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## Commentary

## Italy's response to vaccine hesitancy: An innovative and cost effective National Immunization Plan based on scientific evidence

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The debate around vaccines has been in the spotlight in Europe over the last few years, both within the scientific community and the general public. In times where vaccines are losing public confidence and several international organizations (WHO, EU, ECDC) warn against the growing phenomenon of 'vaccine hesitancy' and its impact on decreasing vaccine coverage trends [1–3], National Health Authorities have been addressed by the Council of EU to take action to promote and support vaccination policies [4]. The case of Italy was raised on international journals in 2015 [5].

Today, after a two-year long administrative process, Italy achieved the final approval of the new National Immunization Prevention Plan (PNPV) 2017–19 [6]. Throughout this period the Italian Ministry of Health and the Government at large have showed considerable commitment to push the Plan forward and to raise the economic resources needed to support its implementation; this because the Italian National Health Service has always fully financed vaccination programmes for both children and adults [7]. The contribution of the scientific community with a strong partnership of four national scientific and professional associations (the Italian Society of Hygiene, Preventive Medicine and Public Health – SItI, the Italian Society of Pediatrics – SIP, the Italian Federation of Family Pediatricians – FIMP – and the Italian Federation of General Medicine – FIMMG) active in the field has been relevant with the publication of an innovative life-time immunization schedule [8] which contributed to grant a solid basis for the PNPV development.

The new PNPV combines the most evidence-based immunization offer with an innovative approach to its implementation in all Italian Regions and Autonomous Provinces (R&AP). Among the innovative aspects of the PNPV: the introduction of new vaccines, new target populations, the implementation of electronic immunization registries, better training for healthcare professionals (including specific courses in the Schools of Medicine) [9], informa-

tion campaigns, the encouragement to sanction physicians who do not recommend vaccinations and new laws to limit pre-school admissions for unvaccinated children. New vaccinations (Table 1) were added, compared to the previous 2012–14 Plan [3]: immunization against meningococcus B, rotavirus and varicella for children; the quadrivalent meningococcal and HPV vaccines extended to males in adolescence and zoster and anti-pneumococcal disease immunization for elder and at risk populations. The new schedule suggested is illustrated in Fig. 1.

Although some of the new immunization programmes were already recommended in selected R&AP [10,11], the new schedule extends them to the whole country thanks to the inclusion in the new list of Essential Levels of Care (LEA), approved by the Parliament in early 2017 and effective from April 4th, 2017.

Not only the Italian PNPV can be considered one of the most modern and updated immunization schedule on the European scene, but it is also a symbol of equity (all vaccines are offered actively and free of charge). However, the significant increase of vaccinations and sessions compared to the previous schedule (estimated to be +65% to +90%) now poses new challenges to the Ministry of Health and R&AP Health Authorities that will need to be faced in the months to come to ensure that the ambitious vaccine coverage targets set in the PNPV can be met.

**Table 1**Summary of vaccines included in the new PNPV 2017–19.<sup>a</sup>

Infancy (< 1y)	DTP <sup>c</sup> , Pertussis, HBV <sup>c</sup> , Hib, Pneumococcus Meningococcus B <sup>b</sup> , Rotavirus <sup>b</sup>
Post-infancy (>1 y)	MPR + Varicella <sup>b</sup> , Meningococcus C
Adolecency	HPV (both sexes) <sup>b</sup> , Meningococcus ACWY <sup>b</sup>
Adult-Elderly <sup>d</sup>	Influenza, Pneumococcus <sup>b</sup> , Zoster <sup>b</sup>

<sup>a</sup> Buster doses non mentioned in this summary table.<sup>b</sup> New vaccines (not included in the 2012–14 National Plan).<sup>c</sup> Mandatory vaccinations in Italy (when the 2017–2019 PNPV was approved).<sup>d</sup> Multi-indications including at risk categories and elderly population (≥65 y).

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Vaccine	Birth First 30 days	3rd month	4th month	5th month	6th month	7th month	11th month	13th month	15th month	↔	6th year	12th-18th year	19-49 years	50-64 years	> 64 years	High risk groups	
DTaP**		DTaP		DTaP			DTaP				DTaP***	dTapiPV	dTap**** every 10 years			(1)	
IPV		IPV		IPV			IPV				IPV						
Hepatitis B	HepB - HepB*	Hep B		Hep B*			Hep B									(2)	
Hib		Hib		Hib			Hib									(3)	
PCV - PPSV^^		PCV		PCV			PCV								PCV+PPSV	(4)	
MMRV								MMRV or MMR + V			MMRV or MMR + v^ *****					(6)	
MMR																	
Varicella																(6)	
Men-C								Men C <sup>§</sup>				conjugate Men ACWY				(7)	
Men-B^A		Men B	Men B		Men B			Men B									
HPV												HPV <sup>°</sup> : 2-3 doses (according to the age and the type of vaccine)				(8)	
Influenza ° °															1 dose every year	(9)	
Herpes Zoster															1 dose#	(10)	
Rotavirus		Rotavirus## (2 or 3 doses according to the type of vaccine)															
Hepatitis A																	(11)

  

Simultaneous administration	Immunizations for risk groups
Immunizations in sequential administrations	

**Fig. 1.** Immunization schedule included in the Italian National Immunization Plan (PNPV), 2017–19. For children born from HBsAg positive mothers. It's a four-dose schedule: the 1st dose within the first 12–24 h of life concurrently with specific Hepatitis B immunoglobulins; the 2nd dose after 4 weeks, 3rd dose following the lifetime immunization schedule, after the 60th day of life, in co-administration with the hexavalent vaccine. Even leaving the final decision to the local administration regarding the best possible schedule according to the local vaccine offer and its timing, it seems useful to suggest a scheme to introduce the Meningococcal B vaccine. This is the recommended sequence of immunization (the days are suggestive and not mandatory): Hexavalent vaccine + Pneumococcal vaccine (PCV) at the start of the 3rd month of life (61st day of life), Meningococcal B vaccine after 15 days (76th day), Meningococcal B vaccine after 1 month (106th day), Hexavalent vaccine + Pneumococcal vaccine (PCV) after 15 days, at the start of the 5th month of life (121st day of life), Meningococcal B vaccine after 1 month, at the start of the 6th month of life (151st day of life), Hexavalent vaccine + Pneumococcal vaccine (PCV) at the start of the 12th month of age, Meningococcal B vaccine starting from the 13th month of life, Meningococcal C vaccine, always after the 1st year of life. The third dose must be administered at least 6 months after the second dose. The fourth dose, the last of the first cycle, must be administered during the 5th - 6th year of age. It's also possible to use the adult formulation (dTapi) at the start of the 5th year of life if parents receive adequate information high coverage rates are reached in adolescent populations. Subsequent booster every 10 years. In response to the outbreaks occurred in the past years, the catch-up of the susceptible individuals and an active research of unvaccinated individuals (mop-up) is strictly recommended. Individuals without history of varicella: Administration of two doses of vaccine. The second administration 30 days after the first. It's necessary to give two doses to the children who begin the administration during the second year of life. It's required just one dose if they begin the administration during the third year of life. One dose of PCV against a higher number of pneumococcal serotypes is recommended to unvaccinated children or children vaccinated with PCV7. Two doses are recommended for high-risk children. One dose. Meningococcal C vaccine is administered for birth cohort at the 13th–15th month of life. For the second birth cohort (12–14 years) one dose of Men ACWY vaccine is recommended for unvaccinated individuals and for the adolescent who were already vaccinated during childhood with the Men C or Conjugate Men ACWY vaccine. Meningococcal C vaccine could be administered to at-risk individuals from the third month of life following a three dose scheme: the third dose after the 1st year of life. Administrate: two doses at 0 and 6 months (bivalent vaccine for individuals aged 9–14 years; quadrivalent vaccine for individuals aged 9–13 years), three doses at 0, 1 and 6 months (bivalent) or 0, 2 and 6 months (quadrivalent) for older individuals. Immunization with the seasonal vaccine for the individuals considered at risk by the Italian Minister of Health (Ministerial Circular). Administration is recommended for one 65 years of age cohort. It's recommended to offer the vaccine universally, it's co-administrable with all the vaccines of the first months of life. **Immunizations recommendations for high-risk groups:** (1) dTapi: number of doses depending if complete cycle or booster. For all pregnant women recommended during the third trimester of pregnancy (ideally at 28 weeks). (2) Hepatitis B: Pre-exposure: 3 doses (0, 1, 6 months). Postexposure: 4 doses (0, 2, 6 weeks + booster after 1 year). Immediate Pre-exposure: 4 doses (0, 1, 2, 12 months?). (3) Hib: for unvaccinated high risk subjects: number of doses to be decided on the basis of age and according to the product information template. (4) PCV: for children aged 0–5 years, PCV/PPSV after 5 year of age. (5) MMR: 2 doses with a minimum interval of 4 weeks; co-administration with monovalent varicella vaccine (V) or with quadrivalent vaccine (MMRV) is available/possible on the basis of age and of immunity against varicella. (6) Varicella: 2 doses with a minimum interval of 4 weeks; co-administration with monovalent varicella vaccine (V) or with quadrivalent vaccine (MMRV) is available/possible on the basis of age and of immunity against measles, mumps and rubella. (7) For high risk individuals it is recommended to offer Men ACWY and Men B, number of doses on the basis of age and according to the product information template. (8) HPV: recommended to subjects of all ages according to the product information template - number of doses on the basis of age and according to the product information template. (9) Influenza: for all ages according to the product information template - number of doses on the basis of age and according to the product information template. (10) Herpes Zoster: recommended to subjects aged ≥50 years. (11) Hepatitis A: number of doses on the basis of the product information template.

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