Infant immunization coverage in Italy (2000-2016)

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Abstract

Background. In Italy, national-level immunization polices are included in the National Immunization Prevention Plan (PNPV), whose latest edition – 2017-2019 PNPV – was finally approved in February 2017. Coverage rates are a key measure of immunization system performance; it can inform and support national and regional polices’ implementation monitoring, as well as measure the impact of interventions aimed at increasing vaccine uptake.

Methods. We collected, analysed and critically interpreted 2000-2016 Italian national infant immunization coverage trends, by different vaccine, target population, and by Region. Data were provided by the Directorate General for Prevention of the Italian Ministry of Health.

Results. In 2016, none of the mandatory or recommended vaccines reached the 95% national coverage target set in the PNPV. Weighted average national coverage for currently mandatory vaccines (against Polio, Tetanus, Diphtheria, Hepatitis B) and other antigens included in the hexavalent vaccine (Pertussis, and Haemophilus influenzae type b) ranged between 93.0% for Hepatitis B and 93.7% for Tetanus; it was lower for Measles, Mumps and Rubella vaccines (87.2%), pneumococcal (88.4%) and meningococcal C conjugate vaccines (80.7%), with a high degree of heterogeneity by Region. Both hexavalent and MMR vaccines coverage rates have been decreasing in the last years, respectively from 2012 (-2.8%) and from 2010 (-3.6%).

Discussion. Further efforts are needed to increase vaccine uptake in Italy, to improve data collection and reporting, as well as to fight the growing phenomenon of the vaccine hesitancy so that PNPV’s objectives and targets can be met in the near future.

BACKGROUND

In Italy, immunization programs are managed in the context of the National Health Service (NHS) which provides universal health coverage: the national level defines the core benefit package of health services to be guaranteed to all citizens (Essential levels of care or LEA) and fund them through the National Health Fund; Regions are responsible for planning and implementing healthcare services [1]. In the field of immunization, the Ministry of Health (MoH), in agreement with the State-Region Conference, issues the Italian National Immunization Prevention Plan (Piano Nazionale di Prevenzione Vaccinale, PNPV), a guidance document for immunization polices aimed at harmonizing immunization strategies across the country and which defines vaccines to be actively offered free-of-charge to target populations. On the basis of this document, each Region adopts its own Regional Immunization Plan and schedule.

Coverage is a key measure of immunization system performance [2]; it can support national and regional immunization polices’ implementation monitoring, as well as inform on the impact of interventions aimed at increasing vaccine uptake. In a well-functioning health systems coverage data are routinely collected by health authorities [3, 4] but rarely shared within the scientific community. In 2015 we reported to the international scientific community the structure and content of the PNPV 2012-2014, we systematically reported how the PNPV was transposed into regional immunization programs and, most importantly, we analyzed national-level coverage data to assess to which extent the 2012-2014 PNPV objectives and coverage targets had been met [5]. We concluded that, despite being a milestone for prevention in the Italian health policy agenda, the 2012-2014 PNPV had only partially succeed in reaching its aims, that coverage rates were
decreasing and much work was left to be done. In the paper we also discussed the barriers to effective implementation of immunization programmes in Italy that would needed to be tackled in the next edition of the PNPV.

Aim of the current study is to report Italian vaccine coverage trends over the last 16 years, by different vaccines, target populations and selected geographical factors, as well as to interpret them in the context of Italian national immunization polices implemented throughout the study period.

METHODS

In this paper we pool, analyse and critically interpret national-level infant immunization coverage rates for the period 2000-2016. Data were provided by the Directorate General for Prevention (DGP) of the Italian Ministry of Health.

Infant immunization coverage rates are calculated computing number of immunised subjects by resident target population, expressed as percentages. The MoH has reported, on a year-basis since 2000, 24 months of age coverage rates of mandatory and recommended infant vaccinations included in the National Immunization Schedule, by Region, as well as by residents-weighted national average. Since 2013 coverage rates are also calculated at 36 months of age, at 5-6 years of age (for booster doses) and by single antigen.

Reporting flow of immunization data in Italy

In Italy the reporting flow of immunization data mirrors the heterogeneous structure of the different Regional Health Services. Regions on a year-basis report to the MoH on absolute numbers of immunised subjects (numerators) and target populations (denominators). Some Regions use the national standard Immunization Information Systems (IIS), while others have local IISs. In the latter case, Departments of Prevention of Local Health Authorities (LHAs) – which implement and manage immunization services at the local level – periodically provide Regions with vaccines’ programmes monitoring data, including immunisation data and adverse events (AEs) reporting. Regions are responsible for collecting data from all local health authorities, pooling and sending them to the central level, (DGP of the MoH) on a yearly periodicity (deadline April of the year after data are referring to), using a standardized data collection form.

The central level is responsible for:
1. defining the reporting system for immunization coverage data in terms of: timing, responsibilities and data requirements;
2. collecting from the different Regions, harmonizing and pooling coverage rates on a year-basis;
3. analysing data, calculating vaccination coverages and interpreting them, carrying out comparisons by different LHAs and regional settings, also on the basis of infectious diseases surveillance trends;
4. disseminating national-level immunization coverage rates through the website of the MoH, identifying critical issues on where to focus to improve vaccine uptake.

Coverage targets

The PNPV sets, for each vaccine included in the PNPV National Immunization Schedule, 24 months of age coverage targets (for completed vaccines courses and for MMR first dose) to be met by Regions. Coverage targets are set taking into account pathogens’ specific herd immunity thresholds needed to interrupt infectious diseases transmission at the population level. The coverage targets defined in the last edition of the PNPV (2012-2014 PNPV) [5] and currently applied to mandatory and recommended infant immunization programmes are set at ≥ 95% for the following vaccines: Tetanus, Diptheria, Acellular Pertussis, Hepatitis B, Inactivated Polio, Haemophilus influenzae type b, Measles, Mumps, Rubella, Pneumococcal and Meningococcal C.

Analysis

We carried out descriptive analysis on national-level coverage data for all vaccines programmes included in the 2012-2014 PNPV’s National Immunization Schedule. All data were provided by the DGP of the Italian MoH and compiled in a comprehensive database. Although throughout the study period the MoH has collected coverage rates from Regions by different vaccine formulations (i.e Diptheria, Tetanus and acellular Pertussis vaccine – DTaP or Diphtheria and Tetanus vaccine + Diphtheria, Tetanus, and acellular Pertussis vaccine – DT-DTaP; [6]), we present coverage figures by single preventable disease and by single vaccine. Based on data availability, we carried out descriptive analysis for the national and a regional level.

Primary outcomes were vaccine coverage rates at 24 months (for the period 2000-2016) and 36 months (for the period 2013-2015) for the following vaccines:

- Inactivated Poliomelitis, Diptheria, Tetanus and acellular Pertussis; Haemophilus influenzae type b; Hepatitis B;
- Measles, Mumps, and Rubella;
- Pneumococcal conjugate;
- Meningococcal C conjugate vaccines;
- Varicella.

In particular, we report on two sets of analyses: i) we present current immunization coverage data, expressed as the most updated coverage rates (year 2016) by preventable disease (cross sectional design analysis), then ii) we present immunization coverage trends over time, expressed as percentage change in vaccine coverage over different time periods. Of note, Pneumococcal and Meningococcal C conjugate vaccines coverage is only available for the period 2013-2016, as those two vaccines were included in the National Immunization Schedule to be actively offered free of charge to the target population starting from year 2012 (2012-2014 edition of the PNPV). Varicella immunization coverage is reported from year 2013 and has been actively offered free of charge – as a pilot project – only in eight Regions (Apulia, Basilicata, Calabria, Friuli Venezia Giulia, Sardegna, Sicily, Tuscany and Veneto).

RESULTS

National level immunization coverage rates for the period 2000-2016 by single antigen are reported in Table.
In Table 1. At the national level, none of the currently mandatory (against Polio, Tetanus, Diphtheria, Hepatitis B) or recommended vaccines reached the 95% coverage target set in the PNPV. In 2016 coverage rates exceeded 90% for Polio (93.3%), Tetanus (93.7%), Diphtheria (93.6%), Pertussis (93.6%), Hepatitis B (93.0%) and Haemophilus influenzae type b (Hib; 93.1%) vaccines; they ranged between 85% and 90% for Measles (87.3%), Mumps (87.2%), Rubella (87.2%) and Pneumococcal Conjugate (88.4%) vaccines and was 80.7% for Meningococcal C Conjugate vaccine.

Regional level coverage rates for year 2016 are reported in Table 2. Seven (33%) Regions out of 21 met the 95% PNPV coverage target for Polio, Tetanus, Diphtheria and Pertussis vaccines, 6 (28.6%) Regions met the 95% PNPV coverage target for Hepatitis B and Hib vaccines. Regional vaccine coverages for those vaccines ranged from 97% to 85%, with highest rates reported in the Basilicata, Molise, Abruzzo, Calabria, Lazio and Calabria Regions and lowest in the Veneto, Sicilia and Valle d’Aosta Regions and the Autonomous Province of Bolzano (Table 2). Only one Region (Basilicata) met the 95% PNPV coverage target for Pneumococcal Conjugate vaccine (regional range: 97%, Basilicata-81%, Autonomous Province of Bolzano).

None of the Regions met the 95% coverage target for Measles, Mumps, Rubella or Men C conjugate vaccines, with regional ranges ranging between 93% and 68% for Measles, Mumps and Rubella vaccines and between 91% and 61% for Men C conjugate vaccine (Table 2). Measles, Mumps and Rubella coverage was highest in the Lombardy and Piemonte Regions, the only two Region exceeding 91% coverage, and lowest (below 80%) in the Molise Region, together with the Autonomous Province of Bolzano.

Looking at trends, national-level 2000-2016 coverage rates are reported in Table 1 and Figure 1. With regard to mandatory vaccines (Polio, Hepatitis B, Tetanus and Diphtheria) coverage rates were maintained above the 95% coverage target from 2002 to 2013 and have been decreasing since then. In particular, mandatory vaccines coverage has decreased by, on average, 2.8% in the last four years (2012-2016; percentage decrease being highest for hepatitis B vaccine, -3.1% and lowest for Tetanus vaccine, -2.6%). This decreasing trend have been reported in almost all Regions: between 2012 and 2016 five Regions (Friuli Venezia Giulia, Valle d’Aosta, Marche, Sicily and the Autonomous Province of Bolzano) reported ≥ 4% decrease in mandatory vaccines coverage, while only one Region (Sardinia) reported a positive figure (+2.5%). Coverage trends for all Regions are reported in details in the Supplementary Material.

Over the study period, Measles, Mumps and Rubella vaccine coverage has never met the 95% coverage targets (Figure 1). MMR vaccine coverage has been increasing from 2000 to 2010, it was highest in 2010 (90.6%) and has drastically decreased since then. In the 2010-2016 study period, Measles vaccine coverage in Italy decreased by 3.6%, with decreasing trends reported in all Regions. In 9 (43%) Regions, the percentage decrease was greater than 5% and in 3 Regions (Friuli Venezia Giulia, Marche and Molise) greater than 9.5% (see supplementary material). Of note, measles, mumps and rubella coverage rates increased at the national level between 2015 and 2016 by 2.3%, this increase being greater than 2% in all but eight Regions (range: -5% – +4.1%)

Coverage rates at 36 months of age are available since 2013. In Table 3 coverage rates at, respectively, 24 and 36 months of age are compared for birth cohorts 2010, 2011, 2012 and 2013. As emerges from the table, for birth cohorts 2010, 2011 and 2012, 95% coverage targets were met at 36 months of age for mandatory vaccines, pertussis and Hib. In particular, the percentage of non-vaccinated subjects who got vaccinated at 36 months of age was highest in the 2012 birth cohort, exceeding 11% for all vaccines (Table 3). The highest percentages were reported for Measles, Mumps and Rubella vaccines for birth cohorts 2010 (23% for Measles and 27.8% for Mumps and Rubella), 2012 and 2013, exceeding 18% for all three vaccines. In the eight regions that piloted varicella, universal immunization coverage in 2016 ranged between 85.5% in the Veneto region and 64.5% in the Calabria Region, with heterogeneous regional 2013-2015 trends (see Table 2 and Supplementary Material).

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Hib: Haemophilus influenzae type b; Men C: Meningococcal C Conjugate; Hep B: Hepatitis B; *weighted average.
DISCUSSION

We present a comprehensive, reliable and relevant set of Italian national-level immunization coverage data, focusing on vaccine programmes for infants and children over the last sixteen years (2010-2016).

Overall in Italy coverage rates have been decreasing since 2012 and are – as for now – still below the targets established by the MoH. We report a high degree of heterogeneity within the different Italian Regions and by vaccine.

With regard to mandatory immunizations, together with the other antigens contained in the hexavalent vaccine (i.e Hib and Pertussis) just about one third of Italian Regions reached the 95% coverage targets in 2016, with other Regions reporting coverage rates lower than 90%. Measles, Mumps and Rubella coverage rates are lower, averaging 87% at the national level, with heterogeneous regional patterns. Of great importance, both hexavalent and MMR vaccines coverage rates have been decreasing in the last years, respectively from 2012 (-2.8%) and from 2010 (-3.6%).

Detailed data on varicella immunization programmes in selected regions since its introduction are provided by the Inter-regional Group on Varicella Vaccination (IGVV) [7]. Of particular note, four out of the 8 pilot Regions that implemented a two-dose schedule Varicella immunization have MMR coverage rates higher than the national average. Data on Pneumococcal and Meningococcal C conjugate vaccines, included in the National Immunization Schedule for the first time in 2012, suggest that – although far from meeting PNPV targets – both vaccines have been well introduced in infant immunization schedules in all Regions reaching, respectively, over 88% and 81% coverage at the national level in 2016.

The case of the Veneto Region is peculiar: being the only Italian Region that in 2007 suspended mandatory vaccination [8], after more than seven years it reports one of the lowest regional coverage rate for the hexavalent vaccine. Such figure is to be interpreted and further discussed as it could inform the debate on whether to change regional immunization policies.

Overall, it is worth recalling that factors responsible for the reported wide variability of coverage among Regions include: different and heterogeneous immunization offer models across LHAs and Regions, varying political commitment to support immunization at the local and regional level, and differentially distributed general population attitudes towards vaccine, by geographical setting.

Coverage rates at 36 months of age, which are available starting from year 2013, and which are higher than rates at 24 months of age, suggest that a considerable share of the population get their children vaccinated with delay, a characteristic comprised in the definition of vaccine hesitancy [9, 10].

Our study has some limitations. First, data come...
from administrative sources whose quality might partially differ by Region. In fact, Regions use slightly different denominators sources to compute coverage rates including civil registries, healthcare registries or Italian National Institute of Statistics data on residents. As progress are being made to harmonize immunization information systems and implement electronic vaccination registries in the whole country, data quality will improve and regional comparisons will become more reliable. Scant data are available on Pneumococcal, and meningococcal C vaccines whose coverage rates are only reported since 2013 or in the context of ad hoc projects [11], nor allow us to distinguish between different available vaccines. With regard to data analysis, a limitation is that we kept a descriptive approach. Although we acknowledge that accounting in our analysis for ecological-level factors that might impact on vaccine uptake over time and in different Regions might have provided us with elements useful to understand how vaccine coverage can be increased – that was not the aim of this study. Last, we did not present vaccine preventable diseases’ (VPDs) burden in terms of notifications and hospitalization, nor we speculated on VPDs burden prevented through immunization – the most important indicators to assess immunization programmes’ effectiveness – as this would have broadened too much the scope of our work. Further studies will explore in depth these issues.

CONCLUSION

National immunization coverage targets are only partially met in Italy. Furthermore, Italy, similarly to other European countries is facing the threatening phenomenon of the vaccine hesitancy and has reported in recent years alarming decreasing trends in infant vaccine coverage.

The debate around vaccine uptake and immunization policies and practices has recently flourished; if on one hand international and national health authorities have recently renewed their commitment to promote (VPDs) prevention and to strengthen immunization programs [12, 13]; on the other hand, recent evidence suggests that vaccines are losing public confidence [14].

Different and setting-specific determinants have been identified to lower vaccine uptake or willingness to get vaccinated [9, 14, 15]. In Italy key events including: news – later disproved – of vaccine-associated deaths [16], court decisions – later reversed – allowing financial compensation for vaccines-associated adverse events, together with the action of anti-vaccination movements have largely contributed to decrease general population’s positive attitudes toward vaccines and, ultimately, have negatively impacted on vaccine uptake.

In February 2017, the Ministry of Health issued the 2017-2019 National Immunization Prevention Plan [17]; the new Plan introduces evidence-based immunization recommendations to new vaccines and new target populations and is considered within the most innovative public national immunization plans in Europe [18, 19]. The new 2017-2019 PNPV [17], was approved after a two-year long administrative process and political debate, and demonstrates the commitment of the Italian MoH and the entire Government to promote immunization policies in Italy [18]. The Italian scientific community, with a strong partnership of four national scientific and professional associations (Italian Society of Hygiene, Preventive Medicine and Public Health – StI, Italian Society of Pediatrics – SIP, Italian Federation of Family Pediatricians - FIMP, Italian Federation of General Medicine - FIMMG) has greatly contributed to the technical part of the process [20, 21]. In line with 2017-2019 PNPV principles and taking into consideration the reported decreasing cov-
Immunization coverage trends: some Regions have recently approved regional laws making attendance to childcare conditional on immunization, while, at the central level, there is political will to increase the number of mandatory vaccines programmes. As a matter of fact, there is recent evidence from California, US supporting the positive impact of a mandatory approach to children immunization on vaccine uptake [22]. Now, for the new PNPV to be effectively implemented and – most importantly – for vaccine uptake trends to start increasing again, the political commitment and the scientific community advocacy action [23] need to be complemented with renewed efforts to carry out effective training, information and communication interventions to promote immunization among healthcare professionals and to increase the demand for immunization in the general population [24-26]. In particular, the potential offered by Information and Communication Technologies and “new media” should be leveraged by institutions and the public health community to inform and educate the general public on the benefits of vaccination [27-32]. Immunization coverage data are of crucial importance to inform the planning, and implementation of those actions, as well as to assess their impact. As vaccine coverage for mandatory and recommended vaccines is included in the set of the health indicators identified to monitor LEAs provision at the national level, we urge strengthened efforts will be devoted in the years to come to its rigorous collection through IIS implementation, to its analysis, its interpretation and dissemination at the national and international level.

**Conflict of interest statement**

There are no potential conflicts of interest or any financial or personal relationships with other people or organizations that could inappropriately bias conduct and findings of this study.

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