



Vaccination in Older Adults: An Underutilized Opportunity to Promote Healthy Aging in India

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Abstract

Over the last 50 years, the Indian population aged 50 years and above (older adults) has quadrupled and is expected to comprise 404 million people in 2036, representing 27% of the country's projected population. Consequently, the contribution of chronic disease to older adults' total burden of diseases in India is likely to escalate. Disease burden is notably amplified by immunosenescence, a deterioration of the immune system that develops with age, leading to increasing susceptibility to infectious diseases and other comorbidities. Older adults with infectious diseases have a higher incidence and likelihood of life-threatening comorbidities such as coronary artery disease, arrhythmia, stroke, myocardial infarction, hypertension, dyslipidemia, and diabetes mellitus. Therefore, immunization of older adults through vaccination might greatly reduce the burden imposed by vaccine preventable infectious diseases in this population. Here, we review evidence relevant to the disease burden among adults aged ≥ 50 years in India, and existing vaccination recommendations. Furthermore, we suggest a set of routine vaccinations for healthy older adults in India. There is a clear mandate to recognize the contributions of older adults to society and embrace strategies promoting healthy aging, which is described by the World Health Organization as the process of developing and maintaining functional ability and well-being in older age. Increasing vaccination awareness and coverage among older adults is an important step in that direction for India.

Key Points

Over the last 50 years, the population of India aged ≥ 50 years (older adults) has quadrupled and is expected to increase further.

People aged ≥ 50 years are prone to infectious diseases due to immunosenescence and other declining physiological functions.

Increasing vaccination awareness and coverage among older adults in India is an important step towards healthy aging.

1 Introduction

Projections show that India will soon surpass China as the most populous country in the world [1]. In parallel to India's rapid socioeconomic development in these last decades, life expectancy at birth has substantially improved to 70.3 years for women and 66.9 years for men in 2016; the corresponding figures in 1990 were 59.7 and 58.3 years [2]. Over the last 50 years, therefore, the Indian population aged ≥ 50 years has quadrupled [1], exceeding 260 million persons in 2020 [1], and is expected to increase more in the near future [1, 3]. As a consequence, the contribution of non-communicable diseases such as cardiovascular disease (CVD), chronic respiratory diseases, and diabetes mellitus to the total disease burden increased from 30% in 1990 to 55% in 2016 [2]. Similarly, the susceptibility to infectious diseases along with other comorbidities also increases with increasing age [4]. The globalization of economies and the high frequency of international travel has also greatly increased the probability of exposure to infectious agents, both within and between countries [5] as dramatically exemplified by the rapid worldwide spread of the coronavirus disease 2019 (COVID-19).

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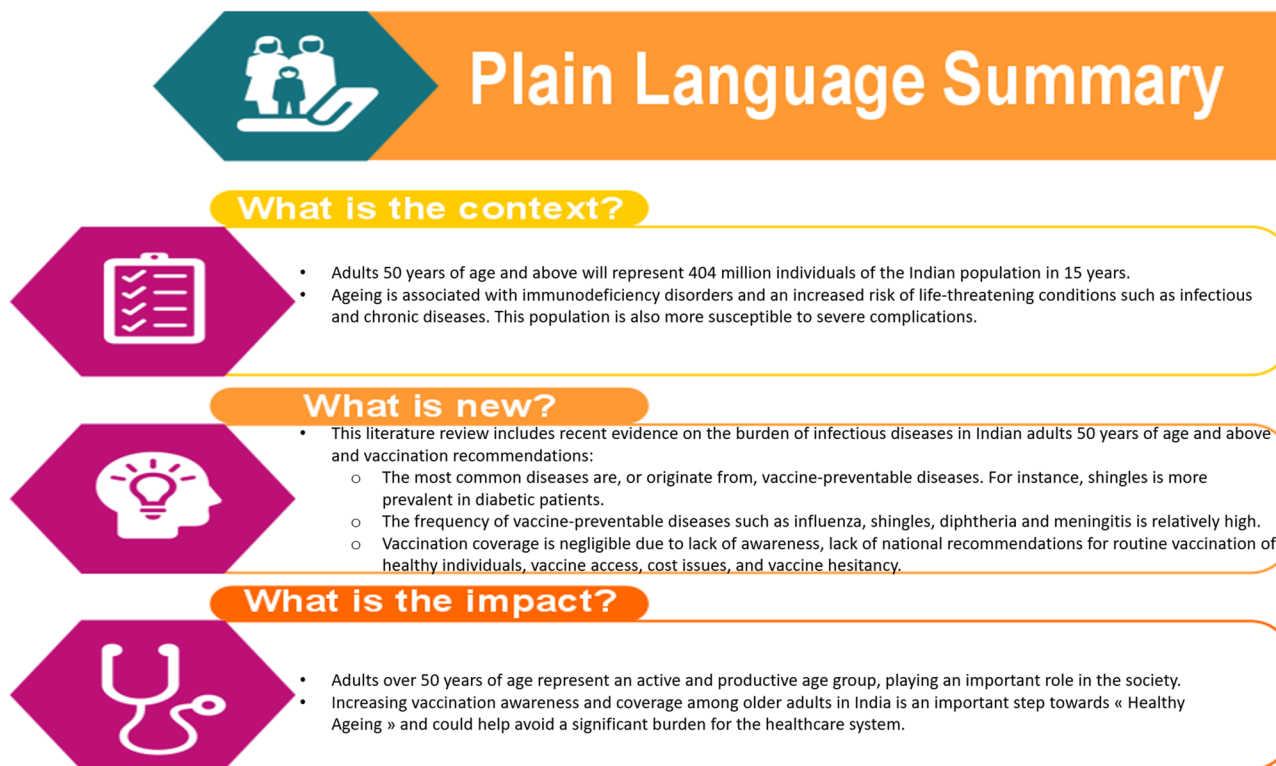


Fig. 1 Plain language summary

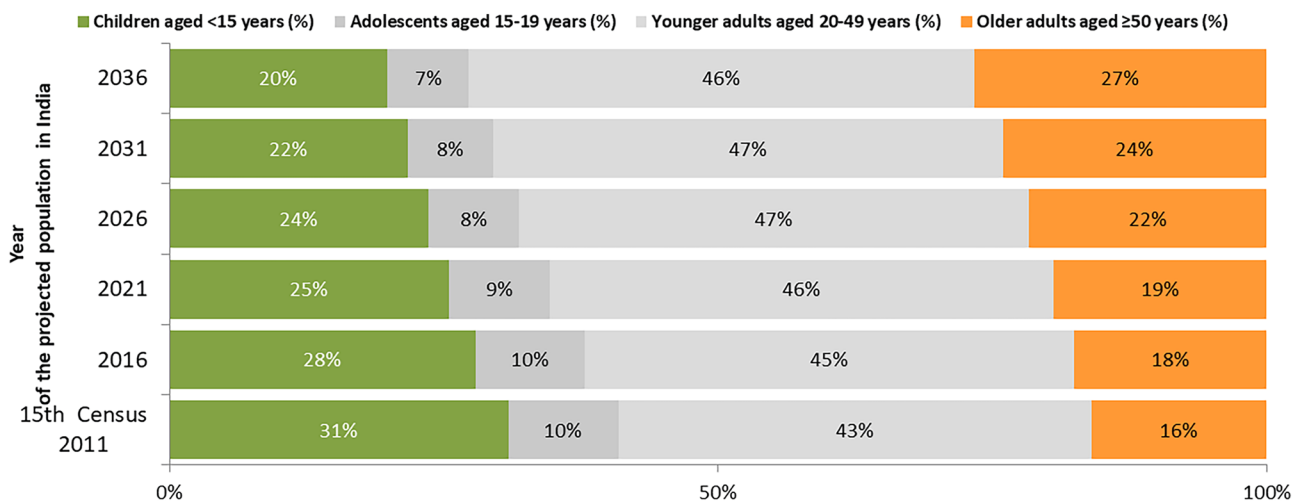
The demographic and socioeconomic changes demand adaptation of health strategies and policies to promote health through increasing access to vaccination of older adults. Immunization beyond infancy is a global priority for the World Health Organization (WHO) [4]. Several industrialized countries have developed immunization plans for older adults to increase suboptimal vaccination coverage but such plans, even when fully implemented, need time to produce optimal results. Nevertheless, such precautionary policies have been largely neglected in low-income and middle-income countries [4]. This situation has been highlighted by the WHO and the organization is calling for countries across the world to implement urgently needed ‘Healthy Aging’ strategies and to “align health systems to the needs of the older populations” [6]. In India, national immunization programs focus solely on pediatric immunization, neglecting preventive immunization for older adults [7]. The available adult immunization recommendations are limited in their applicability and focus on the older adult, while others focus on special populations with specific morbidities [7, 8].

In this review, we therefore discuss the importance of immunization in older adults, and the relevance of vaccination towards healthy aging in India. However, no single definition or standard numerical criterion for the term ‘old’ exists [4, 9]. In developed countries, becoming eligible for

an occupational retirement pension is often used as the informal cut-off for “old age”, while a shorter life expectancy lowers the threshold for being “old” in Africa [9]. The 2007 WHO meeting on immunization in older adults defined older adults as “people in the second half of life, i.e. over half of the life expectancy” for their respective country [4]. In this review, we follow a more conservative definition for older age, in agreement with the International Council on Adult Immunization definition of older adults [10], and thus focus on the population aged ≥ 50 years. The incidence of comorbidities is higher in this age group, and therefore this is the population in greater need of preventive healthcare [10, 11]. We also summarize existing adult immunization policies and discuss the older population’s susceptibility to infectious diseases. Furthermore, we summarize existing barriers, challenges, opportunities, and benefits of older adult vaccination. Figure 1 elaborates on the findings in a form that could be shared with patients by healthcare individuals.

2 Vaccination Coverage in India

In India, the Ministry of Health and Family Welfare conducts approximately nine million sessions of vaccinations every year, targeting one of the largest populations in the



Percentage (%) distribution of age-groups within the total population of India

Fig. 2 Projections of population distribution by age group in India based on the 2011 Census data; years 2011, 2016, 2021, 2026, 2031, and 2036. Created from: Census of India 2011. Population projections for India and States 2011–36. Report of the Technical Group

on Population Projections, November 2019. National Commission on Population. Ministry of Health and Family Welfare, Government of India [3]

world consisting of 27 million newborns, 100 million children aged 1–5 years, and 30 million pregnant women [12]. In 2019, after having implemented for the past 10 years a series of interventions such as strengthening surveillance and cold chain systems and improving communication strategies [7], high coverage rates were achieved in children by age 35 months: 92% for Bacillus Calmette-Guerin, 91% for three doses of diphtheria, tetanus, and pertussis vaccine, 90% for three doses of polio vaccine, and 95% for the first dose of the measles vaccine [13].

Very little data are available for older adult immunizations, and vaccine uptake. Adult vaccination coverage even among at-risk populations, such as healthcare workers, appears negligible [7, 8]. Lahariya and Bhardwaj report that in an adult vaccination center in Jodhpur, pre-exposure vaccination coverage was 8% for hepatitis B, 7% for pneumococcal, 3% for typhoid, and 1% for influenza [7]. Four percent of adults had received one or some of the following vaccinations: meningococcal, hepatitis A, varicella-zoster, and polio [7]. Vaccination coverage post-exposure was 42% for tetanus toxoid vaccines, and 20% for rabies vaccination [7].

3 Older Population and Burden of Disease in India

According to the 2019 findings of the Ministry of Health and Family Welfare Technical Group on Population Projections, the older population, aged ≥ 50 years, is expected to

double from 193 million in 2011 to 404 million in 2036 [3]. Consequently, the age group of older adults aged ≥ 50 years will account for 27% of the total population in India by 2036, while the proportion of the total population of the age group < 15 years will decrease from 31% in 2011 to 20% in 2036 (Fig. 2) [3].

The 2017 Report on Medical Certification of Cause of Death of the Ministry of Home Affairs mentions that, among older adults aged > 45 years, CVD was the leading cause of death, with a range from 35.9% in the 45–54 years of age group to 44.5% in ≥ 70 years [14]. The Global Burden of Disease Study 1990–2016 reported that 28.1% of total deaths in India were caused by CVD, primarily ischemic diseases (17.8% of total deaths), followed by stroke (7.1%), hypertension (1.3%), and rheumatic heart disease (1.1%) [15]. Based on the Global Burden of Disease Study estimates, CVD, diabetes, and chronic respiratory diseases have been increasing. The prevalence of CVD reached 54.5 million in 2016 from 25.7 million in 1990 [15]. Diabetes estimates for 2016 were 65 million, a two-fold increase from the 26.0 million in 1990 [16]. The prevalence of overweight among adults also substantially increased across all states, from 9.0% in 1990 to 20.4% in 2016 [16]. These increases in the prevalence of chronic diseases will most likely lead to increased infectious diseases burden as well, given that chronic diseases are associated with an increased risk for infectious diseases [17–20]. Among patients with chronic obstructive pulmonary disease, diabetes, asthma, chronic kidney disease, or inflammatory bowel disease, older adults aged ≥ 50 years

are at least two times more likely to experience herpes zoster (HZ) [21].

Furthermore, older populations are vulnerable to vaccine-preventable diseases (VPDs) such as influenza, pneumococcal, HZ, and tetanus [22]. The 2004 Global Burden of Disease Project estimated that infectious diseases in India accounted for approximately 30% of the total disease burden [23].

It is also shown that vaccination protects older adults with chronic conditions from developing complications and significantly reduces the frequency of hospitalizations [24], intensive care and cardiac care unit admissions, and mortality [25]. Moreover, worldwide evidence clearly demonstrates that older adult patients with VPDs are at an increased risk of experiencing life-threatening chronic comorbid diseases compared with their peers without VPDs [26]. Coronary artery disease, arrhythmias, hypertension, dyslipidemia, diabetes, myocardial infarction, anxiety, depression, stroke, and transient ischemic attack are more frequent among older adults aged ≥ 50 years with a history of HZ compared with their peers without a history of HZ [27, 28]. Large studies conducted in the USA have shown an association between HZ and the risk of stroke [27, 29]. Asthma is more frequent among patients with HZ than among non-HZ patients [30]. Following HZ, older adults aged ≥ 50 years have a 38% [29] to 53% increased likelihood of experiencing a stroke [27], and a 60% increased likelihood for a transient ischemic attack compared with peers without a history of HZ [29]. Neurologic complications occur in 25–70% patients with infectious endocarditis [31]. Most of these are cerebrovascular in nature, mostly corresponding to ischemic (70%) or hemorrhagic (15%) strokes [31]. Bacterial meningitis and tuberculous meningitis may also lead to stroke in 17–43% and 26% of cases, respectively [31].

3.1 Vaccine-Preventable Diseases in India

Based on the limited data available to the WHO in 2017, a significant proportion of the world's cases of some VPDs occurred in India: 60% of diphtheria cases, 40% of tetanus cases, 17% of pertussis cases, and 17% of rubella cases [8]. Although it is reasonable for the second most populous country in the world to have a high proportion of global cases, the fact that the prevalence of certain VPDs were 2.2–3.4 times higher than the global prevalence gives cause for concern [8]. In the absence of real-time infectious disease reporting [23], there are no adequate data on the overall disease burden due to VPDs in the Indian population. Therefore, the actual VPD disease burden is expected to be higher than reported because of poor surveillance networks, under-diagnosis, and under-reporting [23].

Although epidemiological data stratified by age are not available, there are several reports on VPD outbreaks in recent years (varicella, diphtheria, hepatitis A, influenza, measles) showing that adults were the most frequently affected age group [8]. All other available epidemiological data on VPDs in India refer only to the whole population. It can be assumed, however, that much of the burden of some VPDs is in adults: data available for human papillomavirus disease estimate that every year there are about 97,000 new cases, and 60,000 deaths in human papillomavirus-related cancer [32]. Likewise, regarding HZ, hospital data published within the last 5 years suggest that a substantial proportion of the total population of patients with HZ could be aged ≥ 40 years [33–37].

An analysis of influenza surveillance data from 2010 to 2013 showed that 58.6% of influenza-related respiratory deaths and 52.9% of influenza-related circulatory deaths were among adults aged ≥ 65 years [38]. Influenza vaccination has a low priority in India, and as such is labeled by the Ministry of Health and Family Welfare as 'desirable' for those aged ≥ 65 years [38]. Older adults are also at an increased risk for pneumococcal disease, including meningitis, pneumonia, and sepsis [39, 40].

4 Healthy Aging

Aging is the lifelong process of progressive functional and structural changes in the physical, mental, and social status of individuals [41]. With increasing chronological age, the body organs change at different rates [42]. Neuronal [42, 43] and musculoskeletal [43] system deteriorations influence an individual's strength and mobility and induce frailty. Multiple organ systems such as the lungs, the gastrointestinal system, and the cardiovascular system are undergoing structural and functional modifications through aging [42]. The deteriorations induced are not linear and have differential impacts on the intrinsic capacities of individuals, i.e., the combination of mental and physical capacities [6]. Frailty as a combination of decreased physical activity, energy, muscle weakness, unintentional weight loss, and exhaustion might develop at later life stages [43]. Some older adults might become clinically frail while others might not share such an experience [43]. These trajectories are also influenced by lifestyle conditions, the social and political environment, and their interactions [6].

As the global population increases both in size and in age, it is important for societies to understand the challenges and opportunities of this epidemiological trend and embrace healthy aging, defined by the WHO as the process of developing and maintaining the functional ability that enables well-being in older age [6, 44]. Furthermore, with increasing life expectancy, more family generations are alive at the

same time, family members may be more widely distributed as younger generations might migrate for work, and the trend is that an increasing number of older people live alone instead of together with children, which used to be the norm [44]. Consequently, these people need to feel confident that they have a healthcare sector at their disposal that provides all the necessary provisions to help them attain and maintain good health [44].

Unfortunately, according to the WHO, older adults around the world have poorer health trajectories than anticipated [6]. Specifically for India, in the WHO Strategic Advisory Group of Experts 2013 Survey on Global Ageing, the percentage of participants reporting self-rated good health ranged from 12% among those aged > 80 years to 37% among those aged 50–59 years; only 31% of the overall population of older adults aged ≥ 50 years rated their health as ‘good’ [45].

Most health problems in older adults have their origin in preventable conditions, or conditions that could have been delayed, as pointed out by the WHO [6] and described here. Providing primary healthcare to older people that would slow or reverse declines in intrinsic capacities would help them maximize their functional abilities, in accordance with the WHO Healthy Aging strategic objectives [6]

4.1 Immune System and Aging

The immune system evolves from birth throughout life [46]. With aging, innate and adaptive immune cells undergo a number of alterations that affect their function and therefore the immune system response [47, 48]. Under a life-long adaptive process, the immune system constantly remodels to ensure host survival [42]. At birth, the immune system is still immature and starts developing to become more efficient during the childhood period, in part following challenges from bacteria, viruses, parasites, and fungi [46]. At birth, the innate immune system is not fully functioning, and infants are at an increased risk of infectious diseases [46]. Furthermore, infant T cells of the adaptive immune system differ significantly from those in adulthood, as they have responded to few stimuli while in utero [46]. Gradually, the immune system matures to offer improved protection against infectious diseases; with the aid of vaccinations during childhood, the immune system is stimulated without most of the possible negative effects of natural infections [46]. At this point, it should be noted that most older adults in India aged ≥ 50 years have probably never received any childhood vaccinations, as the Expanded Programme of Immunization was first implemented in India in 1978 [8].

As we age, many biological phenomena, including gradual alterations to immune system cell levels, cause immune system remodeling and changes, some leading to immunosenescence, a deterioration in the functions of the immune system (Fig. 3) [49]. Immunosenescence has been associated

with increased susceptibility to infectious, neurodegenerative, cardiovascular, and autoimmune diseases [42]. The clinical significance of immunosenescence is illustrated by the higher burden of infectious diseases in older adults than in young individuals. For instance, in young ages, CD4⁺ T-cell responsiveness to *Bordetella pertussis* is increased especially compared with decayed older age responsiveness [50]. Current evidence from the field of influenza vaccines indicates CD8⁺ T cells function as a key target towards increasing vaccine effectiveness in older adults [51].

Gradual development of subclinical inflammation, known as ‘inflammaging’, may be at least partially contributing to frailty and increased susceptibility to chronic diseases associated with aging such as atherosclerosis, obesity, diabetes, and neurodegenerative diseases [49]. All modifications together lead to a decreased response to new infections, endogenous injuries, and a decrease in immunity to previously encountered pathogens [49, 51].

Overall, the mortality rate due to infectious diseases is estimated to be three times higher among older adults than in younger adults [46]. In a study in New Delhi, the mortality of patients with *Streptococcus pneumoniae* aged > 50 years was nearly 2.5 times higher than in patients aged < 50 years [22]. For example, *S. pneumoniae* was the most common bacterium among older adults with community-acquired acute bacterial meningitis in a study in Puducherry in India [22].

Nevertheless, an effective immune response can be generated in older adults if the immune system is appropriately activated, for instance through vaccination [52, 53]. It is therefore highly relevant to ascertain older adults’ vaccination coverage, especially among the presumably unvaccinated Indian population of older adults.

5 Recommendations for Older Adult Vaccination

Table 1 summarizes selected vaccination recommendations that involve older adults aged ≥ 50 years and further presents the respective authors’ proposal. Older adult immunization in India is barely accounted for in national vaccination recommendations beyond WHO recommendations for routine immunizations (Table 1) [54]. This is not the case, for example, in other countries in the developed world. For example, in adult vaccination recommendations from the Centers for Disease Control and Prevention in the USA, the adult vaccination program begins at 19 years of age and covers the whole life span [55]. In India, the only adult vaccinations included in the Universal Immunisation Program are tetanus and diphtheria during pregnancy and Japanese encephalitis in certain endemic areas [7, 8]. Medical societies have introduced additional vaccination guidelines. However, these

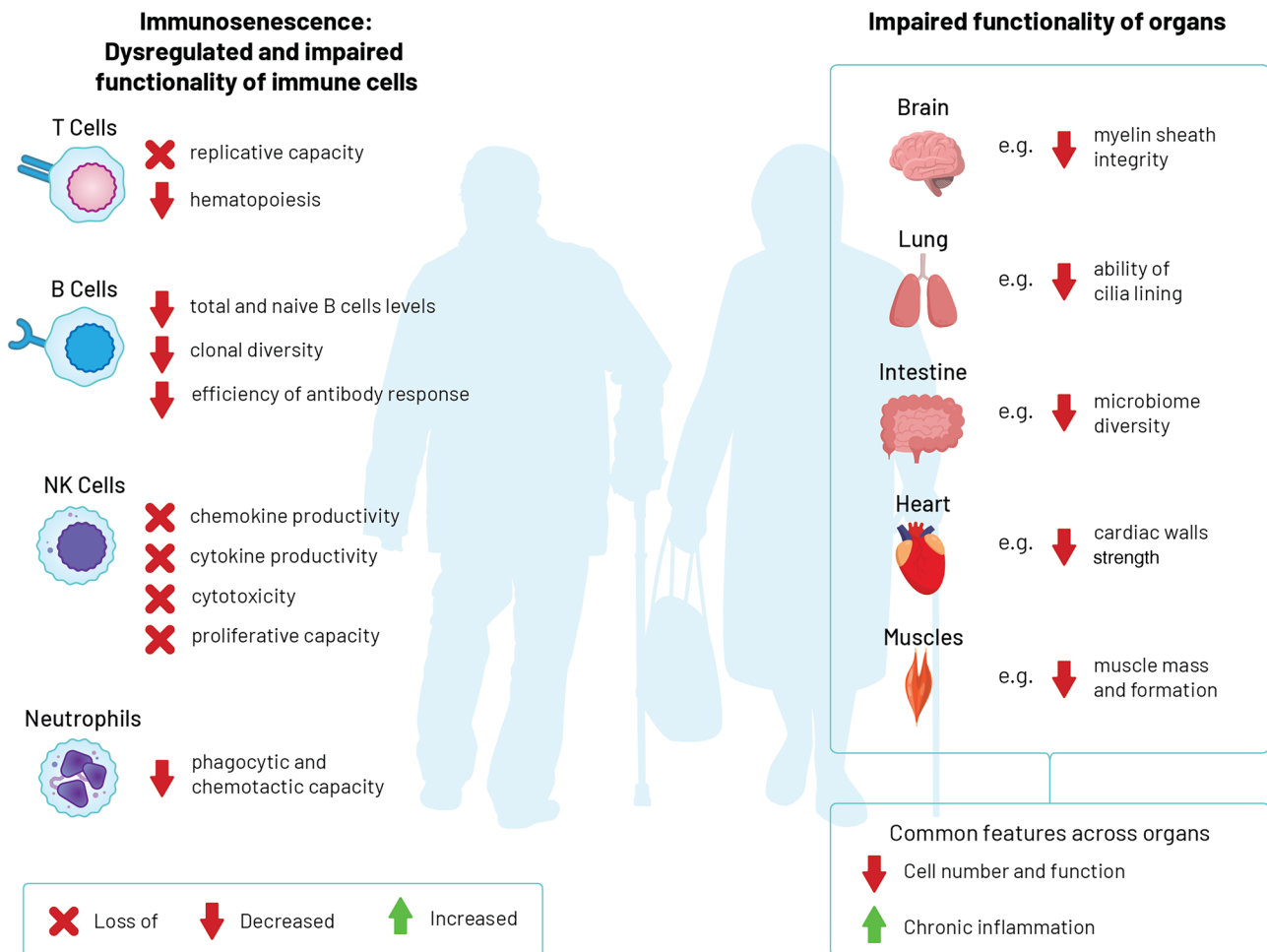


Fig. 3 Biological aging and its impact on the functionality of organs and the immune system. Created from [42]. *NK* natural killer

mainly involve at-risk adults, and discrepancies between them do not allow the dissemination of clear vaccination guidance for adults [8]. Professional association guidelines in India for adult vaccination include the pneumococcal and influenza vaccination from the Geriatric Society of India [56], the Association of Physicians of India [57–60], the Research Society for Study of Diabetes in India, the Indian Society of Nephrology, and the Indian Medical Association [61, 62].

6 Barriers and Opportunities

Some barriers to the immunization of older adults in India are systemic and therefore relevant to any type of vaccination, regardless of the age groups targeted [63–65]. Such barriers include issues of disease surveillance systems, vaccine confidence, and access to vaccines (Fig. 4). Regarding surveillance, no real-time disease reporting [23] system has been implemented for VPDs in India. Moreover, VPDs are

not included in any other formal surveillance system [23]. By surveillance, we consider both disease and vaccination coverage monitoring. Therefore, the VPD burden or vaccination coverage among older adults can only be based on data collected in studies from patients attending primary health centers representing only a small fraction of the overall patient population [23], which are inadequate to cover the whole country.

Prospective epidemiological studies could help improve our knowledge on the epidemiological profile of VPDs among older adults in India. Creating a network of collaborating institutes and hospitals across rural and urban regions of the country would improve multidisciplinary scientific collaboration and facilitate guideline harmonization (Fig. 4). A lack of simple diagnostic tools with non-sophisticated instruments or training for some VPDs [63] could also be addressed within harmonized consensus guidelines.

Other barriers notably include access to vaccines and difficulties in reaching isolated and mobile populations, and vaccine hesitancy because of misinformation [64]. Provision

Table 1 Recommendations for routine vaccinations of healthy older adults without risk factors as per age group

Disease	Age (years)	USA [55]	Europe		Indian Geriatric Society [56]	Author's proposal
			UK [71]	Germany [72, 73]		
Diphtheria, tetanus, pertussis	≥ 50–64 ≥ 65	1 Tdap + Td/Tdap booster every 10 years	– –	1 Tdap booster every 10 years (≥ 60 years)	1 Tdap + Td booster every 10 years	1 Tdap + Td/Tdap booster every 10 years
Measles, mumps, rubella ^f	≥ 50–59 ≥ 60	1–2 doses (if born in 1957 or later)	– –	– –	–	1–2 doses –
Varicella ^f	≥ 50–64 ≥ 65	2 doses	– –	– –	–	1–2 doses
Influenza	≥ 50–64 ≥ 65	1 dose annually	– 1 dose annually	1 dose annually (≥ 60 years)	1 dose annually	1 dose annually
Herpes zoster	≥ 50–64 ≥ 65	1 ^a (≥ 60 years) or 2 ^b (≥ 50 years) doses	– 1 dose (≥ 70 years)	1 ^b dose (≥ 60 years)	–	1 ^a or 2 ^b doses
Pneumococcal disease	≥ 50–64 ≥ 65	– 1 ^c dose	– 1 ^c dose	1 ^c dose (≥ 60 years)	1 dose ^{e or c} 1 dose ^{e or c}	– 1 dose ^{e or c}
Hepatitis A	≥ 50–64 ≥ 65	2 or 3 doses ^d	– –	– –	–	1 or 2 doses ^d
Hepatitis B	≥ 50–64 7 ≥ 65	2 or 3 doses ^d	– –	– –	–	2 or 3 doses ^d
Meningococcal A, C, W, Y	≥ 50–64 ≥ 65	1 dose ^d	– –	– –	–	1 dose
Meningococcal B	Recommendations to specific populations at risk and based on local recommendations					
COVID-19	1 or 2 doses depending on vaccine and local recommendations					

Td tetanus-diphtheria vaccine, *Tdap* tetanus-diphtheria-acellular pertussis vaccine

^aLive vaccine

^bInactivated vaccine

^cPolysaccharide vaccine

^dDepending on vaccine and/or local recommendations

^e13-valent conjugate vaccine

^fWithout known history of vaccination or disease

of transparent information on the effectiveness and safety of vaccines would help combat vaccine hesitancy [66]. Raising a healthcare provider's awareness also has potential to substantially improve vaccination coverage [66]. We suggest that specialized training themes be designed for healthcare providers, and vaccination campaigns be tailored to citizens aged ≥ 50 years [67]. Senior citizens should be able to benefit from their country's healthcare resources and vaccine access should be ensured for them.

Finally, there is also a need for cost-effectiveness data evaluating vaccinations to support decision making. We believe that such estimations should take into account the role of older adults in society as family members and workers, a perspective that would help reverse the existing negative bias towards older adult vaccinations by showing its full value (Fig. 4). Moreover, cost-effectiveness analyses in this setting should include complications of infectious diseases among unvaccinated individuals, burden of the chronic

diseases, polypharmacy, loss of employment and independence, and costs of rehabilitation centers [43].

7 Conclusions

Historically, the primary focus of vaccinations was on immunizations during childhood and pregnancy [5, 7]. However, after having achieved high vaccination rates in these populations, it is time to shift our attention to another rapidly growing and also vulnerable population: older adults. In the age of a globalized economy, with rapidly improving healthcare knowledge and extended life expectancy, 'older adults' constitute an increasingly populous age group that is active and productive, with highly specific skills accumulated over many years. Moreover, they are central members of families and an integral part of societies. One of the biological effects of aging, however, is the decline in intrinsic physical resilience, making

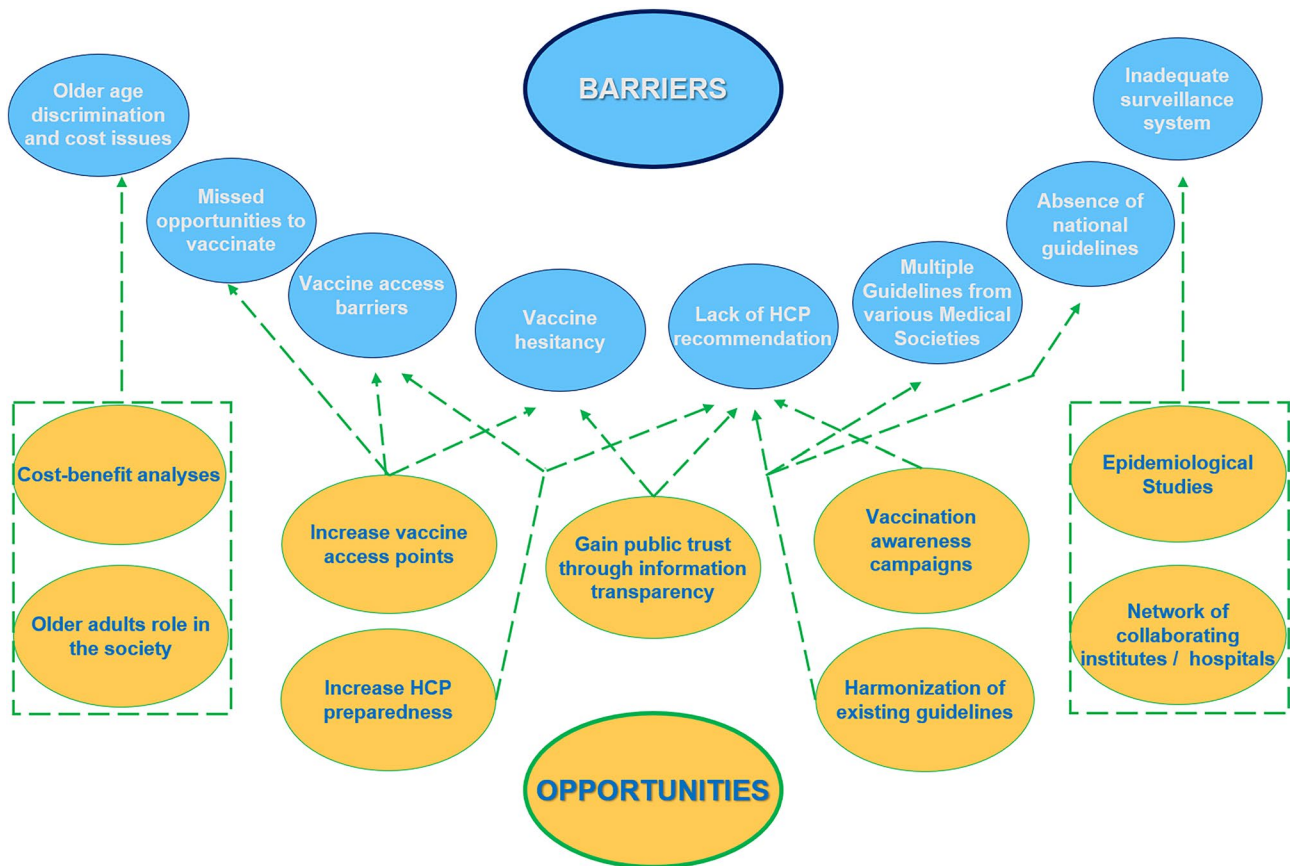


Fig. 4 Barriers and opportunities regarding older adults' vaccination. Created based on [8, 23, 41, 64, 67]. *HCP* healthcare professionals

older adults more prone to infectious and chronic diseases, the burden of which can be reduced by preventive medicine [4]. In India, the public healthcare system is overwhelmed by offering care to patients, many of whom have diseases that could have been prevented [23]. A framework promoting healthy aging, introduced by the WHO, encourages countries to implement strategies promoting good health for all [41].

It is now the time to consider older adult immunization as a new healthcare priority [68]. Adult immunization is a needed key component of a country's approach to building a healthcare program inclusive for all populations [4]. Any such program should consider factors that will promote its successful implementation because it has been shown in countries with established adult vaccination recommendations that vaccination coverage is frequently suboptimal [68, 69]. Especially in light of the COVID-19 pandemic, the WHO is recommending VPD vaccination programs for older adults, and for high-risk populations, as this will help free up beds that would otherwise be occupied by patients with pneumococcal diseases, complications of influenza, and pertussis. It would also help avoid the possibility of coinfections with simultaneous occurrence of

some of these VPDs and COVID-19, and free up medical supplies and medications for the treatment of patients with COVID-19 [70].

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