>2</sup>Dip. Prevenzione, ASL 4-Prato, Italy; <sup>3</sup>Dip. Scienze della salute, Università di Firenze, Italy; <sup>4</sup>ASL 2-Lucca, Italy; <sup>5</sup>ASL 3-Pistoia, Italy; <sup>6</sup>ASL 5-Pisa, Italy; <sup>7</sup>ASL 6-Livorno, Italy; <sup>8</sup>ASL 7-Siena, Italy; <sup>9</sup>ASL 8-Arezzo, Italy; <sup>10</sup>ASL 9-Grosseto, Italy; <sup>11</sup>ASL 10-Florence, Italy; <sup>12</sup>ASL 11-Empoli, Italy; <sup>13</sup>ASL 12-Versilia, Italy

### References/Bibliografia

- Seward JF, Zhang JX, Maupin TJ, Mascola L, Jumaan AO. Contagiousness of varicella in vaccinated cases: a household contact study. *JAMA* 2004;292:704-708.
- Takahashi M, Otsuka T, Okuno Y, Asano Y, Yazaki T. Live vaccine used to prevent the spread of varicella in children in hospital. *Lancet* 1974;304:1288-90.
- Centers for Disease Control and Prevention. Prevention of varicella: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 1996;45(RR-11):1-36.
- Marin M, Guris D, Chaves SS, Schmid S, Seward JF. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2007;56:1-40.
- European Centre for Disease Prevention and Control. *Varicella vaccination in the European Union*. Stockholm, ECDC, 2015.
- Bonanni P, Breuer J, Gershon A, et al. Varicella vaccination in Europe – taking the practical approach. *BMC Med* 2009;7:26.
- Bechini A, Boccalini S, Baldo V, et al. Impact of universal vaccination against varicella in Italy. *Hum Vaccin Immunother* 2015;11:63-71.
- ISTAT. Demo ISTAT. <http://demo.istat.it>
- Regione Toscana. Calendario vaccinale della Regione Toscana e direttive in materia di vaccinazioni. Aggiornamento aprile 2015. Deliberazione Giunta Regionale n. 571 del 27.04.2015. Allegato 1. [http://www301.regione.toscana.it/bancadati/atti/Contenuto.xml?id=5099142&nomeFile=Delibera\\_n.571\\_del\\_27-04-2015-Allegato-1](http://www301.regione.toscana.it/bancadati/atti/Contenuto.xml?id=5099142&nomeFile=Delibera_n.571_del_27-04-2015-Allegato-1)
- SIMI. Sistema Informatizzato Malattie Infettive. <http://www.simi.iss.it>
- Bechini A, Pieralli F, Roselli A, et al. Valutazione dell'efficacia del programma di vaccinazione antivariella in Toscana, nella ASL di Firenze e nella ASL di Prato nel periodo 2009-2013. Atti Congresso SItI 2014. <http://www.societaitalianaigiene.org/site/new/images/docs/atticongressi/2014/riccione/poster.pdf>
- Farrington CP. Estimation of Vaccine Effectiveness using the screening method. *Int J Epidemiol* 1993; 22:742-46.
- Lopalco PL. Assessing Vaccines and Vaccination Programmes in the Field. *IJPH* 2009;6:189-93.
- Chen RT, Orenstein WA. Epidemiologic methods in immunization programs. *Epidemiol Rev* 1996;18:99-117.
- García Cenoz M, Castilla J, Chamorro J, et al. Impact of universal two-dose vaccination on varicella epidemiology in Navarre, Spain, 2006 to 2012. *Euro Surveill* 2013;18:20552.
- Tafari S, Fortunato F, Cappelli MG, et al. Effectiveness of vaccination against varicella in children under 5 years in Puglia, Italy 2006-2012. *Hum Vaccin Immunother* 2015;11(1):214-19.
- Bonanni P, Gershon A, Gershon M, et al. Primary Versus Secondary Failure After Varicella Vaccination: Implications for Interval Between 2 Doses. *Pediatr Infect Dis J* 2013;32(7):e305-13.
- Bechini A, Levi M, Boccalini S, et al. Progress in the elimination of measles and congenital rubella in Central Italy. *Hum Vaccin Immunother* 2013;9:649-56.
- American Academy of Pediatrics Committee on Infectious Diseases. Prevention of varicella: recommendations for use of varicella vaccines in children, including a recommendation for a routine 2 dose varicella immunization schedule. *Pediatrics* 2007;120:221-31.
- STIKO. German Standing Committee on Vaccination. Recommendations of the Standing Committee on Vaccination (STIKO). *Epid Bull* 2014;34:305-39. [http://www.rki.de/EN/Content/Prevention/Vaccination/recommendations/34\\_2014\\_engl\\_19215.pdf?](http://www.rki.de/EN/Content/Prevention/Vaccination/recommendations/34_2014_engl_19215.pdf?)