

Adult Immunization in Italy: successes, lessons learned and the way forward

Meeting Report

AIB Country Meeting, December 6 - 7, 2023, Florence, Italy



University of Antwerp and University of Florence

The Adult Immunization Board (AIB) (www.adultimmunizationboard.org) is an independent multidisciplinary advisory board created in November 2022. The purpose of the AIB is to contribute to the reduction of mortality and morbidity from vaccine-preventable infections and diseases in European adults by providing evidence-based guidance on fundamental technical and strategic issues while monitoring the progress of adult immunization programmes at regional, national, and European levels.

The AIB comprises a group of prominent experts from various fields of adult immunization and representing different European regions. Board members come from a broad array of adult immunization stakeholders (academia, public health, and international organisations) but act in their personal capacity for the board. The AIB is supported by an unrestricted grant from Vaccines Europe (www.vaccineseurope.eu) and applies the ethical rules of its hosting universities, the University of Antwerp and the University of Florence, to guarantee strict operational and scientific independence throughout its activities. The AIB and its board members pledge to work independently, transparently, and collaboratively.

The AIB leverages the long-standing experience of the Viral Hepatitis Prevention Board (VHPB, created in 1992; www.vhpb.org) and the HPV Prevention and Control Board (HPV Board, created in 2015; www.hpvboard.org). In line with the *modus operandi* of the VHPB and HPV Board, the AIB organises two live meetings per year: a technical meeting to discuss specific technical aspects on adult immunization with subject-matter experts, and a country meeting to discuss country and region-specific issues on adult immunization together with local experts. All meeting presentations and reports are available on the AIB website (www.adultimmunizationboard.org).

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Abbreviations list

AEFI	Adverse event following immunization
AIB	Adult Immunization Board
AIFA	Italian medicines agency, <i>Agenzia Italiana del Farmaco</i>
ASL	Local health authority, <i>Azienda Sanitaria Locale</i>
AUSL	Local health unit, <i>Azienda Unità Sanitaria Locale</i>
ASST	Local social health authority, <i>Azienda Socio Sanitaria Territoriale</i>
ATS	Health Protection Agency, <i>Agenzia per la Tutela della Salute</i>
COP	Correlates of protection
ECDC	European Centre for Disease Control
EEA	European economic area
EMA	European Medicines Agency
EU	European union
GPs	General practitioners
HBV	Hepatitis B virus
HCPs	Health care Providers
HIV	Human Immunodeficiency Virus
HPV	Human papilloma virus
HZ	Herpes zoster
IBD	Invasive bacterial disease
IC	Immunocompromised
ICU	Intensive care unit
ILI	Influenza-like illness
IPD	Invasive pneumococcal disease
ISS	National Institute of Health, <i>Istituto Superiore di Sanità</i>
Istat	National Institute of Statistics, <i>Istituto Nazionale di Statistica</i>
LEA	Essential levels of assistance, <i>Livelli Essenziali di Assistenza</i>
LHA	Local health authority – <i>Azienda Sanitaria Locale</i> (same as ASL)
LTCF	Long-term care facility
mAb	Monoclonal antibodies
MoH	Ministry of Health
MMR	Measles Mumps Rubella
MMR-V	Measles Mumps Rubella - Varicella
NHS	National health service
NITAG	National immunization technical advisory group
NVP	National vaccination plan
NVR	National vaccine registry
OECD	Organisation for Economic Co-operation and Development
PCV	Pneumococcal conjugate vaccine
PHN	Post-herpetic neuralgia
PNPV	National Immunization Plan, <i>Piano nazionale prevenzione vaccinale</i>
RCT	Randomised clinical trials
RSV	Respiratory syncytial virus
RZV	Recombinant zoster vaccine
SARI	Severe acute respiratory infections
SSN	National Health Service, <i>Servizio Sanitario Nazionale</i>
Tdap	Tetanus diphtheria acellular pertussis
VHPB	Viral Hepatitis Prevention Board
VPDs	Vaccine-preventable diseases
VPIs	Vaccine-preventable infections
WHO	World Health Organization
YF	Yellow fever

1. Introduction

This report covers the first Adult Immunization Board (AIB) country meeting, which took place in Florence, Italy, on December 6-7, 2023. The purpose of the AIB's country meetings is to establish a collaborative network of national experts in different fields, creating a platform for the exchange of knowledge and best practices in adult immunization. For these meetings, the AIB invites local academics, health care professionals, public health representatives and policymakers to present on adult immunization strategies implemented in the country, as well as educational and communicative initiatives aimed at increasing adult vaccine acceptance and coverage rates.

The specific meeting objectives were the following:

1. Provide an overview of the epidemiology and disease burden of vaccine-preventable infections (VPI) among adults in Italy. Explain the functioning of infectious disease surveillance and control programmes in Italy.
2. Provide an overview of the health care system in Italy, and review how (adult) immunization programmes are structured within the Italian health care system.
3. Explain the evaluation and market authorisation process of (adult) vaccines in Italy.
4. Present the Italian Life-course Immunization Schedule and provide an overview of the new National Immunization Plan (PNPV 2023-25); discuss the decision-making process and criteria according to which vaccines are evaluated and included.
5. Discuss the purchase, distribution, and financing of adult vaccines.
6. Explore the organisation and delivery of adult vaccination services in different regions of Italy.
7. Discuss the recording and reporting of vaccination data in Italy, including coverage rate monitoring and the national registry, as well as vaccine impact monitoring and vigilance practices.
8. Analyse the population's vaccination demand and acceptance, addressing issues such as vaccine confidence and compulsory vaccination policies for specific adult population groups.
9. Present the strategies and programmes implemented in Italy to vaccinate specific adult population groups, highlighting the challenges and opportunities.
10. Explore future prospects and potential solutions to overcome barriers and enhance adult immunization efforts in Italy and other European countries.

This report summarises the presentations, discussions, and lessons learned during the two-day meeting. A selection of keynote presentations given during the meeting were not specific to Italy (*The pricing of drugs and vaccines in Europe; Artificial intelligence to improve vaccination strategies; New platforms and technologies to develop adult vaccines*) and are not included in this report. However, the presentations of these keynote lectures, alongside all other meeting presentations, are available on the AIB website (www.adultimmunizationboard.org).

2. Overview of the epidemiology and disease burden of vaccine-preventable infections among adults in Italy.

2.1. The national surveillance system of vaccine-preventable infections

The national surveillance of infectious diseases in Italy is a competence of the Ministry of Health (MoH), supported by the regional health authorities and the National Institute of Health (ISS, *Istituto Superiore di Sanità*). The surveillance system falls under the European Union (EU) and European Centre for Disease Control (ECDC) umbrella and regulations.

Italy's national surveillance of infectious diseases is defined in the decree law of March 7, 2022 "*Revisione del sistema di segnalazione delle malattie infettive (PREMAL)*"(1). It includes over 50 infections or groups of diseases. It is organised into two main surveillance pathways, the *mandatory notification of infectious diseases* and the *special surveillance systems*.

2.1.1. Mandatory notification system of infectious diseases

A defined list of infectious diseases is mandatory to declare to the health authorities (2, 3). These are defined using the corresponding ECDC case definitions. The system allows for flexibility, with the addition of new elements to the list when necessary (e.g., mpox was included in response to the European outbreak of 2022). The MoH coordinates the mandatory notification system.

2.1.2. Special surveillance systems

For a selection of infections or infectious syndromes, dedicated and tailored surveillance systems are in place (4, 5). These enhanced systems are implemented when the disease surveillance requires additional infrastructure and/or data than that which is obtained through the mandatory notification system (e.g., further laboratory testing). The ISS coordinates these special surveillance systems. Currently, vaccine-preventable infections (VPIs) are targeted by several of these surveillance systems, including vaccine-preventable invasive bacterial diseases (IBD), measles, influenza-like illness (ILI), and SARS-CoV-2/COVID-19 (5). Waste-water surveillance is not yet in place in Italy but it is under consideration as a supplementary special surveillance system for multi-pathogen monitoring.

RespiVirNet is one of the special surveillance systems in place (6). RespiVirNet collects epidemiological and virological data on ILI, using a network of general practitioners (GPs) and paediatricians. This sentinel surveillance system has an estimated national coverage of at least four percent (minimum requirement). The incorporation of RSV and SARS-CoV-2 within this surveillance system is currently under evaluation. RespiVirNet is complemented by a sentinel hospital-based severe acute respiratory infection (SARI) surveillance.

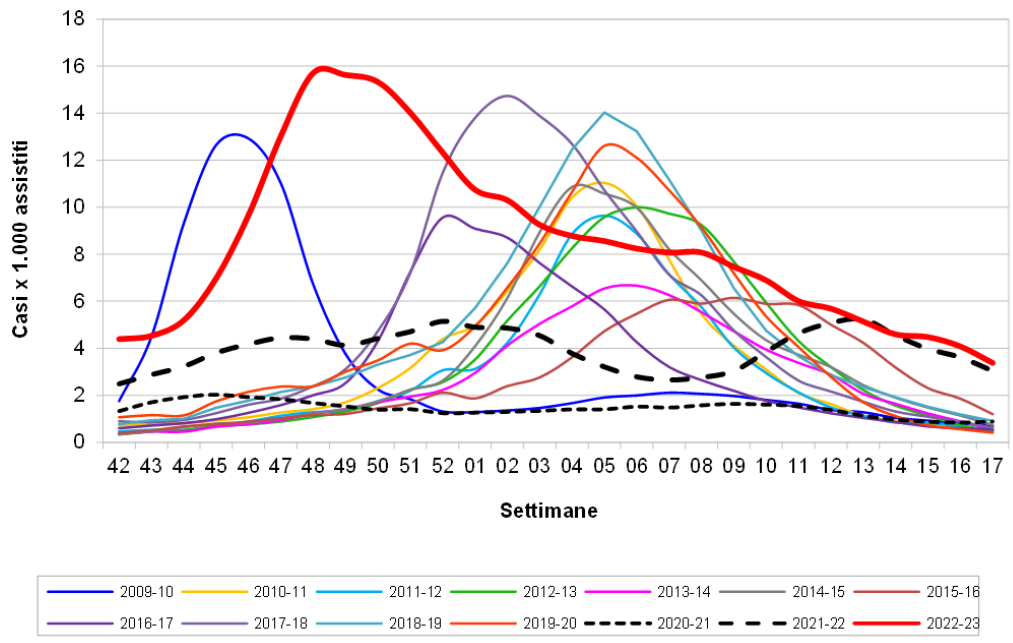
2.2. Epidemiology and disease burden of a selection of VPI

This section covers the epidemiology and disease burden of a selection of key VPI in Italy. Vaccine coverage and vaccine effectiveness monitoring in Italy is detailed in section 8.1.

2.2.1. Vaccine-preventable respiratory viruses

Influenza and ILI: in Italy, the last three years have been characterised by atypical ILI waves, going from the near absence of circulation during the 2020-2021 season (due to COVID-19–related measures) to a circulation and corresponding high disease burden in the 2022-2023 season (Figure 1).

Figure 1. Incidence of influenza-like illness in Italy, Season 2009/10 to 2022/23. Source: RespiVirNet, ISS.



During the 2022-2023 season, 14 million ILI cases were recorded, and a higher peak incidence was reached compared to pre-pandemic seasons. Causal pathogen distribution varied according to age group, with influenza, SARS-CoV-2 and RSV paying a heavy tribute to ILI in the adult population. Overall, influenza was identified in 22% of the positive samples (80% influenza type A, with 92% subtype H3N2).

SARS-CoV-2/COVID-19: with 16 million infections and more than 160,000 SARS-CoV-2-related deaths recorded between March 2020 and April 2022, Italy was one of the most pandemic-affected countries in the EU, especially during its first phase (Source: EpiCentro ¹).

Results from the ISS national SARS-CoV-2 surveillance system have shown a progressive decline in the proportion of severe COVID-19 cases between early 2020 and end of 2023. This evolution is presumably also related to increasing hybrid population immunity (infection-acquired immunity and vaccine-acquired immunity), changes in virulence of circulating SARS-CoV-2 variant, and improvement in patient care. In addition, the assessment of COVID-19 severity and disease burden is complex, being affected by the changes in SARS-CoV-2 testing capacity, guidelines and strategies (e.g., testing only severe cases in the initial months of the

¹ EpiCentro is an online tool to improve access to Italy’s epidemiological information on specific conditions and diseases, as well as population surveillance. EpiCentro was created in 2000 under the direction of the Epidemiology and Biostatistics Laboratory (Laboratorio di Epidemiologia e Biostatistica, LEB) of the ISS, in collaboration with other ISS departments, Regional Health Authorities, Local Health Authorities, Research Institutes, epidemiological associations, and individual workers in public health (Available at <https://www.epicentro.iss.it/en/>).

pandemic; home-based auto-testing of non-severe cases in later periods). Nonetheless, the observed trend is supported by a modelling study by Marziano et al. showing a 22 to 44-fold reduction in the risk of COVID-19 hospitalisation, ICU, and death in Italy between February 2020 to February 2022(7).

Overall, more than 8 million SARS-CoV-2 infections, 260,000 hospital admissions, 31,000 intensive care unit (ICU) admissions, and 150,000 deaths were averted between January 2021 and January 2022 thanks to the anti-COVID-19 immunization campaign in Italy (8). Conversely, the incidence of SARS-CoV-2 infections remains high, with elevated rates of reinfection as both infection and vaccine-acquired immunity rapidly wane over the course of a couple of months. As a result, despite the reduction in disease severity, the weight of COVID-19 on the Italian public health system remains substantial.

Respiratory syncytial virus (RSV): a high RSV burden was reported for the 2021-2022 season in Lombardy (9), one of Italy's northern regions, at least partially ascribed to a higher incidence of primary RSV infection among young individuals. A marked increase in the population-level susceptibility to RSV during the COVID-19 pandemic (~60% increase in the proportion of the RSV infection-naïve population), particularly in the very young population, presumably contributed to the observed increase in RSV primary infections (10).

2.2.2. Invasive pneumococcal disease

Vaccine-preventable Invasive Bacterial Diseases (IBD), including invasive pneumococcal diseases (IPD), are monitored through a special surveillance system of the ISS (11). As with other respiratory pathogens, a drop in IPD incidence was observed during the COVID-19 pandemic. This was a result of the interruption of possible pathogen transmission pathways by the restriction measures in place (e.g., social distancing, face masks), and of an indirect negative impact on the quality and rate of reporting of non-COVID-19 diseases due to an overburdened health system.

In the pre-pandemic years, an increase in the number of IPD cases reported through the ISS's special surveillance system was recorded in Italy. Comparing results to hospital records revealed that this trend was related to an improvement of the surveillance system with increasing reporting rates, rather than a change in the epidemiology of IPD (12).

2.2.3. Herpes Zoster

According to data published in 2010 and 2017, the incidence of herpes zoster (HZ) in Italy is aligned with current EU/EEA incidences, with 5-10 cases per 1,000 person-years (13, 14). This incidence translates into an estimated 150,000 to 300,000 cases per year, with 1% requiring hospital admission. HZ and its complications, including post-herpetic neuralgia (PHN), disproportionately affect older adults from 50 years onwards.

2.2.4. Tetanus-Diphtheria-Pertussis

Tetanus: Between 2017 and 2021, Italy accounted for ~40% of all tetanus cases reported by EU/EEA countries to ECDC. This result could be attributable to the use of a case definition for tetanus different from the EU case definition (15). Overall, 90% of the Italian cases occurred in persons 65 years or older (16).

Diphtheria: Despite the multi-country 2022-2023 European outbreak of diphtheria related to migrant populations, three cases were detected in Italy in 2022 (16, 17). They occurred in male adults (two cases in the age group 25-44 years and one case in the age group 45-64 years); two cases were travel associated. No further cases have been notified in Italy in 2023 (18).

Pertussis: Data shows a strong decrease in 2020-2021, likely due to the COVID-19 pandemic. When comparing to the epidemiologic data of other EU/EEA countries (16), Italy shows a different age distribution: the proportion of cases reported in adults 30 years or older is lower than the European average. This observation may be the result of underreporting, rather than an epidemiological trend (19).

3. Overview of the health care system & review how (adult) immunization programmes are structured within the Italian health care system.

3.1. The evolution of the Italian national health service

The **Constitution** of the Italian Republic was ratified in December 1947. Its Article 32 states that *the Republic safeguards health as a fundamental right of the individual and as a collective interest, and guarantees free medical care to the indigent.*

Following the enactment of the Constitution, a **social health insurance system** was instituted in the country (1948 -1978), in which health insurance was entitled based on employment rather than residency. This system led to major social inequalities.

In 1978, the national health service (**SSN, Servizio Sanitario Nazionale**) replaced the social health insurance system. The advent of the SSN was associated with an exponential decline in infant deaths and an increase in the country's average life expectancy. The SSN has been repeatedly rated by the Organisation for Economic Co-operation and Development (OECD) among the highest rating countries worldwide for life expectancy and among the lowest in health care spending (20).

In 2001, the organisation of the SSN was profoundly altered following the **constitutional reform**, which resulted in an increase in regional competencies with regard to health and prevention. This fragmentation of the SSN has been associated with growing disparities in health care at the regional level with a notable life expectancy gap between the poorer southern regions and the north of the country (21).

3.2. Immunization programmes within the national health service

Since 2001, immunization-programme-related mandates have been split between Italy's central health authority (MoH) and 21 regional health authorities (19 regions and two autonomous provinces), as detailed in Figure 2. The approval of agreements concerning national health policies, including immunization, takes place during state-region conferences.

Below the different responsibilities are described:

The Italian MoH

- defines the objectives to improve population health status

- is responsible for national health planning
- determines the Essential Levels of Healthcare (**LEA, Livelli Essenziali di Assistenza**), in agreement with the Ministry of Economy and Finance

LEA are health services and benefits that the SSN is required to provide to all residents, uniformly throughout the whole national territory, free of charge or upon payment of a fee (ticket). All vaccines included in the National Immunization Plan (**PNPV, Piano Nazionale Prevenzione Vaccinale**, see section 5.2) are considered LEA for those identified as the recipients of the vaccine recommendations. The ticket (co-payment) is not required for LEA-vaccines(22).

The **Italian medicine agency (AIFA, Agenzia Italiana del Farmaco)**

The definition of the reimbursement and supply regime for authorised medicines is managed centrally, by the Italian medicine agency (**AIFA, Agenzia Italiana del Farmaco**), by negotiating the price of drugs charged to the NHS (23). In particular, AIFA manages the authorisation processes for clinical trials, the production of medicinal products and active substances, the inspection and pharmacovigilance activities. In addition, AIFA is responsible for the definition of the system of reimbursability and supply of all authorised medicinal products, the negotiation of the price of those charged to the SSN, following negotiations with pharmaceutical companies. AIFA operates under the guidance and supervision of the MoH and supervision of the Ministry of Economy and Finance.

The **regional health authorities**

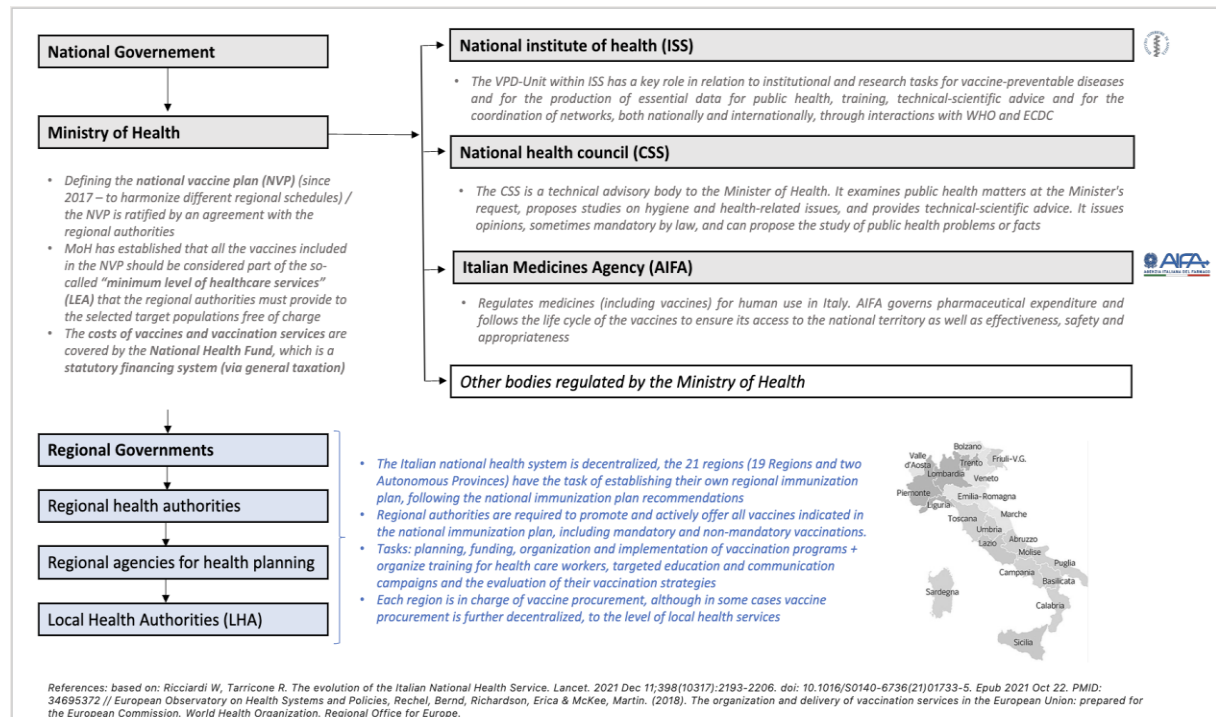
The **regional health authorities** are autonomous in operating strategies. They are responsible for planning, financing, organising, and implementing vaccination services following the PNPV and for promoting vaccination, both mandatory and non-mandatory. The regional health authorities have the ability to legislate on health issues, respecting the general principles, and to determine further LEA that are to be provided uniformly at regional level, so that vaccines or preventive mAb (monoclonal antibodies) that are not included in the PNPV immunization schedule may be locally procured and financed.

The **local entities**

Overall, **local entities** involved in Italy's immunization programmes include 110 Local Health Authorities (LHAs, or *ASL, Azienda Sanitaria Locale*), 57 public hospital enterprises, 30 University hospitals, 64 IRCSS (high-level clinical research centres), and almost 1,400 hospital facilities spread across the country. Notably, while this is the common framework of action among the different regions, the organization of the health systems can differ, and certain competencies are differently decentralized. Lombardy features a system with ATS (Health Protection Agencies - *Agenzie di Tutela della Salute*) for public health coordination and ASST (Local Health and Social Care Organizations - *Azienda Socio-Sanitaria Territoriale*, which are part of the ATSs) managing direct healthcare services through hospitals and clinics (24). In Tuscany, on the other hand, the local health entities are divided into three geographical clusters (*Area Vasta*: North-West, Central, and South-East) that include three AUSLs (Local Health

Authority, Azienda Unità Sanitaria Locale), and 4 AOU (University Hospitals, Azienda Ospedaliero-Universitaria) (25).

Figure 2. Organisation of the Italian health care system, focus on Immunization. Source: AIB figure based on Ricciardi et al., Lancet 2021(20); European Observatory on Health Systems and Policies, WHO 2018(26).



3.3. Immunization policy-making in Italy

Immunization policies are defined at the central level (MoH) through laws, decrees, plans, and circular letters. Circular letters are technical recommendations or explanations of a law, decree or plan. These are not legally binding but allow for flexibility and rapid response.

Immunization-related laws, decrees, and plans currently in place:

- Mandatory vaccination in children (*Law, see section 9.3*) (27)
- List of authorised yellow fever vaccination centres (*Decree*) (28)
- COVID-19 national strategic vaccine plan for the prevention of SARS-CoV-2 (*Decree*) (29)
- 2023-2025 National Vaccination Plan (*Plan*) (30)
- 2019 National preparedness and response plan for a polio epidemic (*Plan*)(31)
- 2010-2015 National plan for the elimination of measles and congenital rubella (*Plan*) (32)

Examples of circular letters (Circolari):

- Annual circular for prevention and control of influenza, indicating the new vaccines’ composition and reporting recommendations for the prevention of influenza through vaccination and other measures of hygiene and personal protection
- Circular letters on COVID-19 vaccine recommendations, used throughout the campaign

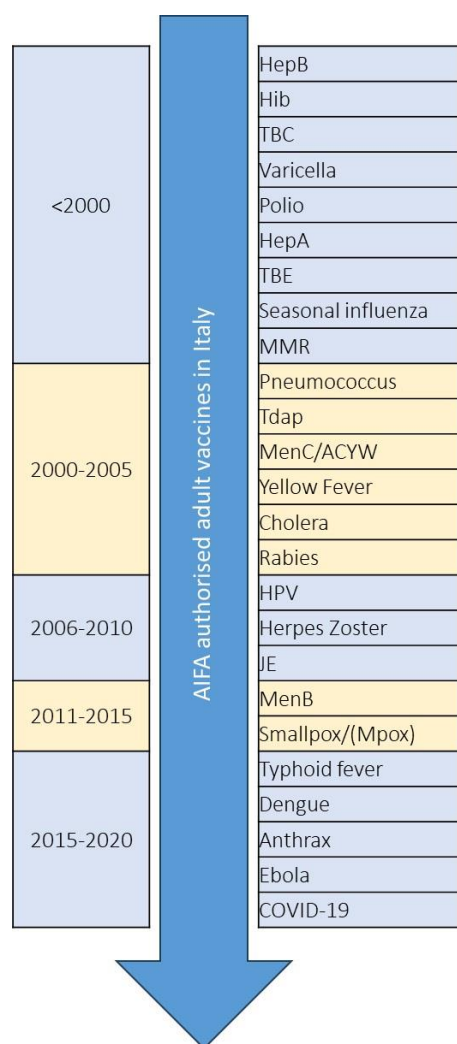
- Circular letters on mpox (EU outbreak of 2022), giving interim guidance on immunization and description of logistics

Italy's **National Immunization Technical Advisory Group** (NITAG) plays an advisory role for the PNPV, its immunization schedule (Section 5.1), and the circular letters on immunization strategies. The last PNPV 2023-2025 is structured in two documents: the National Immunization Plan, which includes the preventive objectives and targets to be reached) and the Immunization Schedule (vaccination schedule), which can be updated independently of the update of the National Immunization Plan. The NITAG is an independent board, appointed by the MoH. Its secretariat resides within the MoH. Italy's first NITAG was appointed in 2017. Since 2021, the country's third NITAG has been in place, chaired by Professor Carlo Signorelli, and composed of 29 core members: public health physicians, an epidemiologist, an immunologist, an infectious diseases specialist, communication experts, a psychologist and behavioural science expert, a forensic medicine expert, an expert in ethics, paediatricians, public health nurses, and GPs (33). Currently, the NITAG is working on a new immunization schedule for 2024, with three working groups addressing different tasks: the first working on the current schedule update, the second on vaccine recommendations in high-risk populations, and the third on recommendations for vaccines in workers and travellers. Other topics in discussion include the integration of seasonal COVID-19 vaccination into the national schedule, meningococcal B vaccination in adolescents, and RSV immunization (vaccines and mAbs). As an advisory body, the NITAG organises hearings with different key immunization stakeholders (e.g., vaccine companies, professional associations, boards such as the Board of the Lifetime Immunization Schedule).

4. Evaluation and market authorisation process of (adult) vaccines in Italy.

Market authorisation of vaccines in Europe can go through three different regulatory pathways, a centralised procedure, a mutual recognition procedure (authorisation of a medicine in one EU member state is recognised by another), or a de-centralised (national) procedure. The centralised procedure is obligatory for a series of products, including those produced through biotechnological processes such as recombinant DNA vaccines. In practice, most vaccines now go through this pathway. The centralised procedure is well defined, with fixed delays (210 days from validation to opinion). Pharmaceutical companies submit a single marketing authorisation application to the European Medicines Agency (EMA), which will perform a scientific assessment of the application and give a recommendation. Approval for market authorisation is granted by the EU Commission, based on EMA's recommendation. This pathway allows for a single trade name throughout Europe and a common labelling (e.g., package leaflets).

Figure 3. AIFA-authorized vaccines for adults in Italy. Source: AIB figure based on AIFA data



Note: Years indicate year of first approval of current vaccine platform in use. Year of approval may differ from the year of effective implementation in the different Italian regions. Abbreviations: Hep: hepatitis; Hib: Haemophilus influenzae; HPV: Human papilloma virus; JE: Japanese encephalitis; Men: meningococcal; MMR: measles-mumps-rubella; Mpx: Monkeypox; RSV: Respiratory syncytial virus; TBC: tuberculosis; TBE: tick-borne encephalitis; Tdap: Tetanus-diphtheria-acellular pertussis.

For a vaccine to be authorised by the EU, the product must meet a series of requirements including evidence of efficacy and safety. Absolute protective efficacy of the vaccine shown in prospective individually randomised and double-blind clinical trials remains the gold standard. In situations where a vaccine is already on the market, the use of a placebo may be unethical. In this case, trials may be designed to estimate the relative efficacy compared to the licensed vaccines. The typical endpoint of the clinical trials used for licensure is laboratory-confirmed symptomatic disease. However, when an immune correlate of protection (ICP) is available, it may be used as a surrogate endpoint, and clinical immunogenicity data will suffice for licensure. In the absence of ICP and when field efficacy trials are problematic, the agency is open to alternative strategies, including immune-bridging studies or, more rarely, controlled human infection models. Regarding vaccine safety, its assessment in clinical trials should cover a population of at least 3000 individuals followed for 6 months or more (minimum 2 months). Plans for post-marketing surveillance of the vaccine effectiveness and safety must be discussed early with regulators, to gain good understanding of what can be achieved after approval.

To enter the Italian market, vaccines authorised for use in Europe through the centralised procedure will also require positive advice from AIFA, Italy’s medicines agency. Vaccines authorised for use in Italy as of December 2023 and year(s) of first approval of current vaccine platform(s) are shown in Figure 3. **Error! Reference source not found..** Of note, the year of approval indicated may differ from the year of effective implementation in the different Italian regions.

5. The Italian Lifetime Immunization Schedule and new National Immunization Plan (PNPV 2023-25).

5.1. Lifetime Immunization Schedule

The **Board of the Lifetime Immunization Schedule** represents a unique alliance of four scientific societies and professional associations: the Italian Society of Hygiene, Preventive Medicine and Public Health (SItI), the Italian Society of Paediatrics (SIP), the Italian Federation of Family Paediatricians (FIMP) and the Italian Federation of General Practitioners (FIMMG). Together these associations represent over 50,000 medical professionals. This collaboration was established to propose 'ideal' vaccination schedules, based on scientific evidence of efficacy, effectiveness, and safety. It was one of the first European initiatives to propose a lifelong approach to immunization, with immunization schedules covering vaccinations from 0 to 100 years old.

The 2014 (34) and 2016 (35) versions of the Lifetime Immunization Schedule produced by the Board were used as the backbone of the PNPV 2017-2019, which was considered one of the most advanced adult vaccination plans in Europe. The Board is now a recognised player in setting up vaccination strategies by Italian health authorities, continuing to propose the best possible vaccination offer for all ages of life. Moreover, the publications of the Board are the object of refreshment courses and meetings for doctors, nurses and public health nurses, and other HCPs involved in vaccination practices. The Lifetime Immunization Schedules of the board have been published in international literature, to make them known, and to offer inspiration for similar initiatives (36). Indeed, this success story shows the major role that scientific societies and professional associations can play in the improvement of (adult) immunization.

5.2. The National Immunization Plan (PNPV)

The PNPV is composed of two documents, the **National Immunization Plan** and the **Immunization Schedule** (vaccination schedule), which can be updated independently of the update of the National Immunization strategy. The **National Immunization plan of the PNPV** outlines the objectives of the national immunization strategy for different age and risk groups and is ratified by an agreement with the regional authorities who are responsible for the implementation of vaccination programmes in their respective regions (37). The PNPV recommends vaccination for people throughout the entire life course and sets clear targets for vaccination coverage, but it also identifies the main priorities (e.g. measles and rubella elimination, polio eradication) and considers many actions to reduce disparities among Italian Regions. As mentioned before, the Italian NITAG has an advisory role on the content of the PNPV (see section 3.3) and the Lifetime Immunization Schedule discussed above can be used to inspire the PNPV. All vaccines included in the Immunization Schedule are defined as LEA and are to be provided free of charge uniformly across the country (see sections 3.3 and 6).

The current PNPV 2023-2025 was issued in August 2023. Its Immunization Schedule is shown in

Figure 4 (38).

Figure 4. Italy's Life-course immunization schedule, August 2023. Source: PNPV 2023-2025 (38), translated to English.

Age (months/years)	2 months	3 months	4 months	5 months	6 months	10 months	12 months	13/14 months	5 years	6 years	11 years	12-18 years	19-59 years	50-64 years	60 years	65 years	>66 years
Hexavalent vaccine: Tetanus, Diphtheria, Pertussis, Hepatitis B, Haemophilus influenzae type b, Polio (DTaP-IPV-HBV-Hib)	█		█			█											
Rotavirus (RV)	█	█	█	█													
Pneumococcal conjugate vaccine (PCV)	█		█			█										█	
Meningococcal B vaccine (MenB)	█	█	█	█			█	█									
Measles, Mumps, Rubella, Varicella (MMRV or MMR+V)							█	█	█								
Meningococcal ACWY vaccine (MenACWY)							█	█				█					
Tetanus, Diphtheria, Pertussis, Polio (Tdap-IPV/Tdap-IPV)									█			█					
Papillomavirus vaccine (HPV)											█	█					
Tetanus, Diphtheria, Pertussis (Tdap)													█	█	█	█	█
Influenza vaccine (Flu)					█	█	█	█	█	█					█	█	█
Herpes zoster vaccine (HZ)																█	█

█ Recommended vaccination by age

NB: months and years are considered completed. Examples: the first dose of DTaP-IPV-HBV-Hib can be offered from 2 months of age, or from 61 days of life; the booster dose DTaP-IPV-HBV-Hib at 10 months, or from 301 days of life.

The **National Immunization Plan** has been updated to address the critical issues of the previous PNPV 2017-2019, in particular vaccination coverage targets failure (in adolescents and adults), regional differences in coverage rates, and organisational heterogeneity across the country. The set goals of the immunization strategy are the following, and those newly included for the PNPV 2023-2025 are in Italics:

1. Maintain polio-free status
2. Eliminate of measles & congenital rubella
3. *Reduce of HPV-related diseases*
4. Reach vaccination coverage targets, *use of pandemic experience in routine vaccinations (extension of immunization sites)*
5. *Vaccinate high-risk groups (e.g., chronic conditions) and highly vulnerable groups for social and economic conditions*
6. Reduce inequalities in vaccination offer
7. Implement the national digital vaccination registry
8. Improve surveillance of VPI
9. *Improve communications on vaccines*
10. Promote vaccine education in Healthcare Providers

Other major changes to the new PNPV compared to the previous version include the possibility of updating the immunization schedule on an annual basis, without modification of the PNPV, and, as an example, the possibility of future introduction of monoclonal antibodies (mAb) for preventive purposes. Moreover, the key role of the NHS' Departments of Prevention in the planning and co-ordination of campaigns is highlighted in the PNPV 2023-25. In the past the

publication of the National immunization strategy has never been constant. The update occurred every 5-7 years.

6. Purchase, distribution and financing of adult vaccines

Purchase, distribution, and additional financing (for supplementary vaccinations not included in the PNPV 2023-25) are organised at the regional level. To explain and discuss these procedures, three regions were used as case examples: Lombardy for Northern Italy, Tuscany for Central Italy, and Puglia for Southern Italy.

Purchase is a mandate of the regions. Regions organise local public tenders, each through different agencies e.g., ARIA S.p.A, in Lombardy (Regional Company for Innovation and Purchasing; www.ariaspa.it), ESTAR in Tuscany (Tuscan Regional Administrative Technical Support Body; www.estar.toscana.it) and InnovaPuglia S.p.A. in Puglia (www.innova.puglia.it).

Assessment of demand is usually estimated by the regions using historical numbers of procurement and uptake, the PNPV uptake targets, and population data issued by the National Institute of Statistics (Istat, *Istituto Nazionale di Statistica*). In Lombardy, assessing vaccine demand is delegated to the Prevention Unit of Directorate General Welfare. As witnessed by Tuscany and Puglia, assessment of demand is particularly tricky in high-risk populations or when historical data do not match with the vaccine coverage targets of the PNPV.

Organisation of procurement and distribution differs across Italy's regions. For example, in Lombardy, the ASST can directly order the vaccines from the vaccine company that won the public tender. In Tuscany, ESTAR, the same agency that organises the public tenders, distributes the vaccines directly to the administration sites, including the region's three AUSLs and public or private pharmacies. In Puglia, the region's six ASLs can order their vaccines from a regionally procured stock.

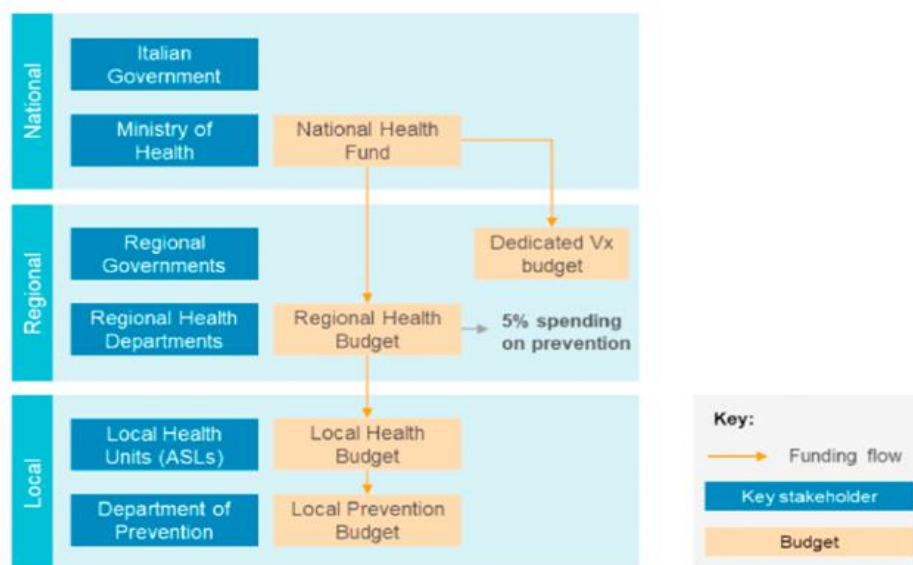
Financing is both central and regional (Figure 5). Vaccines included in the PNPV immunization schedule are LEA (see section 3.2) and are centrally financed by the National Health Fund, a statutory financing system based on general taxation. In addition, since 2017, the National Health Fund has included an additional dedicated budget item for each region to support reimbursement and purchasing of vaccines and innovative (oncology) drugs (39).

Financing of the immunization programmes (costs related to distribution, administration, promotion, infrastructure) and non-PNPV vaccines falls upon the regional health authorities. Overall, an estimated 5% of the regional health budget is dedicated to prevention, with inequalities in levels of investment when comparing regions (39).

Financing strategies differ by region. In Lombardy, a list of vaccines and indications are free of charge those included in the PNPV (e.g., mandatory vaccines, influenza vaccine, Tdap in pregnancy, PCV) and the recombinant zoster vaccine (RZV) in older adults and high-risk patients, while a co-payment system is in place for other vaccines using a controlled cost (sum between a fixed administration fee and the cost of the vaccine awarded by the regional

purchasing center ARIA S.p.A). In Tuscany, vaccines included in the PNPV, as well as vaccines recommended to different categories of workers based on professional risk (e.g., HBV), are offered free of charge. Citizen co-payment is applied for other vaccines, calculated using the discounted public-tender price and the cost of the health care service. Co-payment is nevertheless not generalised throughout the country, as illustrated by Puglia, which does not have such a system in place. For Puglia financing is strictly assured for PNPV vaccines only. Sustainability concerns were raised, as the closed envelope for LEA poses difficulties with regard to the high expenditure costs of pharmaceutical products and the high-priced new vaccines arriving on the market (e.g. RSV immunization).

Figure 5. Italy's budget flow for immunization. Source: Lawlor et al., Health Policy 2022 (39)



Of note, health insurance and employers play a limited role in the financing of vaccines in Italy, with the latter sometimes covering costs related to influenza vaccines or work travel-related vaccines of their employees.

7. Organisation and delivery of adult vaccination services in different regions of Italy

The same three regions were used as case examples to illustrate the organisation of adult vaccination services in Italy: Lombardy for Northern Italy, Tuscany for Central Italy, and Puglia for Southern Italy.

Vaccine administration: across all three regions, multiple administration sites and vaccine administrators are used in their immunization programmes. Vaccines are administered in vaccination centres of local health authorities (ASL), by GPs and paediatricians, by specialist doctors and occupational doctors, in (university) hospitals and at pharmacies, with the involvement also of pharmacists as vaccine administrators. The contribution of each entity to vaccine administration differs by region and by vaccine type. In Puglia, for example, GPs

remain the main vaccinators for influenza, while vaccination centres of ASLs are the main vaccinators for PCV and HZ vaccines. Delays in seasonal vaccination campaigns have occurred in this Region, as the administration of vaccines requires agreement at the regional level with GP unions followed by sub-agreements between the local health authorities and local GP unions.

Outreach programmes: various outreach programmes are organised by the Regions. Successful examples from Lombardy include outreach programmes for homeless vaccination during COVID-19 campaign, vaccination in community homes and long-term care facilities (LTCF), hospital campaigns (e.g., vaccination against HZ in cancer wards), and target-group-specific outreach such as the vaccine project for diabetic patients (40, 41). Another example was shown by Tuscany, with two open days organised for HPV vaccinations in ASLs (42).

Vaccine promotion: regional similarities and specificities are found with regard to vaccine promotion. In Tuscany, tailored communication and campaigns, and engagement of GPs and pharmacists to recommend vaccination to elderly, frail people and patients with special risk conditions are among the current strategies to promote vaccine acceptance.

Success stories: all three regions staged immunization success stories during the COVID-19 pandemic. Lombardy successfully integrated pharmacists as vaccine administrators, who ultimately were responsible for 46% of COVID-19 vaccine administrations (versus 28% by ASST and 17% by GPs). In Tuscany, vaccination centres guaranteed extended openings, even on weekends, the booking system was simplified with a dedicated web portal, and the workflow was designed to ensure low waiting times and manage a large number of people. Puglia successfully reached its highest vaccine coverage for primary COVID-19 schedule ever (99.9% in 60 years and older). Other success stories reported by Puglia included high influenza adult vaccine rates in HCPs related to mandatory vaccination and a new law proposal to be soon discussed in the regional council for the implementation throughout the regional territory of an individual call program for those who have acquired the right to HPV vaccination.

8. Recording and reporting of vaccination data in Italy, including coverage rate monitoring and the national registry, as well as vaccine impact monitoring and vigilance practices.

8.1. Monitoring of vaccine coverage and vaccine effectiveness.

Accurate recording and reporting of data represent crucial components of public health campaigns, and the monitoring of vaccination coverage and effectiveness plays an important role in determining and improving immunization programmes and strategies.

The **national vaccination registry (NVR)** was created in 2017, in parallel with the implementation of new childhood mandatory vaccinations (see Section 9.3). The registry was built to track vaccinations, vaccinated people, target populations, doses and administration times, side effects, and exempted individuals. The data are also used to calculate **vaccine uptake** and for assessment of the country's immunization programmes and are shared with international institutions such as the World Health Organization (WHO) and ECDC.

The data collected within the NVR is fed by the regions and autonomous provinces registries, every quarter. Although regional vaccine databases communicate with the national vaccine registry, the different systems are not yet fully integrated. This results in multiple challenges, such as difficulties in obtaining the vaccine history if a person is being treated outside the region of residence. Moreover, regional vaccine databases use different software and access rights. Considering accuracy and completeness, these are ensured in the regional databases through alerts and mandatory fields.

Since January 2021, a fully integrated **National COVID-19 Data vaccine registry** was put in place. This registry is updated daily, allowing for a vaccination uptake dashboard and close monitoring (43).

Other specific databases and surveillance systems used for coverage uptake include the *influenza vaccination coverage data collection*, a register coordinated by the National Institute of Health that produces detailed vaccine coverage data by vaccine type, brand, risk group, and age group for every season; the *Istat multipurpose survey on households* (44), which collects self-reported vaccinations from a sample population; and population surveillances *PASSI* (45) and *PASSI d'Argento* (46). *PASSI* is a population surveillance system monitoring health in Italy's adult population, while *PASSI d'Argento* monitors health in the older population. Besides the specific indicators on vaccine compliance among the general population living in Italy and its specific subgroups (e.g., people with chronic conditions or HCPs), these Italian surveillance systems allow further analysis by sociodemographic or other modifiable lifestyle risk factors. Further information and reports can be found on EpiCentro (47).

Vaccine effectiveness can be monitored using various approaches, including cohort studies, case-cohort studies, case-control studies (including test-negative case-control studies) or rapid screening methods. The surveillance of COVID-19 vaccine effectiveness was successfully managed in Italy through retrospective cohort design, generating brand-specific and age-group-specific results (48, 49). This was achieved through the linking of the COVID-19 vaccine registry and the national SARS-CoV-2 surveillance system through individual fiscal codes. The screening method has been previously used at the regional level to evaluate vaccine effectiveness of the meningococcal C conjugate vaccine during a serogroup C/cc11 *Neisseria meningitidis* outbreak in Tuscany (50). National linking of vaccine registries and surveillance systems through fiscal codes is currently not possible to apply for other infectious diseases due to issues with the Italian law on the protection of personal data (Legislative Decree, 30 June 2003, n. 196)

8.2. Pharmacovigilance

Monitoring the safety of medicines, including vaccines, is a mandate of Italy's medicines agency, AIFA. Italy's pharmacovigilance system is considered robust by local experts.

In Italy, based on AIFA data, adverse event following immunization (AEFI) rates with non-COVID-19 vaccines reach 78 events per 100,000 doses (51). Importantly, AEFI are untoward medical events occurring after vaccination and that do not necessarily have a causal relationship. This means that AEFI may not only be vaccine-product related, but also include quality defects, immunization errors (e.g., unnecessary dose), anxiety-related events, or co-

incidental events. Most AEFI are classified as mild, with severe AEFI rates in Italy estimated at 3.6 events per 100,000 doses (51). AIFA-published results have shown that the simultaneous administration of vaccines does not influence the risk of reporting serious AEFI (52).

AEFI rates for COVID-vaccines have been slightly higher, with 97 events per 100,000 doses, mainly related to the most used mRNA vaccines (52). During the COVID-19 pandemic, AIFA participated in additional pharmacovigilance collaborations, such as the CovidVaccineMonitor.eu project. This project is an EMA-funded prospective and multi-country European pharmacovigilance surveillance study (53, 54). Sixteen EU countries were involved, with 12 actively participating in the prospective monitoring. The study used active surveillance via a smartphone web app, collecting both solicited and unsolicited safety events. In total, 2982 persons participated in Italy. Local events and non-severe systemic AEFI were all higher with mRNA vaccine produced by Moderna. Unsolicited events were the same across vaccine types. Special cohort monitoring was also performed within the project, with the University of Verona coordinating the monitoring of safety in special cohorts, including pregnant and breastfeeding women. Interestingly, projects and dedicated studies (Progetto MAGNOLIA, A multilayer framework to enhance pharmacological knowledge among women in reproductive age, pregnancy, and post-partum; (55)) have shown a request for greater information on the safety of vaccines by both pregnant and breastfeeding women to allow for decision-making.

9. Analysis of the population's vaccination demand and acceptance, addressing issues such as vaccine confidence and compulsory vaccination policies for specific adult population groups.

9.1. Vaccine confidence

Vaccine confidence is a quantitative predictor of vaccine uptake and is therefore essential to monitor (56). The Vaccine Confidence Project, in order of the European commission, is a survey tool (conducted in 2018, 2020 and 2022) that allows the monitoring and comparison of national vaccine confidence trends in Europe. The results from 2022 were presented (57), with a focus on Italy . In Italy, vaccine confidence was high in the **general population**, with a percent of survey participants agreeing that vaccines are important, safe, effective, and compatible with beliefs above the EU average. However, specific vaccine confidence towards HPV and MMR vaccines tended to be lower. No sociodemographic factors were identified as significant predictors of vaccine confidence, yet a growing vaccine confidence age gap was observed in the EU, with signals indicating higher confidence in age groups 45 years and older. As such, vaccine confidence should be particularly monitored for the 18–34-year-olds' perception towards MMR, with additional research showing its low uptake in young adults (medical students, Rome (58)).

Vaccine confidence among Italy's **HCPs** was also high but with lower vaccine confidence for the vaccination of pregnant women against both influenza and COVID-19. Vaccine confidence among health care providers is of particular importance, as it will not only define the chances of this high-exposure group to be vaccinated but also influence the probability that the HCPs

recommend vaccines to their patients. In a mixed-methods study of health care professionals' attitudes towards vaccination in 15 European countries, the lowest vaccine confidence was found in nurses, midwives and in HCPs from Italy, Hungary, Romania, and Switzerland (59). A lack of trust in health authorities and in the information they provide was identified as one of the drivers of this low vaccine confidence. Moreover, although Italy's health care professionals had a high likelihood of recommending COVID-19 vaccines, the likelihood was lower for HPV and MMR, mirroring the results found in the Vaccine Confidence Project. Importantly, the interviewed HCPs were least comfortable communicating on safety and in particular adjuvants, while communication on the value of vaccines was not perceived as an issue.

Parental vaccine hesitancy was investigated in Italy in 2016 by the ISS. Overall, across 3130 completed questionnaires, 83.7% of parents were in favour of vaccines, 15.6% were classified as hesitant, and <1% were classified as anti-vaccine (60). To increase vaccine acceptance and coverage, this hesitant group could benefit from appropriate communication interventions.

9.2. Actions to counteract vaccine hesitancy and increase vaccine acceptance

In 2022, the Italian Society of Public Health recommended ten actions to counteract vaccine hesitancy (61):

1. Establishment of a National Multidisciplinary Working Group on Vaccine Hesitancy
2. Activation of a National Monitoring/Surveillance System on Vaccine Hesitancy
3. Identification and Dissemination of Tools and Methods to Measure and Understand Vaccine Hesitancy
4. Identification, Testing, and Dissemination of Local and National Good Practices to Counteract Vaccine Hesitancy
5. Widespread and Interdisciplinary Training on Vaccine Hesitancy
6. Training on Risk Communication, Community Engagement and Infodemiology
7. Inclusion of Effective Interventions to Counteract Vaccine Hesitancy within the National Immunization Plan (NIP)
8. Promoting the Establishment and Growth of a Community of Practice and Research in the Field of Vaccine Hesitancy
9. Promoting Collaborations between Scientific Societies
10. Promoting Knowledge from the Behavioural Sciences

These recommendations were successfully incorporated in the PNPV 2023-2025, in which countering vaccine hesitancy was identified as both an objective and a strategy. Moreover, a specific chapter detailing a framework for vaccine communication was included in the new plan, built upon the monitoring and response to vaccine hesitancy, training, and education, strengthening of alliances for optimised advocacy and community engagement, and rebuilding of trust.

The successful translation of this framework into action requires dedicated tools, such as reliable references for the general population (e.g., VaccinarSi) (62). Identification of determinants of vaccine confidence through social media is another key tool, allowing signal detection of vaccine hesitancy and its main themes in order to convey targeted communication

strategies. The evidence produced can guide and promote the implementation of risk communication programmes in public health.

9.3. Impact of the law on compulsory vaccination on vaccine uptake in Italy

Prior to 2017, four vaccines were mandatory for children residing in Italy: poliomyelitis, diphtheria, tetanus, and hepatitis B. However, penalties for non-compliance were not applied. Moreover, in 2007, the Veneto region officially suspended mandatory vaccination, leading to other regions officially eliminating the penalties.

End of July 2017, a new law was approved; it increased the number of compulsory vaccines for children aged 0–16 years to ten, extending the original list to include *Haemophilus influenzae* b, pertussis, measles-mumps-rubella (MMR), and varicella. This decision was driven by worrisome declines in vaccine coverage, the relative ineffectiveness of the "light" obligation strategies in place (without penalties), and the measles epidemic of 2017-2018 which severely hit Italy and resulted in the country being put under trial by the WHO for its low MMR coverage.

The new law not only expands the number of compulsory vaccines, but also encompasses catch-up vaccinations in previously unvaccinated children. The law also enforces specific penalties in the event of non-compliance with the legislation. Children 0-6 years old who are not vaccinated cannot be enrolled in nursery school or day care centres. Children between the ages of 7 and 16, attending compulsory school, must be vaccinated and submitted to all required booster doses, although a delay in complying with the vaccination schedule will not prevent school enrolment. If one or more vaccines have not been administered, the school is required by law to report the violation to the local health agency, which will summon parents, requiring them to comply with their obligations. If parents do not comply with the request, they can be subject to fines, which can range between 100 and 500 Euros.

The making of the law met multiple challenges, leading to both political and public discussions and antivax-driven obstacles (e.g., disinformation, trials). Nevertheless, the law has had a positive impact on vaccine acceptance in the country. Firstly, everyone started talking about vaccines, with greater focus on the HCPs on the issue, and there was a high mediatic impact in which the media finally took a clear position in favour of the law. The law also supported the importance of vaccine monitoring and led to the creation of the NVR. Finally, a favourable impact on vaccine coverage was observed. Between 2016 and 2022, the vaccine uptake for polio went from 93% to 95%, and, more markedly, from 87% to 94% for MMR. Additionally, an increase in vaccine uptake for non-mandatory vaccines was also registered, such as an increase in PCV coverage from 88% to 91% (63). Conversely, vaccine uptake of HPV remains below its target (see Table 5).

Currently, there are no adult compulsory vaccination laws in Italy at the National Level. However, for HCPs, some Regions have instituted compulsory vaccinations (especially influenza) in their Regional Laws. During the pandemic, COVID-19 vaccination was mandatory for HCPs.

10. Strategies and programmes implemented in Italy to vaccinate specific adult population groups, highlighting the challenges and opportunities

Specific recommendations, vaccine strategies, vaccine coverage rates, success stories, challenges, and opportunities were reviewed for seven adult population groups, namely older adults, pregnant women, HCPs, immunocompromised, migrants, young adults, and travellers. These are summarised in Tables 1 to 7.

Table 1. Vaccine strategies and programmes in older adults, Italy.

Specific recommendations	PNPV: Influenza vaccine, PCV, HZ vaccine and Tdap are recommended in older adults. Specific Circular 2023/24: High-dose or adjuvanted influenza vaccines are to be used for seasonal flu vaccination of older adults.
Vaccine strategies	Multiple strategies are implemented across Italy's regions and in various settings (LTCF, hospitals, pharmacies etc.) mostly concerning influenza vaccination and some for PCV and HZ vaccine (64). One example comes from the Veneto region where an active call, information letter, and set appointments for co-administration are given to residents 65 years of age (1 st dose HZ and PCV; 2 nd dose HZ and Tdap).
Vaccination coverage (in 65y+)	Coverage varies according to targeted pathogen and region. Decreasing trends have been recorded in recent years. Coverages tend to be higher in patients with frailty (65). <ul style="list-style-type: none"> - Influenza vaccine: 56% - COVID-19 5th dose: from 3 to <18% - PCV: estimated at <30% (<i>no official national coverage data available</i>) - HZ vaccine: estimated at 5-12% (<i>no official national coverage data available</i>)
Success stories/Examples of awareness activities on EU level	Calls to action through a Manifesto (66): authors include the Italian Society of Gerontology and Geriatrics. Establishment of a Parliamentary intergroup on Healthy ageing in March 2023. PROVAX programme: integrated vaccination programmed with information, vaccination, and follow-up during and after a hospital stay. Emilia-Romagna region: mandatory to include specific recommendations for vaccinations in all hospital's discharge letters.
Challenges	Lack of training of HCPs on vaccination of older adults and the benefits of the life-course approach. Lack of awareness of (preventable) disease burden in older adults. Regional disparities in adherence to national guidelines Absence of evaluation of the different vaccine strategies used National coverage data lacking for pneumococcal and HZ vaccines, lack of coordination in the access to the digital vaccination records
Future goals/ Opportunities	To reach coverage targets of PNPV: 75% for influenza & PCV; 50% for HZ vaccine Insert vaccination in specialist guidelines. Geriatric specialist to be included in NITAG membership Expand involvement of NHS professionals and facilities. Involve hospitals and community pharmacies, and improve access to pharmacy network. Give access to the regional registry to all actors involved in the vaccination process.

Table 2. Vaccine strategies and programmes in health care providers (HCPs), Italy.

Specific recommendations	PNPV: HBV, influenza, MMR, Varicella, Tdap, (BCG for specific exposure risks) Specific Circular: Seasonal COVID-19. During the pandemic, COVID-19 vaccination was mandatory for HCPs.
Vaccine strategies	Variable across regions and institutions. Can be offered at the workplace or local vaccination units/centres. Alternatively, by the HCP's general practitioner.

Vaccination coverage	No official national coverage data are available for all HCP-recommended vaccines. Influenza vaccine uptake in HCPs is available through the population surveillance PASSI, showing low coverage rates of <50% (67). Additional vaccine coverage data comes from regional and local initiatives (68). In general, vaccine coverage rates in HCPs are low, fluctuate, generally mirror those found in the general adult population, and tend to be higher for vaccines preventing diseases with an individual perceived risk (e.g., COVID-19 during pandemic).
Success stories/Examples of awareness activities on EU level	COVID-19 vaccine uptake, reaching 94% for primary schedule among HCPs of the University Hospital of Palermo
Challenges	Lack of coordination, no uniformity of offer at regional or national level Lack of awareness of benefits
Future goals/ Opportunities	Incentives (e.g., paid vacation days; inter-department competition for best rates) Increase accessibility through proximity vaccination (on-site, mobile teams in hospitals) Increase and/or improve vaccination training for HCPs.

Table 3. Vaccine strategies and programmes in pregnancy, Italy.

Specific recommendations	PNPV: Vaccinations against diphtheria, tetanus, pertussis (Tdap) are recommended during the 3rd trimester, for each pregnancy. Influenza vaccine recommended (any trimester, according to seasonality). Specific Circular: COVID-19 vaccine during 2nd or 3rd trimester
Vaccine strategies	Vaccines are offered by obstetrics departments and hospital birth centres, as well as family clinics, prevention department clinics, vaccination centres, and GPs. Vaccines are administered by public health specialists, midwives, gynaecologists, nurses, and to a lesser extent by GPs. Direct and free access to vaccines is possible at the prevention departments and vaccination centres, and appointments can be made via a unified booking centre (centralised computerised system). Vaccinations are offered free of charge. Promotion of vaccination during and after pregnancy is part of birth support and/or antenatal programmes. Informative material for women, training of HCPs, and dedicated agenda slots are used to promote vaccination.
Vaccination coverage	No official national data available. Indeed, although collected in NVR, the data are not validated. Pregnancy status is not an obligatory variable in the registry, leading to denominator issues in correctly calculating vaccine coverage. According to regional data (Tuscany): the highest vaccine coverage in pregnancy is reached for Tdap: 43-47% (69). This does not reflect national data.
Success stories/Examples of awareness activities on EU level	In Palermo, implementation of vaccination educational interventions, including counselling by HCPs during childbirth courses, improved vaccination adherence (70).
Challenges	Absence of dedicated vaccine pathways for pregnant women.
Future goals/ Opportunities	Creation of a dedicated vaccine pathways, with better monitoring Increase HCP awareness. Improve accessibility, extend free access to vaccination centres, implement (multilingual) outreach campaigns.

Table 4. Vaccine strategies and programmes in immunocompromised persons, Italy.

Specific recommendations	PNPV: defines specific recommendations for Asplenia, Immunocompromised, HIV patients, solid organ transplant and Haematopoietic stem cell transplantation candidates, and household members of immunocompromised patients. PNPV 2023-2025: RZV and HPV vaccine (for persons living with HIV) Specific Circular: Seasonal COVID-19.
Vaccine strategies	The PNPV 2023-2025 details a framework to promote interventions in high-risk populations. Vaccine strategies are to be integrated within the immunocompromised patient's clinical care pathway. Moreover, immunization requires a proactive approach, both at the hospital and local level.
Vaccination coverage	No national level coverage data or denominator data are available. Only local or regional studies in specific subgroups provide estimates (71, 72).
Success stories/Examples of awareness activities on EU level	The operational proposal for the vaccination of fragile/immunocompromised persons by a collective of Italian scientific societies (73).
Challenges	Specific challenges were exposed during the COVID-19 pandemic. These included the ever-evolving epidemiology, vaccine hesitancy, and communication challenges (74).
Future goals/ Opportunities	Involvement of Specialists and scientific societies in immunization. Increase awareness (e.g., vaccine recommendations in discharge letter) and facilitate access (e.g., appointment booking options). Authorise access to NVR by professionals involved in patient care to improve and facilitate vaccination pathways.

Table 5. Vaccine strategies and programmes in young adults, example of HPV vaccine, Italy.

Specific recommendations	PNPV: HPV vaccination in adolescents, both females and males (targeted age: 11–12-year-olds); 2 or 3 doses according to age: 2-dose vaccination cycle (0 and 6 months) up to 14 years of age and 3-dose vaccination cycle at times 0, 2, 6 months from 15 years. New recommendation introduced by PNPV 2023-25: Free of charge for women who have been treated for CIN2+ or higher-grade lesions. Vaccination may be administered before or after treatment, up to a maximum of three years after treatment. catch-up vaccination is recommended for women at least up to 26 years of age, also using the appropriate opportunity of the call to the first screening for the prevention of cervical cancer (25 years) and for men at least up to 18 years, if they have not been previously vaccinated or have not completed the vaccination course. Vaccination is also recommended for subjects with HIV infection and MSM (Men having Sex with Men). Not a mandatory vaccine.
Vaccine strategies	In Italy the HPV vaccination strategy aims at strengthening prevention of cervical cancer and other related HPV diseases. The main identified actions to be taken in Italy are: - Strengthening the national vaccination campaign against HPV with the active involvement of GPs, paediatricians, specialists (gynaecologists, oncologists), family counselling centres, scientific societies and civil society; - Promotion of vaccination by expanding access to vaccination services, organising open days and catch-up activities, the maintenance of gratuity over time for the target cohorts (up to 26 years for females and up to 18 years for males), the adoption of flexible informatic tools and technologies to support the active call and the management of the reservation to reduce the probability of non-presentation;

	- Analysis of the determinants of HPV vaccine hesitancy and development of an extensive communication and information campaign in support of the national vaccination campaign against HPV, committed on several fronts: schools, meeting points for adolescents and young people, all media (including social media).
Vaccination coverage	Vaccine coverage: varies by region. In 2021, coverage by 15y in males (birth cohort 2006), last dose, estimated at 54.2%, in 15-year-old females it estimated at 69.4% at the national level (75).
Success stories/Examples of awareness activities on EU level	SPERANZA: project on HPV vaccination after surgical treatment for HPV-related diseases. The study showed HPV vaccination to be beneficial as an adjuvant to surgical treatment for relapse prevention. (76)
Challenges	Remaining low coverage and specific vaccine hesitancy towards HPV vaccine, compared to other vaccines.
Future goals/ Opportunities	Research on ideal timing for vaccination after (pre-) cancer lesions: international RCT trial NOVE and HOPE9 (RCT trial involving nine Italian centres). Reach PNPV HPV vaccine coverage target of 95%.

Table 6. Vaccine strategies and programmes for migrants, including refugees and asylum seekers, Italy

Specific recommendations	PNPV: Children: (catch-up) vaccination according to PNPV immunization schedule, and Hepatitis A in risk groups. Adults: (catch-up) vaccinations against poliomyelitis, MMR, varicella, Tdap, and HBV Italian guidelines further detail immunization of migrants (77).
Vaccine strategies	The PNPV 2023-2025 now includes a strategy to reduce inequalities with regard to immunization. However, the strategy will now need to be translated into action.
National vaccination coverage	No national-level coverage data or suitable denominator data are available. Specific studies such as influenza in high-risk patients, rubella in women (PASSI study), or COVID-19 uptake studies have shown lower coverage rates in the migrant population (78, 79)
Success stories/ Examples of awareness activities on EU level	AcToVax4NAM: access to vaccination for newly arrived migrants, including Co-creation of tools and training sessions with and for Professional For Health (80).
Challenges	Although the right to access vaccinations is guaranteed for all migrants from a legislative perspective, this is not always the case in practice. Challenges are multiple and include cultural and linguistic barriers, difficulties to identify by health registries, and contact through usual channels (e.g., invitation letters). Difficulties in health service accessibility and mistrust of local authorities are additional constraints.
Future goals/ Opportunities	Drawing lessons from the COVID-19 pandemic (81). Multidisciplinary approach, including civil society and social services. Enhancing professionals' knowledge about migrants' rights to health care/prevention. Improving reachability through updated data sources and collaboration. Promoting adherence through culturally sensitive health campaigns and strategies. Achieving vaccination coverage through flexible services and better documentation. Evaluating interventions to measure effectiveness. Strengthen NVR, essential for immunization follow-up of 'on-the-move' populations.

Table 7. Vaccine strategies and programmes in travellers, Italy

Specific recommendations	Hep A in children visiting friends and relatives (free of charge) All: (catch-up) vaccinations for HBV, MMR and Tdap (in children) or Tdap (in adults). Vaccination depending on destination, type of travel, and patient specificities. These (e.g., yellow fever, rabies) are not included in PNPV and therefore not LEA.
Vaccine strategies	Consultations of travellers in dedicated travel medicine clinics within many ASL.
National vaccination coverage	No national-level coverage data or denominator data are available (NVR does not include a “traveller” item). Roughly 50% of travellers are seen pre-travel, but this drops to <20% if travellers visit friends and relatives.
Success stories/ Examples of awareness activities on EU level	Good pre-travel counselling results in higher vaccine acceptance (e.g., rabies). Opportunity for catch-up vaccination
Challenges	The COVID-19 pandemic resulted in a total disruption of this preventive medicine. Travel medicine is not a recognised discipline in Italy.
Future goals/ Opportunities	Vaccinology formally taught. Travel medicine recognised as a discipline. Improvement of NVR with regard to denominators.

11. Future prospects and potential solutions to overcome barriers and enhance adult immunization efforts in Italy and other European countries

The two-day meeting concluded with break-out group discussions, where meeting participants identified the strengths, challenges and potential improvement opportunities of Italy’s adult immunization efforts. These are summarised in Table 8 and imply a multisectoral approach. Italy’s strengths and tactics to overcome barriers to immunization are important lessons to learn from and may be useful to other European countries facing similar challenges.

Table 8. Strengths, challenges and potential improvement opportunities of Italy’s adult immunization efforts.

Strengths	Challenges	Potential solutions
The existence of PNPV that defines the national immunization strategy.	The PNPV is not always translated into action. High complexity and regional disparities related to the fragmentation of Italy’s NHS	More regulation on a national level strategy.
Italy’s life-course immunization schedule.	Adults are not prioritised, with certain underserved populations remaining (e.g., older persons, migrants, pregnancy). Ageing population and changes in household composition. Physicians treating high-risk patients are more focused on treatment than on prevention.	Increase prioritisation of adults within the vaccine strategies. Translate into action the PNPV framework for vaccination in high-risk groups and highly vulnerable groups. Collect and learn from best practices and success stories to reach these specific adult populations. Improve the knowledge on the role of prevention in the health of the population among students in Medical

		schools and post graduate university programs
<p>Mandatory vaccinations to address insufficient vaccine coverage.</p> <p>Currently, there are no adult compulsory vaccination laws in Italy at the National Level. However, for HCPs, some Regions have instituted compulsory vaccinations (especially influenza) in their Regional Laws. During the pandemic, COVID-19 vaccination was mandatory for HCPs.</p>	<p>Vaccine coverage remains low for certain VPI, with higher vaccine hesitancy towards certain vaccines such as MMR and HPV.</p> <p>Vaccine hesitancy is increasing since COVID-19, with a possible age gap emerging.</p> <p>HCPs show higher hesitancy for vaccination of pregnant women for influenza and COVID-19.</p>	<p>Targeted campaigns and communications strategies tailored to each audience.</p> <p>Increase collaboration and involvement of scientific societies with better reach to HCPs and patients of specific high-risk groups.</p> <p>Increase knowledge and vaccine literacy of HCPs and in general population.</p> <p>Translate into action the PNPV framework on vaccine communication. Improve communication on safety.</p> <p>Increase accessibility, including increased proximity to more vaccinating sites (e.g., pharmacy).</p>
<p>Vaccines of the NVP are LEA, and therefore free of charge.</p>	<p>Organisational costs of immunization (public tenders, procurement, distribution, promotion etc.) fall upon the regions, resulting in high expenditure and regional inequalities.</p> <p>Only 5% of the National Health Fund is dedicated to prevention. Although a specific budget for vaccination has been in place since 2017, this budget is shared with the highly competitive field of innovative drugs.</p>	<p>Advocate for better funding of prevention.</p>
<p>Multiple success stories and best practices identified at the local and regional levels.</p>	<p>Effectiveness of local vaccine strategies is not always monitored or evaluated.</p> <p>Local problems are also to be considered, including issues with vaccine stocks and ordering systems.</p>	<p>Collect and learn from best practices and organisations in successful regions, tailored to local needs, for better structuring of campaigns.</p> <p>Collect and learn from the COVID-19 pandemic.</p>
<p>Electronic NVR implemented. Strong vaccine vigilance system, and successful post-marketing surveillance system for COVID-19</p>	<p>Lack of integration of NVR with regional vaccine registries.</p> <p>Absence of national vaccine coverage data in high-risk groups (absence of denominators).</p> <p>The epidemiology of certain VPIs (e.g., HZ) is not captured by the</p>	<p>Address the integration issues between regional registries and NVR.</p> <p>Training of HCPs on NVR and reporting of diseases.</p> <p>Improve vaccine data collection with a better capture of denominator data.</p>

vaccines (effectiveness & safety).	national surveillance systems. As such, the impact of vaccine programmes cannot be fully assessed.	Authorise the access to NVR by professionals involved in patient care to improve and facilitate vaccination pathways.
	According to the Italian Data Protection Authority, patient data cannot be used to enrol patients in vaccination campaigns.	

12. Conclusions

Italy has made groundbreaking measures in the field of adult immunization strategies within Europe. The country was one of the first to propose a life-course vaccination schedule, broadening the historical focus on children to include all adults. Moreover, Italy’s PNVP sets targets for vaccination coverage, identifies the main immunization priorities, and considers multiple actions to reduce disparities among Italian Regions. The vaccines included within the PNVP are categorised as LEA and are consequently free of charge for all individuals residing in the country. In 2017, significant gaps in vaccine coverage, particularly for the MMR vaccine that prompted a severe measles outbreak, were positively countered by the expansion of childhood mandatory vaccines for school attendance from four to ten different vaccines up to the age of 16 years. In addition, Italy has a strong vaccine vigilance system and established a successful post-marketing surveillance system for COVID-19 vaccines, for both effectiveness and safety. The COVID-19 pandemic imposed unprecedented resourcefulness, with new vaccine campaign organisation and strategies that can be leveraged, including the use of novel vaccine administration sites such as hospital settings and pharmacies. However, the fragmentation of Italy’s NHS following the constitutional reform of 2001, has led to an increased complexity and regional disparities regarding immunization. Indeed, although LEA vaccines are financed centrally by the National Health Fund, the organisational costs of immunization fall upon the regional authorities. As Italy’s Regions are not financially equal, decentralisation has led to inequalities in vaccine campaign rollout and ultimately vaccine uptake. Other immunization challenges identified include the changing demographics with an ageing population, an increase in vaccine hesitancy in the aftermath of the COVID-19 pandemic, the lack of targeted vaccine campaigns and communication even towards HCPs, and specific issues related to underserved populations, such as migrants and pregnant women. Additionally, the lack of complete integration of the regional vaccine registries to the NVR leads to issues on the field (absence of vaccine history of patients) and vaccine coverage data gaps, particularly for high-risk groups that lack appropriate denominator data (e.g., travellers, immunocompromised, pregnancy, HCPs). Gaps in vaccine coverage data as well as the absence of certain VPI in the national surveillance system (e.g. HZ) impede vaccine campaign monitoring and evaluation. While Italy is often regarded as one of the leading examples in Europe for adult immunization, barriers to vaccination in Italy are well known and multiple future prospects and potential solutions have been identified by the involved Italian stakeholders to enhance adult immunization efforts. At present, the largest challenge remains the effective translation of recommendations into actions.

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