

# The need for vaccination in adults with chronic (noncommunicable) diseases in India – lessons from around the world

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## ABSTRACT

Worldwide, chronic diseases (noncommunicable diseases [NCDs]) cause 41 million (71%) deaths annually. They are the leading cause of mortality in India, contributing to 60% of total deaths each year. Individuals with these diseases are more susceptible to vaccine-preventable diseases (VPDs) and have an increased risk of associated disease severity and complications. This poses a substantial burden on healthcare systems and economies, exemplified by the COVID-19 pandemic. Vaccines are an effective strategy to combat these challenges; however, utilization rates are inadequate. With India running one of the world's largest COVID-19 vaccination programs, this presents an opportunity to improve vaccination coverage for all VPDs. Here we discuss the burden of VPDs in those with NCDs, the benefit of vaccinations, current challenges and possible strategies that may facilitate implementation and accessibility of vaccination programs. Effective vaccination will have a significant impact on the disease burden of both VPDs and NCDs and beyond.

## PLAIN LANGUAGE SUMMARY

### What is already known on this topic?

- Annually, chronic or noncommunicable diseases (NCDs) cause >40 million deaths worldwide and 60% of all deaths in India
- Adults with these diseases are more susceptible to vaccine-preventable diseases (VPDs); however, vaccine utilization is inadequate in this population

### What is added by this report?

- We highlight the benefits of vaccination in adults with NCDs that extend beyond disease prevention
- We discuss key challenges in implementing adult vaccination programs and provide practical solutions

### What are the implications for public health practice?

- Raising awareness about the benefits of vaccinations, particularly for those with NCDs, and providing national guidelines with recommendations from medical societies, will increase vaccine acceptance
- Adequate vaccine acceptance will reduce the VPD burden in this vulnerable population

## ARTICLE HISTORY

Received 27 October 2021  
Revised 25 February 2022  
Accepted 9 March 2022

## KEYWORDS

noncommunicable disease; NCDs; VPDs; vaccines; vaccination; infectious disease; vaccination; India; chronic disease; vaccine-preventable disease

## The unmet need

Noncommunicable diseases (NCDs), also known as chronic diseases, are health-related states that persist over time, limit daily living and activities, and may require ongoing medical attention.<sup>1,2</sup> They include cardiovascular diseases (CVDs), chronic respiratory conditions such as chronic obstructive pulmonary disease (COPD) and asthma, cancers and diabetes, amongst others.<sup>1-3</sup> NCDs are responsible for an estimated 41 million deaths worldwide each year (Table 1),<sup>4-24</sup> representing 71% of all deaths globally; 77% of these occur in low- and middle-income countries (LMICs).<sup>3</sup> By 2030, it is estimated that NCDs will contribute to 52 million deaths annually.<sup>25</sup>

Due to a decline in fertility rates and increased longevity, world population aging will increase. Adults aged 25–65 years represent 50% of the world's population, with 8% aged >65 years.<sup>8,26</sup> Aging populations and changing lifestyles have led to a rise in the prevalence of NCDs.<sup>25,27</sup> Due to immunosenescence,

and a host of other age-related factors, such as declining functional reserves and resilience, older people, especially those with NCDs, are more susceptible to vaccine-preventable diseases (VPDs) and associated complications.<sup>8-15</sup> There is a pressing need for developing and implementing protective strategies against VPDs in this population.<sup>28</sup>

This is profoundly highlighted by the ongoing COVID-19 pandemic.<sup>29</sup> Although the SARS-CoV-2 virus can infect people of all ages, the incidence and severity of infection increase with age.<sup>30</sup> COVID-19-related deaths were highest where a greater proportion of the population was aged ≥60 years. Chronic diseases affecting the immune, cardiovascular and respiratory systems that often accompany older age increased the risk, severity and fatality of COVID-19 for many of the older population.<sup>29,30</sup>

Here we provide an in-depth review of data from around the world highlighting the burden of VPDs in those with NCDs and the urgent need for proactive

**Table 1.** Incidence, YLD, death and YLL in patients with NCDs in 2017.<sup>4,7,10,11,13,16,17,19-22,31,32</sup>

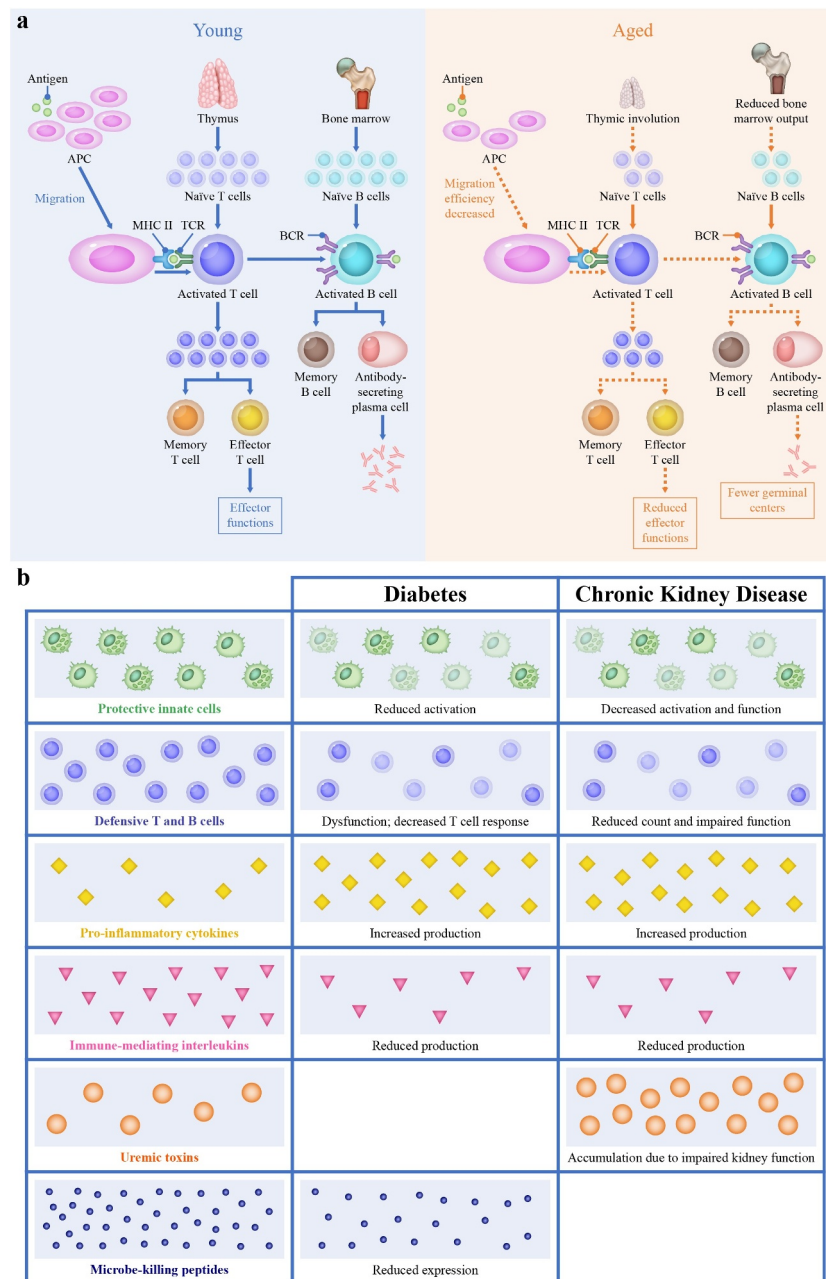
	Incidence <sup>a</sup> (thousands)		YLDs <sup>a</sup> (thousands)			All-age deaths <sup>a</sup> (thousands)			All-age YLLs <sup>a</sup> (thousands)			Risk of VPD
	Global	India	Global	India	Global	India	Global	India	Global	India		
All NCDs	10,813,563	1,854,283	678,294	113,677	41,071	4,679	872,602	141,269	Increased severity of complications <sup>8,15,18</sup> 2x more likely to develop herpes zoster <sup>10</sup> Higher risk of hospitalization or death due to influenza <sup>11</sup> Poorer outcomes when hospitalized with pneumonia <sup>13</sup> 3–16x increased risk of pneumococcal disease <sup>31</sup> Rhino/enteroviruses and influenza in 60–80% and 22–64% of adults with asthma and COPD exacerbations, respectively <sup>19,32</sup> Influenza associated with worse outcomes and excess morbidity and mortality in patients with COPD <sup>20</sup> Risk of hepatitis B infection 43% higher <sup>21</sup> Increased risk of premature death from infectious diseases <sup>22</sup> Increased risk of hospitalization and death due to influenza <sup>17</sup> Increased Associated with worse outcomes <sup>16</sup>			
CVD	72,721	7,385	35,697	3,734	17,790	2,217	330,173	61,699				
Stroke	11,931	1,137	18,695	1,508	6,167	656	113,356	16,530				
Chronic respiratory disease	62,161	8,759	44,312	9,546	3,914	833	68,005	18,976				
COPD	18,476	3,706	30,612	7,724	3,198	-	50,990	-				
Asthma	43,123	4,966	10,623	1,164	495	-	12,140	-				
Diabetes	22,936	3,639	38,575	5,640	1,370	228	29,300	5,952				
CKD	19,736	3,101	7,306	1,246	1,230	224	28,509	6,294 <sup>b</sup>				

CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; NCD, non-communicable disease; VPD, vaccine-preventable disease; YLD, years lived with disability; YLL, years of life lost.  
<sup>a</sup>Numbers rounded to the nearest thousand; <sup>b</sup>Numbers are reported for renal failure listed under NCD in the source reference.

vaccination programs in this vulnerable population. We also discuss some of the current barriers to vaccines and potential solutions to overcome these, with a focus on the Indian population.

### Indian perspective

The world's population is aging, particularly in LMICs. By 2050, almost two-thirds of the world's older population will reside in Asia, and by 2030, India is projected to become the



**Figure 1.** Immunologic differences in (a) older individuals and (b) those with chronic diseases. a) The effect of aging on the immune response.<sup>33</sup> The immune system becomes compromised and dysfunctional with increasing age (immunosenescence), due to a decline in key immune cells that regulate innate and adaptive immune responses.<sup>33</sup> In the older population, the efficiency of APC migration is reduced along with the ability of APCs to form stable contacts with T cells. This results in poor activation and differentiation of T cells. The thymic output is reduced in older patients due to thymic involution that occurs with age, and bone marrow output is also adversely affected with age, leading to a decrease in T-cell and B-cell populations and reduced downstream effects.<sup>33</sup> All these factors have a significant negative impact on the immunity of aged individuals. b) Potential mechanisms for immune impairment in patients with diabetes and CKD.<sup>16,23,24,34,35</sup> Similarly, the immune system can also become comprised in patients with chronic diseases.<sup>16,23,24,34,35</sup> Hyperglycemia in diabetes affects the innate immune system by reducing the production of type I interferon and interleukin-22, which are involved in antiviral activity, chronic inflammation and insulin sensitivity.<sup>16,24</sup> Altered immune responses in patients with CKD, such as a reduction in T and B cells and increased pro-inflammatory cytokines, leave patients more susceptible to infection.<sup>23,35</sup> Infections, such as influenza, increase the risk of adverse coronary and cardiovascular events via direct and indirect mechanisms on the vasculature.<sup>34</sup> Together, this increases the risk of worse outcomes for patients with diabetes and CKD. APC, antigen-presenting cell; BCR, B-cell receptor; CKD, chronic kidney disease; MHC, major histocompatibility complex; TCR, T-cell receptor.

most populous country in the world, with >780 million adults aged 25–64 years (53%) and 128.9 million aged ≥65 years (8.8%).<sup>26,27</sup>

Currently, in India, NCDs are the leading cause of mortality, representing 60% of total deaths in the country and accounting for 15% of all global NCD-related deaths.<sup>36,37</sup> In 2016, the largest contribution to the total mortality burden was attributed to CVDs, which were responsible for 31% of all deaths. Chronic respiratory diseases (CRDs) contributed to 7% of total deaths.<sup>38</sup> The growing burden of NCDs in India has a significant impact on healthcare systems and economies; >20 million productive life-years are lost annually due to NCDs and associated complications, resulting in a significant loss of annual income (~US \$23 billion in 2004). In 2004, Indians spent ~INR 846 billion (~US \$12 billion) on out-of-pocket expenditure associated with healthcare costs for NCDs.<sup>25,39</sup> Treatment for diabetes costs approximately one-third of the total income of low-income households.<sup>25</sup> Thus, there is a critical need to reduce additional healthcare costs, which are significantly impacted by VPDs.

Here we review the growing individual, social and economic burden of some of the key NCDs impacting adults and healthcare systems in India. The diseases discussed are not all-inclusive; for example, cancer is not covered here. Although the literature search was not systematically designed, we use data and evidence from various countries to discuss how adults with NCDs are not only more susceptible to VPDs but are at increased risk of associated disease severity and complications, and we consider how this population would benefit from a routine vaccination program. In India, vaccination programs are primarily focused on children

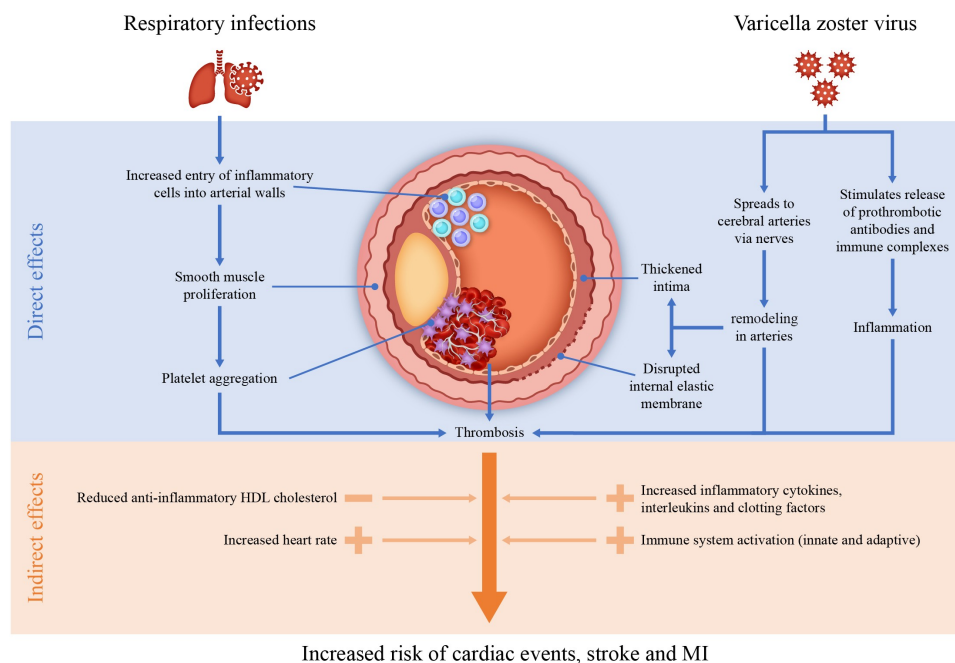
and the adult vaccination coverage is negligible.<sup>40</sup> The COVID-19 pandemic has exemplified that there is an urgent need to increase the coverage of adult vaccinations, particularly amongst those with NCDs. We will discuss how potential strategies, such as increasing awareness and education around VPDs and the benefits of vaccines and implementing vaccination guidelines, may help to overcome the barriers against vaccines and, in turn, positively impact quality of life and promote healthy aging.

## VPDs in adults with NCDs

The immune system becomes compromised and dysfunctional with increasing age (immunosenescence), due to a decline in the numbers and functionality of cells that regulate innate and adaptive immune responses (Figure 1(a)).<sup>33</sup> Similarly, the immune system can become compromised in patients with NCDs (Figure 1(b)).<sup>8</sup> This puts the adult population, particularly those with NCDs, at a major disadvantage who, owing to urbanization, globalization, and increasing international travel, are more at risk of contracting VPDs, thus highlighting the need for routine vaccination programs in this patient population.<sup>8-15</sup>

## CVD

CVD is the leading cause of morbidity and mortality worldwide, with an estimated 17.8 million deaths in 2017 (Table 1).<sup>4</sup> In India, CVDs were responsible for 2.2 million deaths, contributing to 23% of total deaths and 44.5% of mortality in adults aged ≥70 years.<sup>5,41</sup>



**Figure 2.** The effect of VPDs. VPDs and infections can ultimately result in cardiovascular events.<sup>34,42-46</sup> Infection with pathogens associated with influenza-like illness leads to an increased pro-inflammatory response that exacerbates plaque formation in the blood vessels and procoagulant effects, which then contributes to accelerated atherosclerosis.<sup>34</sup> Influenza has also been shown to lower the anti-inflammatory properties of HDL cholesterol particles, which further drives the infiltration of macrophages through the arterial wall.<sup>43</sup> In addition, there is some evidence that influenza may increase the risk of tachycardia, which is associated with major adverse cardiovascular events in hypertensive patients.<sup>43,45</sup> Other viral infections may have similar outcomes: for example, the varicella zoster virus has been shown to directly cause pathologic vascular remodeling, resulting in a thickened intima and vascular occlusion, leading to subsequent thrombosis and rupture.<sup>44,46</sup> Varicella zoster virus also induces systemic inflammatory responses, which cause disruption to pre-existing atherosclerotic plaques and stimulate mediators of the coagulation system.<sup>42,46</sup> Altogether, these events increase the risk of stroke.<sup>42,44,46</sup> HDL, high-density lipoprotein; MI, myocardial infarction; VPD, vaccine-preventable disease.

### Infections and CVD

Influenza and respiratory tract infections are associated with an increased risk of adverse cardiovascular outcomes in the general population.<sup>9,14,15,47</sup> According to a 2015 meta-analysis, patients experiencing acute myocardial infarction (MI) are twice as likely to have had recent influenza or other respiratory tract infections, relative to controls (pooled odds ratio [OR]: 2.01 [95% confidence interval (CI): 1.47–2.76]).<sup>14</sup> Risk of acute MI or stroke was ~3–5 times greater following respiratory infections than baseline in a case-series analysis of 20,486 patients registered in the UK General Practice Research Database (MI: incidence rate ratio [IRR]: 4.95 [95% CI: 4.43–5.53]; stroke: IRR: 3.19 [95% CI: 2.81–3.62]).<sup>15</sup> In a time-series analysis of cardiovascular deaths in New York during influenza season, influenza-like illness was associated with an increase in cardiovascular mortality within 21 days in patients aged ≥65 years.<sup>47</sup> In a matched-cohort study of >3,000 patients, risk of CVD was significantly higher among those hospitalized for pneumonia.<sup>9</sup>

There are two proposed mechanisms by which infections increase the risk of CVD—direct or local effects on vasculature and indirect systemic expression of inflammatory cytokines (Figure 2).<sup>34,42–46</sup>

Interestingly, patients with CVD have an increased risk of morbidity and mortality from infections. In a nationwide population cohort study in Taiwan, patients with heart failure (HF) were twice as likely to develop herpes zoster and had significantly lower event-free survival compared with patients without HF.<sup>10</sup> Similarly, HF and COPD have been identified as independent prognostic factors for influenza-associated hospitalization and mortality.<sup>11</sup> Patients with HF have a higher 30-day mortality rate when hospitalized for pneumonia.<sup>13</sup> In a retrospective analysis of the National Inpatient Sample database, influenza in patients with HF increased the duration of hospitalization and in-hospital morbidity and mortality.<sup>12</sup>

### CRDs

CRDs are one of the leading causes of mortality worldwide, responsible for 3.9 million deaths in 2017 (Table 1).<sup>4</sup> More than 90% of COPD-related deaths occur in LMICs.<sup>4,18,48</sup> In India, CRDs were responsible for >830,000 deaths in 2017 and they were the fourth leading condition accounting for the most disability-adjusted life-years.<sup>5</sup>

Exacerbations (acute worsening of respiratory symptoms) are one of the main causes of morbidity and mortality in patients with CRDs.<sup>19,49,50</sup> In a long-term follow-up of >73,000 patients hospitalized for COPD in Canada, health status declined following severe exacerbations, and risk of successive severe exacerbations increased with each event.<sup>49,50</sup> In a case-series analysis of data from the UK Clinical Practice Research Datalink (CPRD), acute COPD exacerbations were associated with a 65% and 51% increased risk of MI and stroke, respectively, within 91 days of onset.<sup>51</sup> Asthma exacerbations have been shown to accelerate decline in lung function and significantly increase the risk of MI and stroke.<sup>52,53</sup>

VPDs contribute significantly to infection-induced exacerbations in adults with CRDs.<sup>19</sup> Viruses have been detected in 60–80% and 22–64% of adults with asthma and COPD exacerbations, respectively.<sup>54,55</sup> Viral infections are associated with increased

duration of hospitalization, deterioration of lung function and worse hypoxemia in patients with COPD exacerbations.<sup>56</sup> Influenza causes excess morbidity and mortality in patients with COPD.<sup>20</sup> Older adults and those with NCDs are at higher risk of complications associated with influenza infection, including pneumonia and respiratory failure, and admittance to an intensive care unit (ICU).<sup>57</sup> During the 2009 influenza pandemic, hospital-based surveillance data across Central America and the Dominican Republic showed that 61% of patients who died had pre-existing chronic diseases, including asthma (11%) and COPD (5%).<sup>58</sup> In the UK, COPD and asthma were reported in 20% and 19% of influenza-infected patients, respectively,<sup>59</sup> and in Spain COPD was significantly associated with worse outcomes in patients infected with influenza (OR: 1.51 [95% CI: 1.03–2.2];  $p = .002$ ).<sup>60</sup>

There are several proposed mechanisms by which infections may contribute to the pathogenesis and prognosis of CRDs. However, contribution to overall disease burden is not fully understood. Infections have been shown to increase inflammation in the airways and reduce expiratory flow, resulting in dyspnea and exacerbations.<sup>50</sup> Respiratory viral infections have been implicated in the desquamation of epithelial cells, microvascular dilation, edema and infiltration of inflammatory cells, such as CD8 T-lymphocytes, into the airway. This results in reduced muco-ciliary clearance and decreased bacterial removal via macrophages, thus increasing susceptibility to bacterial infection.<sup>20,61–63</sup>

### Diabetes and chronic kidney disease

In 2017, diabetes resulted in 1.4 million deaths worldwide, an increase of 15.1% for type 1 and 43.0% for type 2 since 2007 (Table 1).<sup>4</sup> Diabetes is a leading cause of disability worldwide.<sup>6</sup> In India in 2017, 68 million people had diabetes, a >2-fold increase from the 26 million in 1990, and there were 228,000 deaths, accounting for 2.4% of total deaths.<sup>5,6,64</sup> The incidence and burden of diabetes are predicted to rise in future years.<sup>6</sup> Chronic kidney disease (CKD) was responsible for 1.2 million deaths worldwide in 2017, a 33.7% rise in mortality since 2007.<sup>4,7</sup> In India, CKD was responsible for >220,000 deaths in 2017.<sup>7</sup>

The unfavorable relationship between infections and disease pathology is also true for CKD and diabetes. Patients with diabetes and CKD have an increased risk of infection due to impaired immunity and possible disease complications (Figure 1(b)).<sup>16</sup>

In a retrospective analysis of individual-participant data by the Emerging Risk Factors Collaboration, diabetes significantly increased the risk of premature death from any cause (hazard ratio [HR]: 1.80 [95% CI: 1.71–1.90]), including pneumonia and other infectious diseases.<sup>22</sup> Similarly, CKD has been implicated as a risk factor for all-cause mortality and CVD.<sup>65</sup> In a systematic review and meta-analysis of >610,000 participants, diabetes was associated with higher hospital admissions for seasonal influenza (OR: 9.91 [95% CI: 5.46–17.99]). Pandemic influenza was associated with higher risk of death in patients with diabetes.<sup>17</sup> Similarly, relative risk of hepatitis B infection was 43% higher in those with diabetes compared with those without diabetes in a retrospective study in China.<sup>21</sup>

## Vaccination in patients with NCDs

The risk of infections and severity of associated outcomes are significantly increased in patients with NCDs.<sup>8-15</sup> Vaccination is an effective preventative public health strategy and there are various vaccines available for adults, especially those with NCDs (Table 2).<sup>66-88</sup> Its increased utilization has the potential to reduce the incidence and socioeconomic burden of VPDs in all adults (particularly those with NCDs), and to substantially contribute to a healthier older population. Despite immunosenescence, protective immune responses are still observed in older adults, reducing serious disease and associated complications. Furthermore, the development of vaccine adjuvants and implementation of booster programs have been shown to improve immune responses in this population.<sup>89,90</sup> Despite these benefits, vaccination strategies in adults, particularly in LMICs, have not been widely implemented, and there is a need for a new approach to expand vaccination programs.<sup>89</sup>

Aging is a known risk factor for most NCDs and can increase susceptibility to infectious diseases and VPDs.<sup>91</sup> Furthermore, infections can induce inflammation, which in turn may accelerate aging.<sup>92,93</sup> The World Health Organization (WHO) created the concept of 'healthy aging'—*developing and maintaining the functional ability that enables well-being in older-age*—as a response to the worldwide challenges associated with an increasing aging population.<sup>94</sup> The strategy hopes to improve adult vaccination access worldwide, which may help to defer some of the negative effects of aging.<sup>89</sup>

There is a wealth of evidence that demonstrates the benefits of vaccines in patients with NCDs, such as the following examples assessing the influenza and pneumococcal vaccines in patients with a range of NCDs.

In a systematic review of >12,000 patients who received influenza vaccines or placebo/no-treatment (1991–2009), cardiovascular mortality was significantly reduced in vaccinated patients (relative risk [RR]: .45 [95% CI: .26–.76];  $p = .003$ ).<sup>95</sup> The influenza vaccination has also been shown to decrease the risk of stroke by ~20% (OR: .82 [95% CI: .75–.91];  $p < .001$ ); this effect was consistent across all subgroups, indicating that vaccination may be beneficial in reducing the risk of stroke even in low-risk populations.<sup>96</sup> Similarly, in a population-based study of >27,000 patients aged  $\geq 60$  years in Spain, pneumococcal vaccination was associated with a 35% (95% CI: .01–.58) reduction in the adjusted risk of ischemic stroke.<sup>97</sup> In a large meta-analysis of >230,000 patients, pneumococcal vaccination was associated with significant reduction in the risk of acute coronary syndrome (ACS) events in patients aged  $\geq 65$  years (OR: .83 [95% CI: .71–.97]).<sup>98</sup>

In a systematic review and meta-analysis of >82,000 patients with HF (1990–2013),<sup>99-106</sup> all-cause mortality risk was reduced by ~30% in patients vaccinated against influenza (HR: .69 [95% CI: .51–.87]).<sup>107</sup> In a case-control study (1997–1998), influenza vaccines had a protective effect in patients with known coronary heart disease (CHD), resulting in a 67% reduction in the risk of MI during the subsequent influenza season (OR: .33 [95% CI: .13–.82;  $p = .017$ ]).<sup>43,108</sup>

In patients with COPD, influenza vaccination significantly reduced the incidence of acute exacerbations and respiratory illness (RR: .33;  $p = .005$ ) in a prospective trial in India; the

overall effectiveness of influenza vaccines was 67% in patients with COPD.<sup>109</sup> Yearly influenza vaccinations in Taiwan reduced the risk of hospitalization for ACS by 54% (HR: .46 [95% CI: .39–.55];  $p < .001$ ) and the risk of developing lung cancer by 60% (HR: .40 [95% CI: .35–.45];  $p < .001$ ) in patients with COPD aged  $\geq 55$  years.<sup>110,111</sup> The benefit was more pronounced in those receiving  $\geq 4$  vaccinations.

In patients with diabetes, seasonal influenza vaccination was associated with a significantly reduced risk of all-cause mortality, particularly among those aged  $\geq 65$  years.<sup>112</sup> In a retrospective cohort study of data from the UK CPRD, influenza vaccination was associated with significantly fewer hospital admissions for stroke (IRR: .70 [95% CI: .53–.91]), HF (IRR: .78 [95% CI: .65–.92]), and pneumonia or influenza (IRR: .85 [95% CI: .74–.99]) and all-cause death (IRR: .76 [95% CI: .65–.83]) among diabetic patients.<sup>113</sup> In a multivariate analysis combining data from four influenza seasons (2002–2005), vaccination was associated with a 33% reduction in all-cause mortality among adults aged  $\geq 65$  years with diabetes (OR: .67 [95% CI: .47–.96]).<sup>114</sup> In a retrospective study including >9,000 elderly patients with diabetes, those vaccinated against influenza had lower rates of pneumonia and respiratory failure and were less likely to be admitted to ICU (adjusted HR: .30 [95% CI: .19–.47]).<sup>115</sup> In patients with CKD aged  $\geq 55$  years in Japan, influenza vaccination reduced the risk of hospitalization for HF by 69% (HR: .31 [95% CI: .26–.39];  $p < .001$ ) and ACS by 65% (HR: .35 [95% CI: .30–.42];  $p < .001$ ).<sup>116,117</sup>

The health benefits provided by these vaccines are not only limited to reducing VPDs and related complications in adults with NCDs, but may extend further in minimizing the risk of developing certain chronic diseases. Data from the National Health and Nutrition Examination Survey (2005–2010), conducted in the United States, showed that hepatitis B vaccination was associated with a reduced risk of developing diabetes (OR: .67 [95% CI: .52–.84]).<sup>118</sup> Similarly, the Bacillus Calmette Guérin (BCG) vaccination reduced hemoglobin A1c to near-normal levels in patients with type 1 diabetes.<sup>119</sup> Both the BCG and hepatitis B vaccines are routinely administered to infants through the National Immunization Program in India.<sup>120</sup> An expanded recommendation in high-risk adults to prevent/alleviate diabetes is not currently in place, but is an interesting point for future clinical trials.

## Challenges

In 2003, the WHO urged member states to “*establish and implement strategies to increase vaccination coverage of all people at high risk, including the elderly and persons with underlying diseases, with the goal of attaining vaccination coverage of the elderly population of at least 75% by 2010*”.<sup>75</sup> However, these goals are far from being achieved. Analysis of influenza vaccination uptake in the US and England shows that coverage consistently falls short of these targets.<sup>82, 83</sup> Various recommendations are in place for vaccinations in patients with NCDs; however, they vary across countries and some are incomplete (Table 2).<sup>4,66,69-78</sup> Despite the growing burden of NCDs in India, the Indian National Immunization Program does not include any specific recommendations for the vaccination of adults with NCDs. Some medical societies, such as the Indian Medical

**Table 2.** Recommendations for vaccinations in adults with key chronic diseases provided by various guidelines across the world.<sup>66-88</sup>

Vaccine	Adults with a chronic disease			
	Global <sup>a</sup> US EU <sup>b,c</sup>	WHO CDC ECDC	CVD	CRD
<b>Influenza</b>				
			All with chronic medical conditions All with chronic pulmonary disorders (including asthma)	All with metabolic disorders (including diabetes) All with chronic metabolic disorders
	UK	PHE NHS/NICE	All with CHD or HF	All with chronic medical conditions
	India Global <sup>d</sup>	IMA WHO	All with chronic cardiorespiratory disease	All
	US	CDC	All with CHD (PPV23 1 dose)	All (PPV23 1 dose)
<b>Pneumococcal conjugate vaccine:</b> PCV13	UK <sup>e</sup>	PHE NHS/NICE	All with CHD (PPV23 1 dose)	All (PPV23 2 doses)
<b>Pneumococcal polysaccharide vaccine:</b> PPV23	India	IMA	All with CHD (PCV13 1 dose and PPV23 2 doses)	All (PCV13 1 dose and PPV23 2 doses)
<b>Herpes zoster<sup>f</sup></b>	US	CDC	People with chronic medical conditions may be vaccinated unless a contraindication exists <sup>g</sup>	High-risk individuals who receive dialysis
<b>Hepatitis B</b>	Global	WHO	-	All
	US	CDC	Consider in adults with lung disease if patient has a specific risk factor for hepatitis B	All
	UK <sup>h</sup>	PHE	-	All (stage 4/5)
<b>Tdap</b>	US	CDC	All with lung disease	All
<b>HPV</b>	US	CDC	All with lung disease if aged ≤26 years; maybe in adults aged 27–45 years after discussion with HCP	Adult through age 26 years; less benefit for those aged 27–45 years
<b>MMR</b>	US	CDC	Consider in adults with lung disease if born in 1957 or later	All with CKD if born in 1957 or later or do not have immunity
<b>Varicella</b>	US	CDC	Consider in adults with lung disease	All with CKD if born in 1980 or later or do not have immunity

Other vaccines, such as Hib, Tdap, HPV and meningitis, are recommended in adults with specific risk or conditions.  
 CDC, Centers for Disease Control and Prevention; CHD, coronary heart disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRD, chronic respiratory disease; CVD, cardiovascular disease; ECDC, European Centre for Disease Prevention and Control; ESC, European Society of Cardiology; GINA, Global Initiative for Asthma; GOLD, Global Initiative for Chronic Obstructive Lung Disease; HBV, hepatitis B virus; HCP, healthcare professional; HF, heart failure; HPV, human papillomavirus; IMA, India Medical Association; MMR, measles, mumps and rubella; NHS, National Health Service; NICE, National Institute for Health and Care Excellence; PHE, Public Health England; Tdap, tetanus, diphtheria, pertussis; WHO, World Health Organization.  
<sup>a</sup>GINA guidelines advise administering influenza vaccination in all persons with moderate-to-severe asthma and GOLD guidelines recommend influenza vaccination in all persons with COPD; <sup>b</sup>Individual countries within Europe may have their own guidelines; <sup>c</sup>WHO Europe guidelines note that all persons with CHD are a priority group and ESC guidelines state to consider influenza vaccination in all persons with CHD; <sup>d</sup>GINA guidelines state that there is insufficient evidence to recommend routine pneumococcal vaccination in people with asthma; GOLD guidelines recommend the PCV13 and PPV23 vaccine in adults >65 years of age and the PPV23 vaccine for younger COPD patients with significant comorbid conditions including CHD or lung disease; <sup>e</sup>ESC guidelines recommend pneumococcal vaccination in patients with HF; <sup>f</sup>In the UK, PHE, NHS and NICE guidelines recommend herpes zoster vaccination in all adults >70 years of age; <sup>g</sup>For patients with CKD, herpes zoster vaccine is recommended only if they are aged ≥60 years; <sup>h</sup>WHO Europe recommends hepatitis B vaccination in all adults considered to be at high risk of HBV infection, NHS recommendations note that patients with CKD should be considered for hepatitis B vaccination, and NICE recommends the vaccination in all patients with chronic renal failure; - no specific guidelines provided.

Association, have published vaccination guidelines that include recommendations for adults. However, these guidelines are convoluted by various risk factors and lack clear guidance for adults with NCDs. In addition, there is a need for continuity between different medical guidelines.<sup>88,121–126</sup> Due to the lack of national guidelines there is negligible financial support available, leaving the cost of adult vaccinations solely to the individual. This acts as a major barrier to vaccination uptake.<sup>121</sup>

Several other barriers exist that impact the coverage of adult vaccinations, including those related to access, affordability, reimbursement and infrastructure.<sup>127</sup> The impact of these barriers varies between countries; however, inadequate vaccination coverage is a worldwide problem, even in countries where recommendations, infrastructure and funding are in place to fully support adult vaccination programs.<sup>127</sup> Therefore, some of the most important challenges are those related to psychologic and educational factors.<sup>128</sup> Surveys have shown that many people are hesitant to receive vaccinations, due to a lack of awareness regarding impact of the underlying disease, and possible effectiveness of the vaccine itself. The perception of potential side effects associated with vaccinations is also a predominant barrier to vaccine uptake despite evidence demonstrating they are well tolerated and effective.<sup>127–130</sup> In addition, there is a common misperception that vaccinations are only relevant for children and are not a health priority for adults.<sup>128,131</sup>

In India, additional barriers prevent effective vaccination uptake. Lack of awareness and hesitancy among healthcare professionals (HCPs) and the public, as well as inadequate HCP recommendations, are major barriers to vaccination in adults with NCDs.<sup>121,132,133</sup> In a 2017 study, ~68% of the Indian population were unaware that adult vaccinations existed and believed that they were not necessary as they “felt healthy”.<sup>134</sup> In addition, NCD surveillance in India is insufficient, with reported inconsistencies and lack of standardization, which impede progress in understanding, preventing and treating these diseases.<sup>135</sup> Religious/cultural beliefs, particularly in rural India, may also prevent effective vaccination uptake.<sup>36,121,132,133</sup> Compared with high-income countries, India is under tighter economic constraints, so it is of high importance that effective programs are implemented, as vaccinations are one of the most cost-effective healthcare measures available.<sup>136</sup>

## Solutions

Multidisciplinary recommendations by medical societies, including the Indian Medical Association, to prioritize adult vaccinations may have an impact on future programs; however, standardization of these recommendations is essential. The implementation of national guidelines for adults with NCDs is desirable; however, this would require multidisciplinary coordination and leadership among HCPs and policymakers to promote these guidelines and change the perceived need in this population.<sup>121,137</sup> Raising awareness and educating HCPs and the public on the importance and benefits of adult vaccinations, particularly among those with NCDs, may help increase uptake and compliance, and ultimately reduce the burden of VPDs on the healthcare system in India.<sup>121,137</sup> As patients with NCDs usually require regular medical visits, this provides an opportunity for HCPs to highlight the

recommended vaccines and alleviate concerns over potential side effects to these patients in a one-to-one discussion.<sup>121</sup> The COVID-19 pandemic and subsequent roll-out of the largest vaccination program in India represents a challenge but also an opportunity for implementing a more robust adult vaccination program.

In the US, the 4 Pillars™ Program was developed to provide a step-by-step guide to improve adult vaccination rates. This program focuses on convenient vaccination services, communication with patients about the importance of vaccination and the availability of vaccines, enhanced office systems to facilitate vaccination and motivation through an office champion.<sup>138,139</sup> Implementation of the 4 Pillars™ Program was associated with a significant increase in vaccinations among high-risk groups, including those with chronic diseases, compared with non-high-risk groups (e.g. influenza vaccination increased in patients with chronic lung disease [OR = 1.14] and diabetes [OR = 1.14]).<sup>139</sup>

Some of the key proposals that may help to increase vaccination coverage in adult patients, including those with NCDs, in India include:<sup>121,128,138–140</sup>

- Improving awareness and education of HCPs and patients
  - Educate on the direct and indirect benefits of adult vaccination that extend beyond disease prevention, such as improving quality of life, enabling independent living in the elderly, improving life expectancy, and reducing financial burden
  - Alleviate concerns about vaccine efficacy by changing the narrative to discuss the reduction in risk of disease instead of efficacy rates
  - Address the perception that vaccines are only for children
- Promoting the concept of healthy aging and highlighting the importance of life-course vaccination for continued life-long healthcare
- Implementing and distributing national adult vaccination guidelines and ensuring clear steps and paths of action are provided
- Ensuring there are mechanisms for feedback to monitor desired outcomes
- Involving religious leaders in education activities within the community

## Conclusion

Vaccinations are one of the most cost-effective and efficient healthcare interventions for reducing the incidence and burden of VPDs, not only in children but also in adults, especially those with NCDs. However, utilization rates across the world are inadequate. This leaves adults, particularly those with NCDs, vulnerable to VPDs and their associated complications. There are numerous health and economic benefits of vaccinating adult patients with NCDs, and there should be a global focus on increasing vaccination coverage in this population and among adults in general. It is extremely important to increase awareness and education of HCPs and the public on the widespread benefits of vaccinations and ensure that vaccination programs are adequately



implemented and accessible to all. In India, the lack of guidance, growing burden of NCDs and additional barriers to vaccine uptake highlight the need for action. With India implementing one of the world's largest COVID-19 vaccination programs, now is the time to improve the awareness and accessibility of their adult vaccination programs for all VPDs, particularly among those with NCDs.

## Acknowledgments

Authors thank MediTech Media for editorial assistance and manuscript coordination, on behalf of GSK Vaccines. Zoe Cornhill provided medical writing support and Danielle Lindley coordinated manuscript development and editorial support.

## Disclosure statement

AV declares no conflicts of interest. ADP was previously employed and previously had stock ownership in the GSK Group of Companies. SK, AA and SA are employed by the GSK Group of Companies. SK has stock ownership in the GSK Group of Companies.

## Funding

The author(s) reported there is no funding associated with the work featured in this article.

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