

# Today's vaccination policies in Italy: The National Plan for Vaccine Prevention 2017-2019 and the Law 119/2017 on the mandatory vaccinations

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*Parole chiave: Piano Nazionale per la Prevenzione Vaccinale (PNPV), Calendario vaccinale per la vita, Legge 119/2017, vaccini obbligatori, categorie a rischio*

## Abstract

*The National Plan for Vaccine Prevention 2017-2019 has expanded the vaccination offer including new vaccines, enlarging the target population and introducing for the first time in Italy a life-course approach to vaccination. A "lifetime immunization schedule" is aimed to reduce the burden and the related costs of vaccine-preventable diseases through effective vaccination programs. However, to counteract the national steady downward trend in the uptake of vaccinations that caused a drop of the vaccination coverage below the 95% threshold to allow herd immunity, it was decided to make 10 vaccinations mandatory by the law 119/2017. In particular, in addition to already mandatory vaccinations against diphtheria, tetanus, hepatitis B and poliomyelitis, those against measles, mumps, rubella (MMR), varicella, pertussis and Haemophilus influenzae type b (Hib) were added to the list. According to the law, all unvaccinated children cannot attend preschool services until the age of 6 years and fines (from 100 to 500 Euros) are provided for parents. Moreover, this law provided, in its first application, a catch-up campaign for children up to the age of 16 years and the free-of-charge offer of all mandatory and recommended vaccines to each child not yet vaccinated according to the previous NPVP.*

*The NPVP includes also several at risk categories, such as pregnant women, healthcare workers and subjects suffering from chronic diseases, to whom specific vaccinations, free of charge, are offered. The vaccinations of pregnant women have different purposes. In order to decrease the pertussis risk in newborns in the first months of life, a booster immunization of DTPa is recommended, at every pregnancy, between week 27<sup>th</sup> and 36<sup>th</sup>. Instead, the influenza vaccine administration to pregnant women during the second or third quarter is mainly aimed to avoid the risk of serious disease complications for both the mother and the fetus. Another group of at risk subjects included in the NPVP is that made up by healthcare workers. According to the plan, "an adequate immunization of the healthcare workers is essential for the prevention and control of infections (anti-hepatitis B, anti-influenza, anti-measles-mumps-rubella, anti-varicella, anti-pertussis)". Finally, almost all the vaccinations foreseen by the NPVP are offered free of charge to subjects suffering from specific diseases. These include cardiovascular, respiratory, hepatic, neoplastic, renal and metabolic disorders, in addition to immunosuppression that exposes them to an increased risk of contracting invasive infectious diseases.*

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## Introduction

Vaccinations are considered one of the greatest achievements of public health worldwide. However, in last few years, a distrust about vaccine safety, efficacy and even necessity have led to an alarming number of subjects refusing or delaying vaccinations. This has recently led to the onset of cases, or even real outbreaks, of vaccine-preventable diseases, such as *Haemophilus influenzae* b (Hib) invasive disease, varicella, pneumococcal infections, measles, pertussis, influenza and its complications (1-3).

Even if it is well known that the serious side effects of vaccines currently in use are extremely rare, especially if compared to the benefits that vaccines provide (4), the major cause of vaccine refusal is represented by the totally unfounded fear of serious vaccine-induced diseases. These include the onset of multiple sclerosis following the hepatitis B vaccination or that of autism after MMR vaccination (5).

Despite the scientific evidences about vaccine safety and efficacy, in Italy, starting from 2013, the number of under-vaccinated or unvaccinated subjects alarmingly increased (2), hindering the achievement of the herd immunity, i.e. immunization at least equal to 95% and, consequently, an indirect protection also of the unvaccinated (6).

In order to counteract this threat to public health, a new National Plan for Vaccine Prevention (NPVP) 2017-2019 was approved in Italy (7), followed, in the same year, by the widely debated and criticized Law 119/2017, which increased the number of mandatory vaccinations from four to ten, introducing fines for the “hesitant” and refusing parents (8). The two measures are widely discussed below, underlining the reasons that led to their enactment, and, above all, the goals they intended to achieve.

## The National Plan for Vaccine Prevention 2017-2019

The NPVP 2017-2019 was approved by the State-Regions Conference of 19.01.2017 (9) and aimed to improve the current national vaccine-preventable disease epidemiology through the achievement of several target points, among which to maintain the polio-free status of the Country, to achieve the measles and rubella “elimination” and to guarantee the active and free offer of vaccinations to special age groups and to the groups of population at risk (7).

The NPVP was fully incorporated into the update of the list of Essential Levels of Care (in Italian LEA: Livelli essenziali di assistenza), approved in the same year through the emanation of the Decree of the Prime Minister of the Italian Government (in Italian: DPCM) of 12.01.2017 “Definition and Update of the Essential Levels of Care” (10). The principal contributions of the plan are the extension of the vaccination offer with the introduction of new vaccines and the enlargement of target population. Moreover, the NPVP introduced, for the first time in Italy, a life-course approach to vaccination and the “lifetime immunization schedule” was carefully developed by using as basis the previous shared results of a scientific advice of the partnership of four national Medical Scientific Societies including: a) the Italian Society of Hygiene, Preventive Medicine and Public Health; (SitI), b) the Italian Society of Paediatrics (SIP), c) the Italian Federation of General Practitioners (FIMMG) and d) the Italian Federation of Paediatricians (FIMP) (11). As strongly recommended by national and international health authorities, the NPVP is aimed to reduce the burden and related costs of vaccine preventable diseases (VPDs) through effective vaccination programs (12, 13). Due to the annual reduction of direct costs of vaccine-preventable diseases, it is estimated that National Health System

approximately saves 200 million euros, after deduction of the cost of new vaccinations (~100 million euros per year) (14).

### Law 119/2017

To counteract the growing phenomenon of vaccination refusals and of the “vaccine-hesitancy”, accountable for the worrying decrease of vaccination coverages, in the same year, the highly debated Law 119/2017 on mandatory vaccinations, implementing the Law-Decree 73/2017, was approved (8). The law was felt necessary because the efforts towards a voluntary approach to vaccinations, followed in the last 15 years, had failed their goals. Based on this vaccination policy, only the four previously introduced anti-diphtheria (in 1939), tetanus (in 1963), polio (in 1966) and hepatitis B (in 1991) vaccines were mandatory, with the exception of the Veneto Region, where the obligatoriness for these vaccines was suspended in 2007 by a Regional Law (15). In any case, since 1999, the foreseen penalties were not enforced to people refusing vaccination of their children, who could anyway attend their schools. All the other vaccines provided by the immunization programs, such as *Haemophilus influenzae* type b, acellular pertussis and the measles-mumps-rubella-varicella (MMRV) were only strongly recommended, as well as those against meningococcal and pneumococcal diseases and the anti-HPV vaccine. This caused a substantial drop of the vaccination coverage of both compulsory and recommended vaccinations and, due to the fact that the immunization against measles virus had always remained far below the 95% threshold recommended by the WHO, in January 2017 a severe measles outbreak occurred in Italy. In addition to the 5,408 cases recorded in 2017, the outbreak caused additional 2,427 cases until the 30<sup>th</sup> November 2018; at least one minor complication was reported in

47% of the notified cases and, overall, eight deaths were also reported (16). To reverse this dramatically increased burden of a vaccine-preventable disease, the Italian Ministry of Health, by a Law-Decree enacted on 7 June 2017 and then converted on 31 July 2017 into the Law 119/2017 (8), expanded the vaccinal obligations, bringing them to 10 and making them enforceable. Particularly, in addition to the already mandatory polio, diphtheria, tetanus and hepatitis B vaccines, the obligation was extended to *Haemophilus influenzae* type b, acellular pertussis and the MMRV vaccines. According to the Law, all the unvaccinated children were not allowed to attend preschool education until the age of 6, and fines (from 100 to 500 EUR) were provided for parents. Moreover, this Law provided, in its first application, a catch-up campaign for children up to the age of 16 years and all the previously mandatory and recommended vaccines, according to all the NPVPs preceding the NPVP 2017-2019 were offered actively and free-of-charge to each unvaccinated child. The Law also stated that a National Vaccine Registry had to be set up to monitor vaccination coverages at an individual level and this important tool was expected to become operational in 2018 in agreement with a Ministerial (Health) Decree (17), what did not happen. Consequently, the possibility to verify everybody’s vaccination coverage (including the booster doses administered) in all regions and autonomous provinces was delayed to the near future.

As reported by D’Ancona et al., the data recorded throughout the country in the first months of application of Law 119/2017 highlight a clear trend reversal, with a substantial increase for both previously compulsory and recommended vaccinations (18).

### Novelty in the NPVP 2017-2019

Well integrated by the Law 119/2017, the NPVP offers many other strongly

recommended vaccinations, among which those against *Neisseria meningitidis* B and C, pneumococcal and rotavirus for all newborns, the tetravalent meningococcal (ACWY135) and the HPV vaccination of the adolescents (both females and males, beginning just at 11 years of age) and, for the elderly, the annual anti-influenza, the anti-pneumococcal (PCV13 + PPV23) and the anti-Herpes Zoster vaccines (7).

Many are the news brought by the 2017 NPVP, among which the introduction of the newest anti-meningococcal B vaccine for all the newborns starting from the cohort 2017, the introduction of the tetravalent meningococcal (ACWY<sub>135</sub>) for all the adolescents, the introduction of the anti-HPV vaccine for both sexes starting from 11 years of age and, finally, the introduction of several vaccinations for some “at risk” categories, among which pregnant women, HCWs and subjects suffering from chronic diseases such as diabetes, liver and lung diseases.

### *1. Immunization of pregnant women*

Pregnant women are one of the “at risk” categories included in the new plan and vaccinations actively offered to this group have different purposes. Particularly, in order to decrease the pertussis risk in newborns in the first months of life, before they can be subjected to vaccination, a booster immunization by DTPa is recommended for the mothers, at every pregnancy, between weeks 27 and 36. Acellular pertussis component of DTPa is safe both for mother and infant, and immunogenic in the mother with effective transfer of antibodies to infant, and it has well been shown that this passive immunity is effective in preventing pertussis in young infants, who, this way, can be protected also before the date of active vaccination (19-21).

Further, the recommendation of influenza vaccine to pregnant women during the second or third quarter of pregnancy is mainly aimed to avoid the risk of serious disease

complications for both the mother and the future newborn. Due to immunological changes, involving both the innate and adaptive immune systems (22, 23), an increased susceptibility to influenza and other infections is observed during pregnancy (24), when an increased innate response is coupled to the attenuation of the T-helper type 1 cell-mediated cytotoxic activity and decreased B-cell proliferation (25). Considering safety and effectiveness of the influenza vaccine, since 2012 the WHO stated that pregnant women must be prioritized over other risk groups highly recommending the influenza immunization during all stages of pregnancy (26). In their systematic review Mertz et al. (24) underlined the strong association between pregnancy and severe influenza disease, observing a higher number of community-acquired pneumonia, hospitalization, admission to intensive care units (ICU) and ventilatory support during pregnancy in comparison to non-pregnant woman infected with influenza. Considering the hospitalization, the meta-analysis of several studies, mainly performed during the pandemic influenza A H1N1, showed an odds ratio [OR] equal to 2.44 (95% CI 1.22–4.87) (24). Furthermore, maternal influenza infections also increase the risk of poor outcomes of pregnancy such as a higher probability of spontaneous abortion, stillbirth, prematurity or low birth weight (27, 28). While the last effect can be caused very trivially by the temporary states of macronutrient and micronutrient deficiency induced by influenza, which limits the fetal availability of essential nutrients necessary for normal fetal development and growth, the other harmful effects of maternal influenza disease are due to the activation of innate immunity, increased in pregnancy, as above reported. Therefore, unlike other etiologic agents of infectious diseases, capable of causing the well-known congenital infection due to the transplacental passage of pathogens, the harmful effects of influenza

virus on fetus are indirect (29). Indeed, the pathophysiological responses are not due to vertically transmitted infection, as observed for rubella, cytomegalovirus, herpes simplex virus-2, *Toxoplasma gondii* and others, classically grouped together as the TORCH group infections, to which other agents have been recently added (varicella virus, parvovirus, and Zika virus). In particular, the activation of inflammatory response, triggered by maternal influenza disease, determines placental insufficiency, which in turn can cause fetal hypoxemia reducing the delivery of oxygen and, consequently, spontaneous abortion, stillbirth, preterm birth or prematurity (30). However, the most feared pathophysiological response to the maternal innate immunity activation influenza-induced is the production of soluble immune factors such as cytokines and other mediators of inflammation (IL1b, IL-6 and TNF ). These factors can cross the placental barrier causing fetal inflammation and, consequently the well-known oxidative stress, damaging the finely regulated organogenesis process (31, 32).

## 2. Immunization of HealthCare Workers (HCWs)

Another group of at risk subjects included in the NPVP 2017-2019 is that made up by healthcare workers (HCWs). According to the plan, “an adequate immunization of the HCWs (anti-hepatitis B, anti-influenza, anti-measles-mumps-rubella (MMR), anti-varicella, anti-pertussis) is essential for the prevention and control of infections” (7). To vaccinate HCWs is important to protect not only the patients but the HCWs themselves. Indeed, the World Health Organization (WHO) estimates that about 59 million of HCWs are potentially exposed every day to biological risks, working with infectious patients and coming into contact with contaminated fluids and materials (33).

The HCWs are at high risk of contracting HBV infection, due to a direct or an indirect

contact especially with contaminated blood and other body fluids (34). Infected HCWs could also represent a risk for the patients (35). According to the WHO, about 5.9% of HCWs are exposed to a HBV infection each year; this means that approximately 66,000 HBV infections among HCWs occur each year worldwide (36). About 70% of HCWs in countries with medium to high endemic risk of HBV have biological risk accidents due to needle stick injuries, with an average of two per HCW per year (37). However, the HBV coverage vaccination rates among HCWs are at a suboptimal level. Particularly, a 2-year Italian seroepidemiological study reported that the vaccination rate versus HBV among HCWs was only 70.1%; stratifying the data by areas, 66.8% were in medical wards, 70.1% in surgical wards and 79.2% in intensive care units (38).

Concerning the influenza, this category is considered very important because it has been demonstrated that about 25% of them contract the virus every year and, thus, they can transmit the infection to patients especially during the asymptomatic period (39). Moreover, several studies have shown that the vaccination of this category is a high effective strategy, particularly in reducing all-cause mortality in both patients and residents of healthcare structures (40-42). For all these reasons, influenza vaccination for all HCWs is strongly recommended in almost all European countries (43). However, as demonstrated by a recent Review, coverage rates against influenza in this category are generally low, ranging from 14% in Poland to 45.6% in England (44). Consequently, unvaccinated HCWs may represent the main source of influenza inside the healthcare structures with high risks for patients' health. In Italy, the annual informative note about the prevention and control of influenza (season 2018-2019) considers HCWs a category for whom influenza vaccination is strongly recommended in order to protect themselves, their relatives

and the patients with whom they come into contact during the healthcare activities (45). Influenza vaccination of the HCWs is important not only to reduce the burden of morbidity and mortality of the patients but also to decrease the related remarkable costs for the National Health Service. The costs consequent to nosocomial influenza involve direct costs, related to the care of ill people, and indirect costs, especially consequent to the decreased productivity due to absence from work (46). Indeed, it has been demonstrated that influenza represents one of the principal causes of work absence, causing approximately 10% of all absences from work. In Italy, it has been calculated that the average length of absence from work for influenza is 4.8 days and every case of influenza would cost about 330 Euros (47).

However, despite the ease in the availability of vaccines to the HCWs and the scientifically proven effectiveness in reducing the incidence of the infection, their acceptance by HCWs is still a critical issue. Possible reasons for low influenza vaccination coverages could be a lack of time, especially during the working hours, doubts about the effectiveness, fear for side effects and personal reasons including the “right to become ill” themselves (39). In order to improve the situation and raise awareness about this problem, various recommendations have been made in several countries, including educational strategies and the implementation of strategies to improve vaccine accessibility. However, it has been suggested that these actions may not be sufficient to improve the uptake up to the recommended levels, and that compulsory approaches might be needed (48). These approaches could include, also, the requirement for those refusing HCWs, to complete a ‘declination form’, stating their reasons for non-vaccination. Another possibility would be to include in the job contract the engagement not to refuse all the prescribed vaccinations.

### *3. Categories at “high risk for pathology” included in NPVP 2017-2019*

Almost all the vaccinations foreseen by the NPVP are offered free of charge, regardless of the age, to different groups affected by specific diseases (i.e. categories at “high risk for pathology”). These include cardiovascular (both congenital and acquired cardiopathies), respiratory (including severe asthma, pulmonary dysplasia, cystic fibrosis and COPD), hepatic, neoplastic, renal and metabolic (such as diabetes mellitus or, sometimes, obesity with BMI >30) diseases, in addition to immunosuppression that expose them to an increased risk of contracting invasive infectious diseases, developing serious complications (49-51). In order to protect susceptible subjects affected by these pathological conditions, many vaccines are also recommended to all their cohabitants. In particular, vaccination of cohabitants is the only effective prevention tool available to protect subjects with severe immunosuppression to whom live attenuated vaccines cannot be administered. These are: 1) subjects with AIDS or other clinical manifestations of HIV infection, 2) subjects suffering from cancers that can alter their immune mechanisms, 3) subjects with impaired cellular immunity, 4) subjects with disgamaglobulinemia or hypogammaglobulinemia and 5) subjects undergoing long-term immunosuppressive therapy. Instead, the immunosuppression conditions for which, regardless of the type of vaccine available, the active immunization is strongly recommended are: congenital or acquired immunodeficiencies, including HIV infection without signs of immunodeficiency and with a proportion of CD4+ T lymphocyte counts  $\geq 200/\text{mL}$ ; forms of iatrogenic drug immunosuppression such as subjects awaiting organ transplantation and those affected by acute lymphatic leukemia in remission (at least three months after the end of the last cycle of chemotherapy and with compatible immunological parameters) (52). In all these cases, the condition of susceptibility to the

specific preventable disease is defined on the anamnestic basis, without the need for serological confirmation. Other pathological conditions for which the NPVP 2017-2019 provides the free active vaccination are: 1) chronic alcoholism, 2) adrenal insufficiency, 3) deficiency of complement factors, 4) anatomical or functional asplenia and programmed splenectomy, 5) programmed immunosuppressive therapy, 6) deficiency of coagulation factors, 7) presence of hematological diseases and hemoglobinopathies. The most strongly recommended vaccinations in all these pathological conditions include influenza vaccine (to be administered also in children or adolescents on long-term therapy with acetylsalicylic acid at risk to develop Reye's syndrome and in subjects affected by neuromuscular diseases with an increased risk of aspiration of respiratory secretions), anti-Haemophilus influenzae tipo b (Hib) and anti-Pneumococcal vaccine (in presence of cochlear implant). Moreover, the other vaccines recommended by the NPVP in the groups affected by specific diseases are: 1) anti-Hepatitis B vaccine (in poly-transfused or hemophiliac patients, in uraemic subjects, to whom dialysis is programmed, and in institutionalized subjects with physical and mental disabilities), 2) anti-Hepatitis A vaccine (to prevent the onset of fulminant forms in subjects suffering from chronic liver disease, 3) anti-Herpes zoster vaccine (considering that the presence of diabetes, COPD etc may aggravate the painful syndrome associated with the disease complications) (53).

#### *4. Other Categories included in the NPVP 2017-2019*

The NPVP 2017-2019 guarantees free vaccinations also to some categories of subjects that have an increased risk of exposure to preventable infectious diseases associated with specific behaviours. These groups include children of immigrants (up to six years of age) who come from

endemic countries and the homosexual males to whom anti-Hepatitis A vaccine is strongly recommended (54). As regards the Hepatitis B vaccine, it is freely provided to the cohabitants and contacts of HBsAg positive subjects, regardless of age, to blood donors belonging to rare blood groups, prisoners, subjects engaged in prostitution, drug users and homosexual males (55). In the latter group also Human Papillomavirus (HPV) vaccine is strongly recommended, because of the epidemiology of this virus and the important burden of HPV-related diseases (56-58). Lastly, to prevent the tick-borne encephalitis (TBE), vaccination is recommended for the residents in endemic rural areas, as well as for the professionally exposed subjects.

## **Conclusions**

The NPVP 2017-2019 is an indispensable tool to promote public health, as unanimously recognized by the scientific community also at the international level and, thanks to it, the immunization policies in Italy have reached an important milestone. By the wide and free-of-charge vaccination offer, not exclusively addressed to the pediatric age, the NPVP 2017-2019 represents one of the most complete interventions of public health implemented by a National Health System. As above reported, the main features of the NPVP 2017-2019 are the introduction of new vaccines, a lifetime immunization schedule as well as a wide vaccine offer to several population groups, among which pregnant women, healthcare workers and subjects suffering from chronic diseases (7).

However, similarly to other countries, in Italy worrying decreases of vaccine coverage were reported before the NPVP was approved. Likely, this aspect would have greatly reduced the positive effects on public health. To counteract the alarming increased susceptibility to the preventable

diseases, which was responsible, inter alia, for the measles outbreak above reported, the Law n. 119/2017 on mandatory vaccines for childhood was soon approved (8). Both at the political and social level, the Law triggered a wide debate which was amplified by the media. The debate, to date still active, probably has increased the awareness of the population on the invaluable role of the vaccines and, already a few months after the mandatory vaccination has come into force, an increase of vaccine coverage was observed also for the recommended vaccines included in the NPVP 2017-2019. In particular, at the end of 2017, the percentage of immunization in the children of 24 months against pneumococcal and meningococcal C and B were 90.9, 83.1 and 38.6 respectively (2, 59). Although these values were higher than those recorded previously, a thorough assessment of the effects of the integrated application of the Law and NPVP 2017-2019 (i.e. the decreased incidence of several preventable diseases) is still premature. However, a further data which would seem to confirm the trend reversal of vaccine coverage is represented by the almost complete depletion of the influenza vaccine stocks for the 2018-19 vaccination campaign, highlighting the remarkable adherence to this immunization program.

## Riassunto

### *Attuali politiche vaccinali in Italia: Il Piano Nazionale per la Prevenzione Vaccinale 2017-2019 e la Legge 119/2017 sull'obbligatorietà dei vaccini*

Il Piano Nazionale per la Prevenzione Vaccinale 2017-2019 ha esteso l'offerta di vaccini sia ammettendone nuovi che allargando la popolazione target. Detto Piano ha introdotto per la prima volta in Italia un "calendario vaccinale per la vita". Questo mira a ridurre l'impatto e i costi delle malattie prevenibili da vaccino attraverso efficaci programmi di vaccinazione.

Tuttavia, al fine di contrastare il trend nazionale, registratosi negli ultimi anni, che ha causato una riduzione della copertura vaccinale al di sotto della soglia del 95% tale da non consentire il raggiungimento della "herd

immunity", è stato necessario con la legge 119/2017 rendere obbligatorie 10 vaccinazioni. In particolare, oltre alle vaccinazioni già obbligatorie contro difterite, tetano, epatite B e poliomielite, sono state aggiunte alla lista quelle contro il morbillo, la parotite, la rosolia, la varicella, la pertosse e l'*Haemophilus influenzae* di tipo b. Secondo la suddetta legge, i bambini non vaccinati non possono frequentare i servizi prescolari fino all'età di 6 anni e prevede multe (da 100 a 500 euro) per i genitori. Inoltre, questa legge ha previsto, nella sua prima applicazione, una campagna di recupero per i soggetti fino a 16 anni e tutti i vaccini obbligatori e raccomandati sono stati offerti attivamente e gratuitamente a ciascuna coorte di questi bambini e adolescenti non vaccinati.

Nel Piano Nazionale per la Prevenzione Vaccinale 2017-2019 sono incluse anche le categorie a rischio, quali le donne in gravidanza, a cui vengono gratuitamente offerte specifiche vaccinazioni. Queste hanno finalità diverse, quale ridurre il rischio di pertosse nei neonati nei primi mesi di vita, con una dose di richiamo di DTPa, ad ogni gravidanza, tra la 27<sup>a</sup> e la 36<sup>a</sup> settimana. Invece, la somministrazione del vaccino anti-influenzale durante il secondo o terzo trimestre è principalmente mirata ad evitare il rischio di gravi complicazioni della malattia sia per la madre che per il feto. Un altro gruppo di soggetti a rischio incluso nel Piano è costituito dagli operatori sanitari. Secondo il piano, "un'adeguata immunizzazione del personale sanitario è essenziale per la prevenzione e il controllo delle infezioni (antiepatite B, anti-influenza, antimorbillo-parotite-rosolia, anti-varicella, antipertosse)". Infine, quasi tutte le vaccinazioni previste dal Piano sono offerte gratuitamente ai soggetti affetti da malattie specifiche tra cui malattie cardiovascolari, respiratorie, epatiche, neoplastiche, renali e metaboliche, oltre a condizioni di immunosoppressione che li espone ad un aumentato rischio di contrarre malattie infettive.

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