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Focusing on the implementation of 21st century vaccines for adults

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ABSTRACT

Adult immunization is a priority for public health, particularly in countries where an aging population has become increasingly more numerous. Protection against diseases which typically affect adults (like flu, pneumococcal diseases and Herpes zoster), the shift of age of infections which originally affected children (like measles), the decreasing protection with time for infections which need periodical booster doses of vaccines (Tdap), the availability of vaccines which can also impact on adult health (HPV) are only some examples of the importance of implementing targeted vaccination strategies.

The possibility to reach high coverage with immunizations that can guarantee a fundamental improvement of health for adults and the elderly can only be achieved through a coordinated effort where all stakeholders, under the coordination of public health, contribute to issue recommendations; create a functioning database for vaccine coverage registration; promote formative courses for healthcare workers and continuous information for the public; increase vaccines uptake among healthcare workers, who need to give the first testimony on the relevance of immunization.

1. Background

Vaccination calendars have traditionally been thought for infants and children, and only in relatively recent times, adult vaccination programmes have become a priority [1].

However, such delay is reflected also in the level of implementation and coverage [2,3].

A publication from the Immunization Action Coalition in the United States in 2004 reported a paradigmatic sentence of William Schafner, President of the National Foundation for Infectious Diseases: '*Where we are with adult immunization is where we were 25 years ago with children immunization. It is like a drip coming out of the faucet. For children it's turned on full force*' [4]. Although some progress has occurred in the last decade, we are still facing considerable difficulties in making adult immunizations known, recommended and implemented. Infectious diseases are not a "problem of the past" and there is enough evidence to justify implementing a life-course approach to immunization. As a matter of fact, infectious diseases such as seasonal influenza, pneumococcal diseases (including pneumococcal meningitis, pneumococcal pneumonia and invasive pneumococcal disease), pertussis, herpes zoster, measles, diphtheria and tetanus continue to place a significant burden on individuals of all age groups and also on Europe's ageing society. Between 2000 and 2050, the number of people aged 60 and over is expected to double. In 2050, more than 1 in 5 people will be 60 years or older. In 2012 in Japan, the proportion of people aged 60 years or older exceeded 30% and by the middle of the century, many countries will have a similar proportion (countries in Europe and North America, but also Chile, China, the Russian Federation, Thailand and Viet Nam) [5,6].

The "*World report on ageing and health*" highlights several areas that are likely to be effective in promoting health in adulthood. One of the key areas for action on healthy ageing is ensure access and affordability of medical products such as vaccines [7].

With regard to mortality data in the US, it is estimated that approximately, 200 children die for vaccine-preventable diseases (VPD) each year versus 70,000 adults – an incredible 350-fold difference. In a context of a progressive ageing population, the absolute and relative number of adults ill or dying of VPDs will continue to increase [1,8]. Therefore, the economic burden of some VPD will surely increase if no preventive strategies in adulthood will be implemented [9].

Moreover, according to estimates by Centers for Disease Control and Prevention (CDC), among U.S. adults, nearly 40,000 cases and 4000 deaths attributable to invasive pneumococcal disease occur each year, between 3000 and 49,000 deaths due to seasonal

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influenza [10], 9000 reported cases of pertussis [11], and about 1 million cases of herpes zoster [12]. Moreover, these diseases and their sequelae generated substantial costs. The costs of health and productivity for the society due to influenza alone are estimated to be as high as $87 billion per year [13,14]. A multi-country analysis among 10 EU countries analysed the cost-effectiveness of pneumococcal vaccination, with PPV23 (polysaccharide pneumococcal vaccine 23-valent), for IPD across those aged >65 years. The study observed substantial variation in the Incremental Cost-Effectiveness Ratios (ICERs) across the countries, with older populations generally having higher ICERs [15].

A considerable reduction in pneumococcal disease and its related costs over 5 years is estimated in Italy with the introduction of pneumococcal vaccination, with only PCV13 (pneumococcal conjugate vaccine 13-valent), of one, two or three adult cohorts per year. Vaccination of 65-year-old subjects, albeit more expensive, proved to be more favourable than the vaccination of 70- or 75-year-old cohorts [16]. A cohort-based HZ vaccination program in Italian elderly could have a relevant impact on the reduction of clinical cases and a favourable economic profile for the National Health Service (NHS), as already foreseen in other countries [17–19]. Every €1 invested in adult vaccination, starting at the age of 50 years, would yield €4.02 of future economic income for government over the lifetime of the cohort [20].

The objective of the current work is to give evidence to the importance of spreading the culture of prevention of infectious diseases in an ageing society at different levels. We also address possible strategies to reach high vaccination coverage in adulthood, giving an accent on the correct managing of adult vaccination programmes and communication skills. Our intention in writing this paper is to approach health policy makers and health care workers (HCWs) and give them the opportunity to consider that life-course immunization is a good investment on health and also a cost saving choice in the long term, but strong commitment is needed by all actors to reach the target of the adult population.

2. Why vaccinate Adults?

There are many reasons why adults need to be immunized. As a matter of fact, adults may need vaccination because they were not immunized at all or partially during childhood with paediatric vaccines; in the interval between childhood and adult age, new important vaccines may have become available; booster doses may be needed in case immunity is guaranteed by a high level of neutralizing antibodies that cannot be recalled through the mechanisms of immunological memory (i.e. tetanus), or cannot be reached in time to prevent the disease, because the incubation period is shorter than the time to boost immunity (i.e. meningococcus); older adults and those affected by chronic diseases may be at higher risk of acquiring the preventable disease, or have more serious consequences from being infected, or both [21–23].

The list of vaccinations which may be important to administer to adults is a long one, with influenza, pneumococcal and Herpes zoster vaccines being particularly a priority for the elderly and risk groups of any age [24–26], tetanus-diphtheria-pertussis (Tdap) for all adults, measles-mumps-rubella (MMR) and varicella for susceptible adults who never experienced the diseases and were not immunized, HPV for adolescents and young adults, hepatitis A and B for travellers and certain risk groups [27], meningococcus for adolescents, some professional groups or for particular epidemiological reasons [28,29], tick borne encephalitis, yellow fever, leptospirosis and rabies for leisure or professional exposures in specific geographical areas [30,31].

Of course, there may be other vaccines useful for adults in specific situations. What is important in order to decide on possible vaccines to offer to adults, is to analyze some crucial elements like health factors (presence of chronic diseases or immunodeficiency, pregnancy, history of sexually transmitted infections, etc.); age (≥65 years for influenza, pneumococcus and Herpes zoster in many countries, but with a trend to decrease the age of recommendations to ≥50 years due to the accruing evidence of their relevance since that age; females at fertile age need to be offered vaccines to prevent infections during pregnancies); lifestyle (place of birth and international travels, history of intravenous drugs use); occupation (healthcare workers with exposure to blood, secretions and other body fluids; life in closed communities like colleges and military camps; teachers) [32,33].

3. The importance of ageing and of an ageing society

In several high-income countries, the proportion of elderly people (>65 years) has surpassed that of children (0–14 years) since a long time. The same is increasingly happening in highly populated countries transitioning towards economic growth and better living conditions. Such scenario casts serious doubts on the sustainability of health systems, especially those based on tax payment by working individuals. In this context, vaccination of adults and the elderly people can importantly contribute to decrease healthcare expenditure directly by preventing diseases and expensive complications, but also indirectly by avoiding days of work lost due to the preventable diseases.

The favourable economic impact of immunization is coupled with a positive effect on well being. A longer life represents an important opportunity and provides the chance to carry on new activities, while continuing to make valuable collaborations inside family and community [34]. Nevertheless, the dimensions of these opportunities strictly depends on one essential factor: health. Among the 60-and-over population, non-communicable diseases already account for more than 87% of the burden in low-, middle-, and high-income countries. On the other hand, the continuing health threats from communicable diseases for older people cannot be neglected. During the last century, childhood immunization strategies have eliminated some of these health threats, and outbreaks have been experienced by fewer people. Indeed, paediatric vaccinations have contributed to reduce morbidity and mortality rates. A Swedish study analysing historical mortality data concluded that reduced early exposure to infectious diseases was related to increases in life expectancy and mortality reduction. Some Authors proposed that the reduction in lifetime exposure to infectious diseases and other sources of inflammation, has also made an important contribution to the historical decline in old-age mortality [35]. Avoiding infectious diseases at adult and elderly age means the possibility to preserve a good physical activity even in the late decades of life [36].

And it helps to avoid serious complications, which become progressively very frequent after age 50 years. As a matter of fact, the proportion of US population with 1, 2 or 3 chronic conditions is particularly high in subjects ≥65 years (86%), but is already 73% at age 45–64 years [37] (Table 1). Similar proportions can be envisaged for the European population, meaning that immunization is projected to play a key role in the possibility to achieve better health even at late age.

Moreover, older people, already suffering from one or more underlying chronic medical conditions, are particularly vulnerable to infectious diseases for a variety of reasons such as age-related "immunosenescence" (the progressive reduction of immune function with age) and unwillingness to take booster injections against diseases (such as diphtheria, tetanus or pertussis). There is an evidence that incidence and severity of many infections increases with age (influenza or pneumococcal diseases; at the same time,

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Table 1
Estimated percentage and number of US adult aged ≥18 years with chronic conditions by select characteristics, national health interview survey, 2012. From [37], adapted.

Characteristic	0 Chronic Conditions		1 Chronic Condition		2 Chronic Conditions		≥3 Chronic Conditions	
	% (95% CI)	Population	% (95% CI)	Population[a]	% (95% CI)	Population[a]	% (95% CI)	Population[a]
Total	50.2 (49.5–51.0)	118,000	24.3 (23.7–24.9)	57,154	13.8 (13.3–14.2)	32,350	11.7 (11.2–12.1)	27,416
Sex								
Male	52.2 (51.2–53.4)	59,078	24.1 (23.2–25.0)	27,248	13.0 (12.4–13.7)	14,685	10.7 (10.1–11.3)	12,060
Female	48.4 (47.4–49.3)	58,922	24.5 (23.8–25.3)	29,906	14.5 (13.9–15.1)	17,666	12.6 (12.0–13.2)	15,356

[a] Population: Number × 1000.

the ability of many vaccines to induce an immunogenic and effective response is lower in elderly people, making protection of this weak population a challenge [38–48].

A recent systematic review and meta-analysis has shown a substantial indirect protective effect of childhood pneumococcal conjugate vaccination on invasive pneumococcal disease (IPD) across the whole population within a decade from the beginning of the vaccination programme [49]. But, while a strong herd effect was demonstrated for PCV7, a possible herd effect due to PCV13 is still object of debate and international recommendations suggest the need to protect directly the elderly [50,51].

Based on the results of the CAPITA (Community-Acquired Pneumonia Immunization Trial in Adults) trial performed in the Netherlands, the Advisory Committee on Immunization Practices recommended that all adults 65 and older receive the pneumococcal conjugate vaccine and many countries have already implemented an age-based offer. The CAPITA trial demonstrated a 46% reduction in community-acquired pneumonia and a 75% reduction in vaccine-type invasive]pneumococcal disease [52]. Moreover, a post hoc analysis from the CAPITA trial showed that among immunocompetent elderly over 65 years, vaccine efficacy (VE) of PCV13 was modified by the presence of diabetes mellitus at the moment of vaccination, with a higher VE for subjects with diabetes than those without [53].

Therefore, it is clear we need to vaccinate adults and the elderly, the most difficult question is 'how can we reach high coverage with the most important vaccines?'

4. Strategic issues in the implementation of adult immunization

Vaccination policies for adults are not consistent across Europe, including the meaning of "recommended vaccine" which is not comparable among countries [54].

According to an international survey performed between 2010 and 2011 in 33 countries with advanced economies (as defined by the International Monetary Fund), a correlation between having a comprehensive adult immunization schedule (one-third of the countries) and recommending more vaccines for adults was found. Seasonal influenza, tetanus, pneumococcal polysaccharide, and hepatitis B were the most frequently recommended vaccines, while newer vaccines are less likely to be recommended for adults than older ones [55].

In order to make adult vaccination programmes as effective and successful as childhood programmes, health authorities of each country should strive to include standard recommendations, stable funding and routine vaccine coverage assessment also for their adult populations [56].

An important consideration regarding adult immunization programmes is that the approach is not usually universal, but rather based on selected target groups identified by age, pre-existing chronic diseases, immune deficiency, or conditions like pregnancy, life in institutions, professional activity (for instance, work in healthcare settings) or travels abroad. In particular, vaccinations during pregnancy are recommended not only to prevent diseases in women, but also to prevent infection in the newborns. As a matter of fact, there is an increased risk of malformations associated with influenza virus infection in the pregnant woman during the first trimester of pregnancy [57–60]. Flu vaccination in pregnancy is safe and without consequences for the fetus in terms of abortion, preterm delivery and small for gestational age [61,62]. Moreover, flu vaccination during pregnancy is protective towards fetus, as demonstrated in a recent meta-analysis: women in the influenza vaccine group had a lower likelihood of stillbirth (RR, 0.73; 95% CI, 0.55–0.96), even in case of H1N1pdm09 vaccine administration (RR, 0.69; 95% CI, 0.53–0.90), while the pooled estimate for spontaneous abortion was not significant (RR, 0.91; 95% CI, 0.68–1.22) [63]. Receipt of influenza vaccine during pregnancy is associated with a decreased risk of preterm birth (OR: 0.87; 95% CI: 0.77, 0.98) and low birth weight (OR: 0.74; 95% CI: 0.61, 0.88) [64]. Maternal influenza immunization is a strategy with substantial benefits for both mothers and infants. Inactivated influenza vaccine is effective in reducing influenza illness by 63% in infants up to 6 months of age and averted approximately a third of all febrile respiratory illnesses in mothers and young infants [65]. Infants born to women reporting influenza immunization during pregnancy have risk reductions of 64% for ILI, 70% for laboratory-confirmed influenza, and 81% for influenza hospitalizations in their first 6 months [66].

Pertussis is still common in a highly vaccinated infant population and is a relevant health concern in infants who are unvaccinated or incompletely immunized, both in terms of morbidity and case fatality rate. Clinical manifestation of pertussis can be severe in infants not immunized against pertussis. Paroxysmal cough was more likely reported among children with positive samples for *B. pertussis* (OR 1.96; $p < 0.05$). A statistically significant OR of 2.39 for post-cough vomiting, together with cyanosis and apnea, was found for pertussis positive infants compared with the others [67]. Between January 2000 and December 2012 in Tuscany (Italy) the majority of hospitalised children due to pertussis were infants (75.6%), who had the highest rate of complications (24.2%) of any age group and a crude mortality rate of 9.47/1000 [68]. In the last decade a shift of cases from school-age children to adolescents, adults and particularly, to children under 1 year of age has been described [69–71]. Most identified sources of pertussis infection for infants under 6 months were household contacts, of which 39% (95%CI 33–45%) were mothers, 16% (95%CI 12–21%) fathers, and 5% (95%CI 2–10%) grandparents. Siblings (16–43%) and non-household contacts (4–22%) can be heterogeneous sources, while for 32–52% of infant cases, source remains unidentified. Moreover, asymptomatic pertussis infection can be found in 8–13% of contacts [72,73]. The inability of acellular pertussis vaccines to prevent asymptomatic infection and pertussis transmission is the basis of the failure of the cocooning strategy. Immunizing only postpartum mothers with Tdap vaccine did not reduce pertussis illness in infants ≤6 months of age, and it is still difficult to immunize all household and key contacts of newborns with Tdap [74–76].

A recent systematic review concluded that antenatal combined Tdap vaccine administered during the second or third trimester of

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pregnancy is safe for the women and it is not associated with clinically significant harms for the fetus or neonate [77,78].

The Global Pertussis initiative recommends vaccination during pregnancy as the primary strategy, given its efficacy, safety, and logistic advantages over a cocoon approach. Maternal vaccination against pertussis provides adequate antibody concentration to protect infants in the first months of life [79] and it should be administered between 27 and 36 gestational week [80]. Indeed, maternal pertussis vaccination is cost-effective in the United States according to World Health Organization criteria for industrialized countries [81]. Tdap vaccination in pregnant women is safe and no adverse reactions or any concerning patterns in maternal, infant, or fetal outcomes were identified [82–88]. Maternal tetanus vaccination is effective in reducing neonatal mortality (RR 0.68, 95% CI 0.56–0.82 [89–90].

Finally, respiratory syncytial virus (RSV) is an important cause of severe and fatal respiratory disease in infants, studies on RSV vaccination in pregnancy are in progress. The availability of effective vaccines for maternal immunization in the future could substantially impact the morbidity and mortality of RSV-associated illness in infants worldwide [91]. Currently, vaccine formulations produced have an acceptable safety profile in adults and adjuvanted formulations provided additional immunogenicity benefit as compared to increasing antigen dose alone [92].

Whenever possible, lowering the age of recommendation for a vaccination in case a substantial proportion of those above the threshold age are at risk, is the best way to increase coverage in those most in need to be protected [93].

As a matter of fact, we have ample demonstrations that strategies of immunization aimed at picking every individual at risk based on knowledge of the specific risk condition often fail. In Europe, only few countries reached influenza vaccination coverage objective recommended for the elderly, while for high risk groups, such as subjects with chronic illness or health care workers, immunization coverage is certainly lower and it was decreasing over time in many countries. Recent CDC data (2013–2014 season) suggest that the proportion of US adults who were immunized against influenza was 45.3% and 65.0 % for those aged 50–64 and 65 and older, respectively [94]. In 2009, vaccine coverage for influenza varied by country ranging from 32.9% in Hungary to 71.7% in the Netherlands for clinical risk groups and from 13.4% in the UK to 89.4% in Romania for HCWs. Moreover, many countries that recommend the influenza vaccination do not monitor the coverage in risk groups [95,96].

Some explanations are: difficulty in properly identifying risk subjects for whom vaccination is indicated, regardless of age, resulting in unsatisfactory vaccination coverage and a persistent susceptible population. For many years up to now, numerous independent and international health organizations have officially encouraged flu vaccination. In 2003, the World Health Assembly adopted a resolution to increase influenza vaccination coverage of all people at high risk [97]. The WHO has recommended a 75% vaccination coverage rate for the elderly by 2010–2011. In 2009, the Council of The European Union encouraged Member States to adopt and implement national, regional or local policies to improve seasonal influenza vaccination coverage in order to reach the vaccination coverage objective of 75% for the 'older age groups' and, if possible, for other high-risk groups [98].

Member States are also encouraged to improve general vaccination coverage, particularly among healthcare workers. In February 2010 the CDC Advisory Committee on Immunization Practices (ACIP) recommended universal annual influenza vaccination. Universal vaccination means the inclusion of all people aged 6 months and over. This new recommendation seeks to remove barriers to influenza immunization and signals the importance of preventing influenza across the entire population [99].

On the other hand, offering immunization to all those above a certain age guarantees higher possibility to cover those at risk [100].

Moreover, pneumococcal routine vaccination, with PPV23, of all populations aged ≥65 years in order to prevent invasive pneumococcal disease (IPD) was estimated to be the best strategy, with

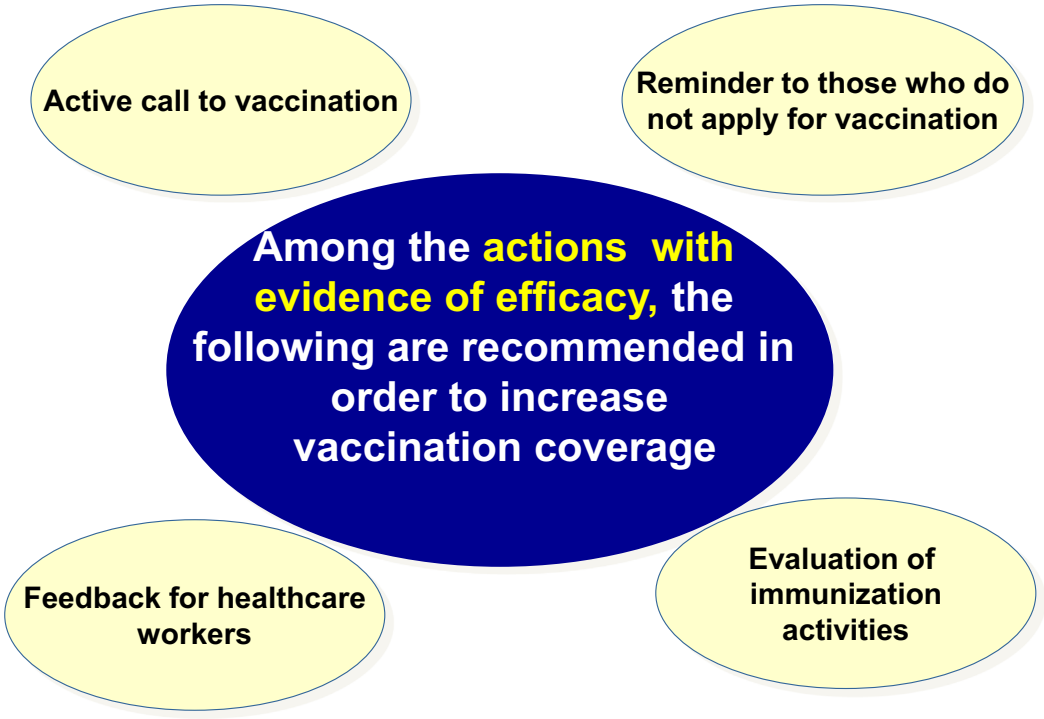

Fig. 1. Actions with evidence of efficacy to increase vaccination coverage. , Source:[102] adapted.

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lower cost per life year gained compared to vaccinating high-risk groups only [101].

However, other strategies are possible and should be jointly implemented, like vaccination of hospitalized patients with at risk or high-risk conditions at discharge, through an integration between hospital and territorial health services; vaccination of those living in residences for the elderly; direct involvement of General Practitioners (GPs) in the selection of candidates and in the administration of vaccines; use of 'opportunistic situations', for example offering lacking immunizations when performing periodical screening tests or visits for the renovation of a driving license, etc.; active involvement of specialists in ambulatories and wards.

Among the actions that have evidence of effectiveness in implementing vaccinations uptake, we can include active call to vaccination, reminders to those who do not apply for vaccination, feedback for HCWs involved, and an evaluation of immunization activities (Fig. 1) [102].

A crucial practical issue to help implement adult vaccination strategies is the availability of computerized registries of 'at risk' and 'high risk' subjects, easy to consult both for public health services and for the GP who takes care of those subjects. Such registry should be linked to a vaccination register able to generate data on coverage sorted by different subjects' characteristics (age, chronic diseases, etc.).

5. Formation, information and communication issues

Adult vaccination (with the exception of influenza) is still a relatively neglected practice, even for HCWs. Therefore, efforts are needed to organize formative courses for public health doctors, GPs, paediatricians and nurses. But also for specialists interested in the prevention, diagnosis and treatment of acute and chronic diseases of infectious origin (i.e. infectious diseases specialists and hepatologists for HBV, gynecologists for HPV, etc.) and for specialists of other chronic diseases (cardiologists, pulmonologists, diabetologists, nephrologists, haematologists, etc.) where vaccination is a key intervention to preserve patients' health. In addition, specific intervention in hospital setting and perioperative medicine, targeting surgeons, anesthesiologists and other specialists should be encouraged in order to increase their awareness on the risk of Overwhelming Post-splenectomy Infection (OPSI), especially due to encapsulated bacteria (mainly pneumococcal, meningococcal, and Haemophilus influenzae type b) in asplenic and hyposplenic patients. Moreover, public health services should be involved in the managing of the appropriate vaccines administrations and booster doses scheduling, according to the international recommendations [103,104]. Skills are also needed for all those involved in the promotion and administration of vaccines to properly communicate the (un)balance between the risk of diseases *vs* the risk of vaccinations.

Unfortunately, while increasing immunization coverage is a slow and hard to reach objective, dramatic drops of uptake frequently occur when communication crises occur, like the one we experienced in Italy in late November 2014. At that time, 3 sudden deaths within 48 h of a specific influenza vaccine administration were notified from two different Regions, which led to the precautionary suspension of the vaccine lot from the Italian drug regulatory agency (AIFA). The deaths were clearly not due to vaccine [105], also because the death reports were well below the expected number of deaths statistically occurring in the population of elderly immunized subjects, and the role of vaccination after looking at the causes of death was highly implausible [106]. Such event, largely covered by media with a frightening approach, caused a dramatic drop of coverage, which reached a record low of 49% at the national level for subjects aged $\geq$64 years. No doubt that the crisis should have been dealt with a different approach, as it was recently pointed out [107]. The end result is that Italian health authorities are now struggling to recover trust in influenza vaccination, but coverage increased by about only 3% in the last 3 years. Moreover, the European Monitoring of Excess Mortality for Public Health Action (EuroMOMO), in the bulletin at the end of March 2017, described, in most European countries, a marked excess of mortality for all causes in early 2017, coinciding with the epidemic peak of influenza. In the last season 2016/2017 the predominant (78%) influenza virus was A (H3N2), particularly virulent and usually associated with an excess of mortality among the elderly. Indeed, Italy was one of the countries in which severe outcomes and higher mortality rates were observed, resulting in pressure on the health care system [108,109].

The widespread attitude towards vaccinations called "vaccine hesitancy" is another important obstacle to achievement of vaccine coverage objectives and must be dealt with appropriate communication strategies towards general population and HCWs, too [110–113].

Skepticism about vaccinations is a phenomenon that exists since the availability of the first vaccines, but nowadays it is certainly supported and amplified by the ease with which anyone can have access to conflicting information or fake news on the internet, classic media and social networks. Such feeling results in a delay in acceptance or refusal of vaccines despite availability of vaccination services, and can explain failures to reach high vaccination coverage. Recognizing the relevance of this phenomenon to the attainment of established health objectives, in 2012 the World Health Organization (WHO) Strategic Advisory Group of Experts (SAGE) on Immunization created a specific working group on the topic, guided by a joint secretariat of the WHO/UNICEF in order to suggest tailored evidence-based strategies to address the causes, to respond promptly to anti-vaccination movements in case of misinformation or potential adverse events and to determine the impact of educational interventions and whether vaccine acceptance has improved [114,115].

Investigation into vaccine safety and pharmacovigilance are essential actions to increase public confidence in vaccinations, but it is likewise essential that journalists publish news on lack of evidence between an adverse event and vaccination with the same emphasis in which alarming news or fake news on supposed vaccines damages are reported [116].

Another major communicative hurdle to vaccination is the often shameful vaccination coverage in HCWs, which is a common problem to many countries. Doctors and nurses need to be an example of coherence, because the strongest testimony on the importance of immunization for the patient is being reassured that the healthcare provider is also vaccinated. Data from 10 European countries collected for the influenza seasons 2008/09 to 2010/11 found an official range of coverage between 12% and 98%. However, in most countries coverage ranged between 14% and 28%, and in virtually all (the only exception being Romania) it was not higher than 50% [117]. These data open a number of questions on the ethical duty of HCWs not to put into danger patients' health and life as a consequence of failure to follow the recommendation to be immunized yearly.

However, other vaccinations are often culpably neglected by HCWs, like MMR. Measles has become a frequent nosocomial infection, due to the epidemiological shift of the disease towards adulthood, and to the high number of susceptibles among HCWs [118,119]. Therefore, a strong educative effort towards HCWs on the benefits and risks of immunization is needed in all countries. Some national initiatives in Italy have been set up during the last years, aimed at increasing awareness on vaccine preventable infectious diseases (VPID) and trust in vaccinations in different target populations such as students and teachers of primary and sec-

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ondary schools, HCWs by means of distance learning course on vaccinations, parents refusing vaccinations for their newborns through home visits, and a national call center was launched to create a direct line from the general population to experts in vaccines and vaccination strategies [120].

6. Management of adult vaccination programmes

Getting a higher level of awareness on the importance of adult vaccination, and a high coverage for recommended immunization is not a single actor's possible achievement. All involved stakeholders need to develop partnerships, create synergies, adopt common formative programmes and agree protocols of intervention. Public health medical services should guarantee the governance of the network, by: organizing vaccination programmes; supplying vaccines to primary care services and to GPs; organizing Continuous Medical Education courses on vaccination; collecting data on coverage and assuring the information feedback to vaccinators and GPs; helping to make policy through recommendations or regulations. In case an incentivating system for HCWs is in place, it should foresee progressively escalating rewards only if the target coverage is reached.

Italy has developed an example of strong collaboration and commitment of different scientific and professional societies involved in planning, counselling and administering vaccines throughout all life, the so-called 'Lifetime Vaccination Calendar' ('*Calendario Vaccinale per la Vita*'). The Lifetime Vaccination Calendar was meant to coagulate the scientific world and healthcare practitioners (public health, paediatricians, GPs) to propose 'the best possible immunization schedule' updated regularly, following the most recent discoveries and scientific evidences. There was no intent to substitute public health decision makers, rather giving a strong support initiative for Regional Health Authorities, to possibly integrate the vaccination offer guaranteed as Essential Level of Assistance by the National Vaccination Plan [121].

But also to supply an important guide to doctors and nurses on what to inform about and to propose in the interest of population health from an individual point of view [122,123].

However, this alliance had an unexpected crucial influence on the National Triennial Vaccination Plan recently adopted by the Italian Ministry of Health [121], which can be presently regarded as the National Vaccination Calendar with the widest free-of-charge offer of vaccinations in the world.

7. Conclusions

Adult immunization is a priority for public health, particularly in countries where an ageing population has become increasingly more numerous. Protection against diseases which typically affect adults (like flu, pneumococcal diseases and Herpes zoster), the shift of age of infections which originally affected children (like measles), the decreasing protection with time for infections which need periodical booster doses of vaccines (Tdap), the availability of vaccines which can also impact on adult health (HPV) are only some examples of the importance of implementing targeted vaccination strategies.

The possibility to reach high coverage with immunizations that can guarantee a fundamental improvement of health for adults and the elderly can only be achieved through a coordinated effort where all stakeholders, under the coordination of public health, contribute to issue recommendations; create a functioning database for vaccine coverage registration; promote formative courses for healthcare workers and continuous information for the public; increase vaccines uptake among healthcare workers, who need to give the first testimony on the relevance of immunization.

Conflict of interest

Authors declare no conflicts of interest.

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