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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.

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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

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E-mail addresses: paolo.bonanni@unifi.it (P. Bonanni), guglielmo.bonaccorsi@ unifi.it (G. Bonaccorsi), chiara.lorini@unifi.it (C. Lorini), francesca.santomauro@ unifi.it (F. Santomauro), emilia.tiscione@unifi.it (E. Tiscione), sara.boccalini@unifi.it (S. Boccalini), angela.bechini@unifi.it (A. Bechini). 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 multicountry analysis among 10 EU countries analysed the cost-effectiveness of pneumococcal vaccination, with PPV23 (polysac-charide 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 \notin 1 invested in adult vaccination, starting at the age of 50 years, would yield \notin 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 <u>health factors</u> (presence of chronic diseases or immunodeficiency, pregnancy, history of sexually transmitted infections, etc.); <u>age</u> (\geq 65 years for influenza, pneumococcus and Herpes zoster in many countries, but with a trend to decrease the age of recommendations to \geq 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); <u>lifestyle</u> (place of birth and international travels, history of intravenous drugs use); <u>occupation</u> (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 oldage 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 \geq 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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