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Review Article

Adult vaccination in India: A rapid review of current status & implementation challenges

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***Background & objectives*: The expanded programme on immunization launched in India in 1978, with its focus on preventing six diseases in children (tetanus, diphtheria, pertussis, poliomyelitis, typhoid, and childhood tuberculosis), was widened in its scope in 1985-86. This new *avtaar,* the Universal Immunization Programme (UIP), incorporated measles vaccine for children and rubella and adult diphtheria vaccines for pregnant women. We conducted this rapid review on adult immunization relevant for India, as recent COVID-19 experience revealed how newly emergent or re-emergent pathogens could have their onslaughts on the elderly and adults with comorbidities.**

***Methods*: Three different bibliographic databases, namely PubMed, Scopus and Ovid were searched electronically to access the articles published in peer-reviewed journals. Relevant consensus guidelines by in-country professional groups were also collated. We conducted deduplication and screening of the outputs of these searches (1242 bibliographical records). Finally, 250 articles were found eligible for inclusion. As trials on the reduction of morbidities, mortalities and hospitalizations in adults due to proposed vaccines under Indian consensus guidelines were not available, no meta-analysis was conducted.**

***Results*: Evidence from articles finally included in this synthesis were grouped under (*i*) preventing viral and bacterial infections in adults; (*ii*) adult vaccination and awareness tools; (*iii*) vaccine hesitancy/ acceptance; and (*iv*) adult vaccination guidelines. In-country research revealed the need for introducing the Human Papilloma Virus (HPV) vaccine in adolescence or early-adulthood to prevent ano-genital cancers in elderly and later life. Importantly HPV prevalence among cervical cancer patients varied between 88 to 98 per cent in Andhra Pradesh, Odisha and Delhi. The importance of conducting regular surveillance of pneumococcal diseases and influenza, as well as tweaking the vaccines accordingly, was revealed in other articles. A poor uptake of influenza vaccine (≤2%) in adults (≥45 yr) was documented.**

The uptake of hepatitis B vaccine in Health Care Workers (HCWs) in Delhi and Mumbai was of concern and ranged from 55 to 64 per cent. The vulnerability of HCWs to rubella was investigated in a paediatric ophthalmic hospital in Madurai: a tenth of the selected HCWs were rubella seronegative and mounted good protective immunity following RA 27/3 vaccine administration. An outbreak of measles in college students in Pune emphasized the phenomenon of waning immunity. Similarly, a study in the infectious disease hospital in Kolkata and in-patients in Delhi revealed a lack of protective immunity against diphtheria and tetanus in adults. The researchers estimated the economic benefits of providing a typhoid vaccine to a household to be US$ 23 in a middle-income neighbourhood and US$ 14 in slum settings.

The authors highlighted the importance of preventive strategies, finding that the cost of severe typhoid fever was US$ 119.1 in 18 centres across India. Both qualitative and quantitative investigations explored vaccine hesitancy, which was studied more during the COVID-19 pandemic than earlier.

***Interpretation & conclusions*: Vaccination programmes in India would require (*i*) increasing awareness around vaccine-preventable diseases among adults and HCWs; (*ii*) actively engaging health care systems and community-based organizations; and (*iii*) developing and producing affordable, safe, and country-appropriate vaccines. Effective communication strategies and tools will be the key to the success of such interventions.**

Key words Adult - gaps in immunization - Indian guidelines - pandemic preparedness - vaccine preventable infections

The Expanded Programme on Immunization (EPI) was launched by the World Health Organization (WHO) in 1974[1]. The idea was to ensure access to life-saving vaccines for every child, irrespective of their geographical origin and socioeconomic status. Since then, its impact has grown over the last five decades. There are now thirteen vaccines recommended for different age groups[1]. EPI was launched in India in 1978, with the objective to reduce the mortality and morbidity from six diseases *i.e*., tetanus, diphtheria, pertussis, poliomyelitis, typhoid and childhood tuberculosis by providing immunization services to all eligible children. Its new incarnation, the Universal Immunization Programme (UIP) was launched in 1985-86, in India, with the inclusion of measles vaccine[2] and exclusion of the injectable typhoid vaccines, which had several side effects and poor protection.

By incorporating Rubella and adult Diphtheria vaccines for pregnant women, the UIP expanded its horizon to the adult population[3]. However, immunization coverage, thus achieved to address the vulnerability of adults to various infections, was inadequate. Notably, the shape of the population pyramid of India has changed considerably between 1978 and 2024. The percentage of the population ≥65 yr of age has increased during this period from 0.9 (both male and female), to 1.4 in males and 1.5 per cent in females[4].

With the world population ageing rapidly, partly due to life saving impact of childhood immunization, it is estimated that by 2030, there will be 34 nations with over 20 per cent population ≥65 yr[5]. Due to the immune-senescence and declining functional reserve and resilience, older people, especially those with non-communicable diseases (NCDs), such as cardiovascular diseases, chronic obstructive pulmonary disease, diabetes, and cancers, are more prone to infections[6]. Therefore, the incidences of various vaccine preventable infections (VPIs) are increasing in the elderly (≥60 yr)[7]. Inclusion of adult vaccines within the ambit of UIP, in this context appears crucial.

Against this background, we conducted a rapid review of the adult vaccination issues in India. The purpose was to understand their nuances and inform policymakers about evidence-based programming. Moreover, worldwide, there is ongoing discussion about pandemic preparedness. In this context, adult vaccination comprises an important intervention element because the recent COVID-19 experience revealed how the elderly in general and adults with comorbidities could suffer most with the emergence of new viral pathogens. We, therefore, conducted this rapid review of adult vaccination to inform the current country-specific programme planning in India and beyond.

Materials & Methods

To conduct a rapid review on various domains around adult immunization in India and to synthesize evidence available in the published articles, an electronic search was conducted. Three different bibliographic databases, namely PubMed, Scopus and Ovid, were used for this purpose. The search was guided by a framed research topic using the PICOS framework. In PICOS, the Population (P) under scrutiny was adults aged ≥18 yr (PubMed allows grouping of population aged 19+ yr). The Intervention (I) was ‘immunization’, further divided into two sub-domains; one was ‘Intervention at individual level’, which included vaccination, vaccine-preventable diseases (VPDs), and different vaccines available for adults. The other sub-domain was ‘Intervention at the policy and programme level’, including issues like vaccination programmes, EPI, UIP, National

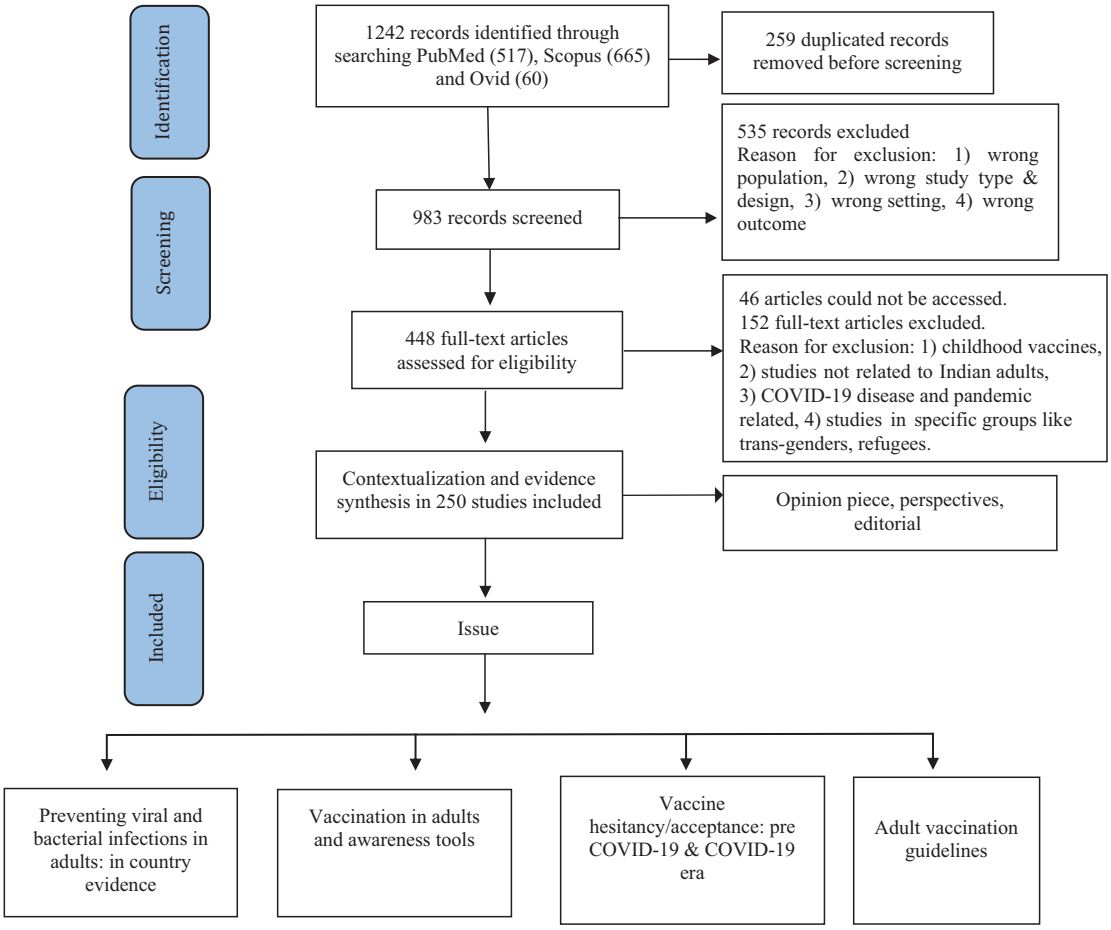

Figure. PRISMA scheme of workflow.

Technical Advisory Group on Immunization (NTAGI), *etc*. The Outcome (O) was captured under qualitative concepts such as hesitancy, denial, anxiety, *etc*. In quantitative terms, the outcome was represented through vaccine uptake, vaccination coverage, out-of-pocket expenses, complications avoided, *etc*. India at the country level and 'its States and union territories' at the regional level served to characterize the Settings (S). No time restriction was imposed on the search strategy. All possible keywords under the domains, as mentioned earlier, were used to develop a comprehensive search strategy (Supplementary Table). Results of the searches (1242 bibliographic records) conducted on June 27, 2024 from the above-mentioned databases were exported to Rayyan software that helped conduct the literature search, deduplication (259 duplicate records), and screening based on pre-decided eligibility criteria for inclusion in our investigation. Initially, the title and abstract screening of 983 articles were undertaken independently by the two authors (AB and SMS) to select only the eligible ones. Any conflict regarding this, between the two authors were resolved through mutual consensus. The access of full texts of 448 articles, thus selected, was needed for final inclusion in the study. However, 46 articles could not be accessed for full text, and 152 articles were excluded following full-text reading due to various reasons (Figure). Finally, 250 articles were found eligible to be included in this study, which were evaluated for their design and implementation details during the qualitative synthesis of evidence. The entire scheme of workflow is presented in the flow diagram (Figure) based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). As trials on the reduction of morbidities, mortalities and hospitalizations in adults due to proposed vaccines under Indian consensus guidelines were not available, no meta-analysis was conducted.

Results

Data categorization: Two hundred and fifty publications were used to synthesize evidence under

the following four subtitles: (*i*) Preventing viral and bacterial infections in adults: in-country evidence, (*ii*) Vaccination in adults and awareness tools, (*iii*) Vaccine hesitancy/acceptance: pre-COVID-19 & COVID-19 era, and (*iv*) Adult vaccination guidelines.

Preventing viral and bacterial infections in adults; in-country evidence: In the following section, viral infection in adults caused by human papillomavirus (HPV), influenza, Japanese encephalitis (JE), measles and rubella (MR) and hepatitis B (HBV), have been dealt with. Subsequently relevant bacterial diseases such as pneumococcal infection, typhoid, diphtheria, and tetanus have been discussed for their relevance to adult vaccination.

HPV-early vaccination in early adulthood & opportunities to avert adult cancer: HPV is a sexually transmitted infection which is acquired through unprotected sex during adolescence or later. The infection predisposes ano-genital cancers in males and females after a long latent phase of incubation. In India, the HPV prevalence has been recorded as 93.8, 87.8 and 98.1 per cent among patients with cervical cancers in Odisha, Andhra Pradesh and Delhi, respectively[8-10]. In contrast, according to the NFHS 5 (2019-2021) report, only two per cent of the women of urban population and 1.7 per cent of the rural population underwent screening test for cervical cancer[11]. Research has emphasized that immunization with the HPV vaccine in adolescents may help address these issues[12].

In a multi-centric cluster randomized trial of quadrivalent HPV vaccination in girls (10-18 yr), 25 per cent of the participants received one dose of HPV vaccine. The trial demonstrated a robust and sustained immune response against HPV 16 and 18, and the antibody levels were stable over a four-yr period. The frequencies of cumulative incidence and persistent HPV 16 and 18 infections up to seven yrs of follow-up were also low in all the vaccinated groups[12]. Noticeably, modelling studies have shown that a single-dose HPV vaccine has the potential to provide short and long term protection[13], and is likely to be cost effective than two dose schedule[14]. Dandapat and colleagues[15] highlighted the need to add HPV vaccine to the UIP. Importantly, the Federation of Obstetric and Gynaecological Societies of India (FOGSI), the Indian Academy of Paediatrics (IAP), and the NTAGI during 2018-2022, endorsed the introduction of two-dose (for girls aged 10-12 yr) and three-dose (for those aged ≥15 yr) schedules of the HPV vaccine[16-18].

Influenza; importance of including circulating strains in the vaccine: In Kashmir, north India, 1219 patients admitted with severe acute respiratory illness (SARI) were tested for influenza viruses. About one-third of them were influenza-positive. Sequencing of the HA genes revealed about fifty per cent of them were infected with influenza B/Victoria, followed by about forty seven per cent with influenza A/H1N1 and the rest were infected with influenza A/H3N2 strain. Among influenza positive patients, 6.8 per cent were vaccinated, whereas vaccination proportion among influenza negative, was 8.6 per cent. Vaccine effectiveness (VE) in this study, for any influenza strain was found to be 13 per cent (95% CI - 42 to 47), and for influenza B, it was zero per cent. Poor VE was due to genetic mismatch between the circulating strain and the strain included in the vaccine[19]. Studies on acceptance, awareness, knowledge, attitude, *etc.,* related to influenza vaccine among adults have also been conducted from different parts of India[20-27].

JE, MR & HBV vaccine; unaddressed issues: A case-control study was conducted among participants aged 15-65 yr to estimate VE in the Sivasagar and Dibrugarh districts, of the northeastern State of Assam. The overall VE was 77 per cent (95% CI: 67–83). The VE decreased from 91 per cent in the first year of vaccination to 71 per cent at six yr post-vaccination[28]. It was found that, adults were more affected in a JE outbreak[29] in Assam. We could retrieve a few more research articles highlighting the evidence of the occurrence of JE in adults and preventive strategies in India[30-32].

In 2024, a retrospective cohort study was conducted to investigate the outbreak of measles among young college students (18-24 yr) in Pune, India. Among 31 suspected cases, 12 were tested, of which seven were positive for measles-specific IgM antibodies. All these cases received the measles vaccine in childhood[33], indicating the waning of immunity over a period of time following childhood immunization. The investigators highlighted the importance of adult measles vaccination. Studies on the measles vaccine were few. They dealt mainly with seroprevalence and susceptibility to measles among adults in India[34-36].

A cross-sectional study[37], from a paediatric ophthalmology hospital in Madurai, south India, highlighted the proneness of healthcare workers (HCWs) to rubella infection. About a tenth of the selected HCWs in this hospital were found to be rubella

seronegative and thus vulnerable. Vaccinating these seronegative HCWs with RA 27/3 rubella vaccine mounted good protective immune responses. Such result prompted the researchers to raise an advocacy point highlighting the need for rubella vaccination among hospital staff. A few other studies from our search reiterated the need for rubella vaccine in adult females before pregnancy in India[38,39].

In two studies from New Delhi, only about 55 per cent of the HCWs were vaccinated against HBV[40,41]. This highlighted the existing gap in vaccine coverage. Another investigation from an institute in Mumbai, recorded the incidence of needle stick injury among HCWs to be 10.4/100 occupied bed per year, and only 64.2 per cent of the HCWs in this investigation had prior vaccination against Hepatitis B[42].

Pneumococcal infection; serotypes included in vaccines *vs.* circulating types: A systematic review and meta-analysis revealed that approximately one fifth of adult Indian patients with community-acquired pneumonia (CAP) had *S pneumonae* infection, contributing a significant burden of CAP in India[43]. Three cross-sectional studies during 2007-2017[44-46], investigated if circulating pneumococcal strains (serotypes) in the communities were covered by the existing pneumococcal vaccines. A study from Vellore[44] revealed that serotype coverage offered by the pneumococcal conjugate vaccines (PCV) PCV7, PCV10, PCV13, and pneumococcal polysaccharide vaccine (PPV) PPV23 were 29, 53, 64, and 73 per cent, respectively. The coverage for the same serotypes was 16, 24, 48 and 66 per cent, respectively in New Delhi[45]. This study also found 30 per cent of the isolates were of non-vaccine serotypes among patients ≥50 yr of age with CAP. In a prospective laboratory survey of Invasive Pneumococcal Diseases (IPDs) among individuals aged ≥18 yr in a South Indian tertiary care referral centre[46], the protective coverage was 58.7 and 67.4 per cent respectively for PCV13 and PPV 23.

Typhoid; benefits of adult vaccination: In 2004, a contingent valuation (CV) survey was conducted in Kolkata, India to generate information on private demand for cholera and typhoid vaccines. The median private economic benefits of providing a typhoid vaccine to a household with five members were estimated to be about US$ 23 in a middle-income neighbourhood, and for a cholera vaccine, it was US$ 27. In this investigation, the estimated benefits were different in slum settings; US$ 14 for typhoid and US$ 15 for a cholera vaccine[47].

A Kolkata-based modelling study done to assess the economic benefits of typhoid vaccine revealed that three typhoid-vaccination strategies (targeting only enrolled school children, targeting all children, and targeting adults and children) were 'very cost-effective'[48]. On the other hand, in an urban slum in New Delhi, the mean total cost (patient and provider) of typhoid fever was US$ 126, with a hospitalized case costing much higher at US$ 636[49]. In a Kolkata-based study, the cost was US$ 72.71[50]. The benefits and cost of vaccination against typhoid were evident through such contrast. The study conducted by Severe Enteric Fever of India (SEFI) network at 18 sites across India (2017-2020), revealed that the mean cost of severe enteric fever was US$ 119.1. This study highlighted that the cost was likely to increase with emerging antimicrobial resistance, and emphasized the importance of preventive measures[51]. The safety, clinical acceptability and immunogenicity of typhoid conjugate vaccine (TCV) among adults was highlighted in another investgation[52]. Importantly, a study in South India is currently ongoing to determine the relative and absolute rate reduction of symptomatic, blood culture-confirmed *S. Typhi* infection with TCV[53].

Diphtheria & tetanus; lack of protective immunity in adults: In the infectious disease hospital, Kolkata, 200 diphtheria patients were evaluated for demographic details, immunization status, clinical features, complications, and outcome. Adults ≥20 yr comprised 32 per cent of the total cases[54]. Another retrospective study was conducted on 241 confirmed diphtheria patients admitted to the same hospital, where the majority (50.6%) were ≥15 yr old. Only 27.4 per cent were fully immunized and the rest were either partially immunized (44.4%) or non-immunized (28.2%)[55]. The Delhi study[56] conducted among 255 healthy adult participants in 2009 revealed that 53 per cent of adults were unprotected against diphtheria, and 47 per cent were susceptible to tetanus. Two more studies[57,58] dealt with the prevalence of diphtheria among adult population in Jaipur, and Dibrugarh. Such findings underlined the needs for adult vaccination against these bacterial infections.

According to NFHS-5 report, 70 per cent mothers had antenatal check up in the first trimester, 58.1 per cent had at least four antenatal visits and 92 per cent of

them were protected against neonatal tetanus in the last birth by adequate immunization[11].

Vaccination in adults and awareness tools: We included maternal health and vaccination articles in the present review. Gandhi *et al*[59], examined the NFHS-4 data and the Public Affairs Index to assess inequalities in the coverage of reproductive maternal new born and child health (RMNCH). It was found that there was erratic distribution of RMNCH coverage.

Another study from the State of Jammu and Kashmir[60] in northern India used NFHS-4 data, the Census of India and Digest of Statistics to reveal a gap of 10.5 per cent for immunization and found a moderate negative correlation between the coverage gap and socioeconomic development[60]. Inadequate coverage of 'quality ante-natal care' was also indicated in other investigations[61-65] using State or nationally representative data sources (NFHS-4 and NFHS-5).

Importantly, in a multi-centric (4 States) community-based study of older adults (>60 yr) in July 2018 on Influenza and respiratory syncytial virus (RSV) in India[66], all four sites reported negligible influenza vaccination uptake (0.1-0.4%), low health insurance coverage (0.4-22%) and high tobacco use (19-52%). In another study on 72,250 adults (aged ≥45 yr), uptake of each of influenza, pneumococcal, typhoid and hepatitis B vaccine was less than two per cent[67].

A few articles[68,69] presented mobile messaging as a potential maternal and child healthcare tool. In a rural community-based study in 2013 in Vellore, Tamil Nadu[68], 70 per cent of the individuals were willing to receive health information *via* text messages, and 98 per cent believed text messages could effectively spread health messages, including vaccination. However, reach, accessibility, and acceptance of different channels for health promotion, such as MobileApp (*Saheli* in Haryana)[69], television, newspapers, health facilities, service providers, radio and other media (posters, pamphlets and various folk-art forms) were explored in large numbers during the COVID-19 pandemic[70].

Vaccine hesitancy/acceptance: pre-COVID-19 & COVID-19 era: Articles dealing with vaccine hesitancy or acceptance in adults in India were published in considerable numbers following the COVID-19 pandemic. Among the 50 articles retrieved, only five were related to diseases other than COVID-19. While the majority of these studies were quantitative, qualitative investigations were few.

A cross-sectional study conducted from December 2020 to June 2021 in Mysuru, identified the factors associated with hesitancy and refusal of vaccines[71]. Although this was conducted during the pandemic time, the investigation focused on vaccines other than COVID-19. The reasons associated with vaccine hesitancy were as follows: (*i*) study participants did not think them as needed (46%); (*ii*) some considered vaccines unsafe (12%); and (*iii*) lack of awareness about places to go to and get vaccinated (7%). The study recorded that UIP vaccines were more acceptable among the public than non-UIP vaccines due to more 'reliability and safety' and their 'worldwide acceptance'. Interestingly, prior to initiation of COVID-19 vaccination programme in India, a group of researchers explored vaccine hesitancy among the medical students and doctors and their immediate family members in Delhi[72]. The reasons for vaccine hesitancy were, (*i*) fear of side effects (51%); (*ii*) lack of awareness about the vaccines (49%); and (*iii*) the lack of national guidelines on adult vaccination (33%). The hesitancy for vaccine was highest for zoster (98%) and least for tetanus toxoid (58%). Significant hesitancy was also observed for pneumococcal, HPV, influenza and varicella-zoster vaccines. A qualitative study[73] to understand the awareness, perceptions and choices while recommending the HPV vaccine to parents of adolescent girls, identified several barriers, faced by physicians: (*i*) lack of national-level guidance on the age, eligibility, and dosage; (*ii*) lack of opportunity to discuss the routine adolescent vaccines due to absence of practice-level contact with well or non-sick adolescents; and (*iii*) out-of-pocket expenditure and vaccine availability.

Similarly, the studies on COVID-19 vaccine hesitancy were cross-sectional in design. In the northern district of Rajasthan[74], psychological antecedents and predictors of COVID-19 vaccine hesitancy among patients with chronic disease were studied. A study by Gupta *et al*[75], described COVID-19 vaccine hesitancy among 80 per cent of pregnant women in Manipur. Another study[76] conducted at a tertiary care centre in Kalyani, West Bengal, measured willingness to pay (WTP) for the COVID-19 vaccines among participants and their children. Although more than half of the adult respondents were unwilling to pay for vaccines for themselves, WTP for COVID-19 vaccination was higher for their children. The Indian Institute of Sciences, Bangalore, dealt with the role of leadership

Box. Indian consensus on recommendation of adult vaccines* based on age[88]

Age group (yr)	Recommended vaccines
18-49	Chicken pox, cholera (at risk), COVID-19 (pandemic or epidemic), HBV, HPV, influenza, MMR, meningococcal, rabies (post exposure), TdaP (every 10 yr), yellow fever (travelling to an endemic country), when there is additional risk factors-typhoid, Japanese encephalitis, HIB, HAV, HIB, rabies (pre exposure)
50–64	HBV, influenza, meningococcal, pneumococcal, TdaP (every 10 yr), shingles, rabies (post exposure), COVID-19 (pandemic or epidemic), yellow fever (travelling to an endemic country), when there is additional risk factors-typhoid, JE, HIB, HAV, HIB, cholera, rabies (pre exposure)
≥65	HBV, influenza, pneumococcal, TdaP (every 10 yr), shingles, RSV (above 60 yr age) rabies (post exposure), COVID-19 (pandemic or epidemic), yellow fever (travelling to an endemic country), when there is additional risk factors-typhoid, Japanese encephalitis, HIB, HAV, rabies (pre exposure)

*HIB, hemophilus influenza B; HAV, hepatitis A virus; RSV, respiratory syncytial virus

and incentive-based programmes in addressing vaccine hesitancy[77]. It concluded that political and community leaders had minimal role in encouraging COVID-19 vaccination. The role of timely, and accurate information, applications of telemedicine, and the need for optimal design of incentive-based vaccination programmes to get adequate coverage were highlighted. Community based studies were conducted in different urban and rural settings of India in Puducherry, Maharashtra (Pune), Tamil Nadu (Chengelput), and Uttar Pradesh (Kanpur). Respondents who had no acceptance for vaccine cited reasons like 'fear of side effects', 'not effective', 'I am healthy', and 'I don't need them'. Association of vaccine hesitancy with specific gender, age group, educational status or socio-economic position were not consistent including those involving health workers[78-80]. A few of the studies, explored trust in the government, source of information about the vaccine and political affiliation as explanatory variables[81].

Among the few qualitative studies, the one conducted in Chennai, Tamil Nadu[82], healthcare workers, religious leaders, community influencers, local administrators and representatives of marginalized communities were interviewed in-depth. The following five domains were explored (*i*) vaccine availability, (*ii*) trust in COVID-19 vaccines, (*iii*) vaccine-related concerns, (*iv*) health/risk balance and (*v*) vaccine prioritization. Eagerness to receive COVID-19 vaccines was linked with 'freedom from fear', 'possible restoration of normalcy', 'protection of family' and 'ability to travel and work abroad'. Doubts surrounding safety and the fear of side effects of the COVID-19 vaccine were feeders to vaccine hesitancy. Despite such hesitancy, 70 per cent of the Indian adult population had been fully vaccinated and 93 per cent had received their first dose, just one yr after the launch of COVID-19 vaccination drive on January 16, 2022. Moreover, India delivered the highest single-day vaccinations of 25 million doses on September 17, 2021[83].

Adult vaccination guidelines: The Geriatric Society of India[84], the Research Society for the study of Diabetes in India[85], the Indian Society of Nephrology[86], and the Federation of Obstetric and Gynaecological Societies of India[87] issued adult vaccination guidelines at various time points. Importantly, the Association of Physicians of India (API), in collaboration with the other associations and 'Societies of Subject Experts' in the country, brought out an exhaustive adult immunization consensus guideline in 2024. 'Bridging the childhood vaccines' in adult healthcare has been underlined in this consensus guideline. Vaccines like rotavirus and BCG (Bacillus Calmette-Guérin), which are conventionally administered in the pediatric age group, may find their role in the adult population in some particular circumstances like immunocompromised conditions and among HCWs, *etc*. Box highlights the consensus recommendation for vaccines in the elderly population belonging to the selected age group in India[88].

Although the measles and rubella (MR) vaccine is included in the national immunization schedule for children in India, mumps is not included. However, MMR (measles, mumps, rubella) vaccination has been recommended for adults by different medical societies like API, FOGSI, *etc*[88]. As there is not enough evidence to suggest that mumps is a disease of public health importance[89], MR vaccine was incorporated in EPI in 2017-19[3].

Indian Consensus Guideline on adult immunization recommends at least one dose of Tdap (Tetanus, diphtheria, acellular pertussis) vaccine during each

pregnancy, preferably between 27 and 36 wk of gestation[88].

Two vaccines for dengue are now prequalified by WHO[90]; however, those vaccines are yet to be licensed in India. A phase 3 trial of India's first indigenous tetravalent dengue vaccine is currently underway[91]. Likewise, efforts are ongoing to prevent infections such as HIV, malaria, tuberculosis and leprosy[88] through adult immunization.

Discussion

This rapid review has synthesized available in-country evidence around gaps in adult vaccination in India and identified programme and policy needs. Researchers all across the country generated information on viral and bacterial infections and their long-term impact, which led to subsequent programmatic discussions and helped develop adult immunization guidelines. For example, globally 27 per cent of the cervical cancer cases are contributed by India. The current estimates indicate that approximately 1,00,000 new cases were diagnosed and 60,000 deaths occurred annually in the country, accounting nearly 1/3rd of the global cervical cancer deaths[92]. HPV vaccination has a huge potential to change this scenario. Noticeably HPV vaccine constitutes a key component of the WHO strategy for worldwide elimination of cervical cancer[12]. However, several barriers, such as high costs and low public awareness, prohibit the introduction of prophylactic vaccines in countries like India, Nepal, Bangladesh, and Srilanka[93].

Noticeably, influenza viral infection has immediate relevance to adults with or without comorbidities. There are indications for influenza vaccines in adults belonging to the high-risk groups in South Asian countries[94]. The National Centre for Disease Control (NCDC) has reported 6351 cases of influenza, with 132 deaths in India as of 2024[95]. In this context, it is important to note that influenza vaccination has recently gained due attention and has found home in recommendations in the national guidelines in South Asian countries, including India[94]. However, the present uptake is less than two per cent among adults aged ≥45 yr[20], which is of great concern.

Similarly, it is important to recognize that respiratory syncytial virus (RSV) is one of the important viral pathogens identified in older adults with acute respiratory tract infection[96]. Though we could not find any Indian data on the same, globally, vaccine trials are ongoing against RSV among older adults[97]. Other than respiratory tract infection (RTI) causing viruses, other viral infections in adults, which are of public health importance are JE, MR and Hepatitis B (Box).

In Japan, the Republic of Korea, and Taiwan (China), the introduction of the JE vaccine in routine childhood vaccination programmes began about 50 yr ago. Combined with this, increased urbanization and improved agricultural practices resulted in the elimination of JE from these countries[98]. JE vaccine was introduced in UIP-India, for children only in the year 2013. On the other hand, occurrence of JE in adults in parts of India are matter of concern, as cited above. The latest consensus guideline addresses this concern (Box).

In contrast, measles vaccine is presently a part of UIP and the consensus guideline recommends it for adults in the age group of 18-49 yr[88]. Similarly, the Hepatitis B vaccine was included in UIP for children. However, the consensus guideline now recommends it for adults, with and without co-morbidities like chronic kidney diseases, chronic liver diseases, *etc*[88]. Further, HCWs constitute a group, which is vulnerable to HBV and rubella due to occupational exposure. Notably, 37% of Hepatitis B Virus (HBV) infections among Health Care Workers (HCWs) are due to percutaneous occupational exposure to body fluids[99]. According to WHO, the estimates of Hepatitis B vaccine, among HCWs vary from 18 per cent in Africa to 77 per cent in Australia and New Zealand[40].

Among bacterial diseases in adults, those caused by pneumococcal infection provides opportunities for prevention through vaccination. In the population aged <2 and ≥ 65 yr, the highest rates of invasive pneumococcal diseases (IPDs), have been reported. The mortality rates in these conditions are very high in individuals ≥ 65 yr of age due to depleting immune mechanisms and associated co-morbid conditions[45]. This highlights the importance of investigations from different regions of India[44-46], which examined the extent of protective coverage offered by existing pneumococcal vaccines in the country, *vis- a-vis* circulating serotypes.

Another bacterial infection in adults of considerable public health importance is typhoid. The estimated economic benefits of providing typhoid vaccines in low- and middle-income settings in India have been captured in this rapid review. The World Health Organization (WHO) recommended introducing

typhoid conjugate vaccine (TCV) in lower- and middle-income countries (LMICs). However, this requires substantial investment. With only 1.15 per cent of gross domestic product public spending towards health care, India's vaccination programme has been slow to introduce new vaccines and relies heavily on out-of-pocket payments for treatment[100].

The lack of protective immunity against diphtheria and tetanus in adults, as highlighted in this review, requires urgent attention. The only existing adult vaccination initiative in India caters to pregnant women. Noticeably, tetanus toxoid (TT) vaccine was replaced by tetanus diphtheria (Td) in UIP-India schedule. As per NHFS-5, there was increased antenatal check-up, antenatal visits, and past protection against neonatal tetanus as compared to NFHS-4[11], which led the country to validate for maternal and neonatal tetanus elimination by mid-April 2015 with the help of multilateral development partners such as WHO, UNICEF and others[101].

Preventing tuberculosis in adults through vaccines poses the greatest hurdle, as an efficacious vaccine is yet to be available for different ages[102-111]. Although the retrospective data analysis of a community-based trial at Chingleput revealed that BCG revaccination in a community could offer modest protection against the development of TB disease at the end of 15 yr[112], researchers have suggested that benefit might be obtained by re-vaccinating adults in the age group of 14-25 yr with BCG[102,103].

In 2015, the WHO Strategic Advisory Group of Experts on Immunization defined vaccine hesitancy as a delay in acceptance or refusal of vaccination despite the availability of vaccination services, which can vary across time, place, and vaccines and is influenced by factors such as complacency, convenience, and confidence. WHO identified it as one of the top ten global health threats in 2019[113]. In recent times the COVID-19 pandemic and vaccination against COVID-19 brought such issues again to the fore. The concerns leading to vaccine hesitancy among the recipients generally constitute safety, science, efficacy, side effects, availability and a belief that they have sufficient immunity to combat. Also, in some studies age, sex, education and religion played important roles[114-119]. Addressing such issues during adult vaccination programmes thus appears paramount.

The lack of an adequate number of studies focussing on the effects of adult vaccination on reducing their morbidity and mortality, as well as hospital admissions following vaccine-preventable infections, did not allow us to present detailed critical insight on the topic.

In conclusion, the implementation of adult vaccination in India would require: (*i*) increasing awareness about the seriousness of vaccine-preventable diseases in the community and HCWs, (*ii*) engaging healthcare systems including government and community-based organizations effectively, and (*iii*) conducting research around development and production of affordable, safe, and effective vaccines in Indian context. Considering the changing epidemiology of the diseases[7], developing appropriate communication strategies and tools[120] will be the key for reaping the benefits of such interventions. The COVID-19 pandemic has also underlined the vulnerabilities of the elderly and adults with comorbidities to emerging and re-emerging microbial pathogens, which further highlights the importance of improving the situation of the poor uptake of adult immunizations across the country.

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Supplementary Table. Search strategy for PubMed as on June 27, 2024 at 11.10 am

#	Conceptualization	Search string	Result
1	Intervention – Individual level	"Immunization" [Mesh] OR "Vaccination" [Mesh] OR "Vaccine-Preventable Diseases" [Mesh] OR Immunization OR Vaccination OR "Vaccine-Preventable Diseases" OR VPD OR "Anthrax Vaccines" [Mesh] OR "Cholera Vaccines" [Mesh] OR "COVID-19 Vaccines" [Mesh] OR "Diphtheria-Tetanus Vaccine" [Mesh] OR "Diphtheria-Tetanus-acellular Pertussis Vaccines" [Mesh] OR "Pertussis Vaccine" [Mesh] OR "Tetanus Toxoid" [Mesh] OR "Influenza Vaccines" [Mesh] OR "Hepatitis A Vaccines" [Mesh] OR "Hepatitis B Vaccines" [Mesh] OR "Papillomavirus Vaccines" [Mesh] OR "Japanese Encephalitis Vaccines" [Mesh] OR "Meningococcal Vaccines" [Mesh] OR "Pneumococcal Vaccines" [Mesh] OR "Poliovirus Vaccines" [Mesh] OR "Rabies Vaccines" [Mesh] OR "Respiratory Syncytial Virus Vaccines" [Mesh] OR "Measles-Mumps-Rubella Vaccine" [Mesh] OR "Measles Vaccine" [Mesh] OR "Rubella Vaccine" [Mesh] OR "Mumps Vaccine" [Mesh] OR "Typhoid-Paratyphoid Vaccines" [Mesh] OR "Herpes Zoster Vaccine" [Mesh] OR "Yellow Fever Vaccine" [Mesh] OR "measles, mumps, rubella, varicella vaccine" [Supplementary Concept] OR "Chickenpox Vaccine" [Mesh] OR "Anthrax Vaccines" OR "Cholera Vaccines" OR "COVID-19 Vaccines" OR "Diphtheria-Tetanus Vaccine" OR "Diphtheria-Tetanus-acellular Pertussis Vaccines" OR "Pertussis Vaccine" OR "Tetanus Toxoid" OR "Influenza Vaccines" OR "Hepatitis A Vaccines" OR "Hepatitis B Vaccines" OR "Papillomavirus Vaccines" OR "Japanese Encephalitis Vaccines" OR "Meningococcal Vaccines" OR "Pneumococcal Vaccines" OR "Poliovirus Vaccines" OR "Rabies Vaccines" OR "Respiratory Syncytial Virus Vaccines" OR "Measles-Mumps-Rubella Vaccine" OR "Measles Vaccine" OR "Rubella Vaccine" OR "Mumps Vaccine" OR "Typhoid-Paratyphoid Vaccines" OR "Herpes Zoster Vaccine" OR "Yellow Fever Vaccine" OR "Varicella Vaccine" OR "Chickenpox Vaccine" OR "MPox Vaccine" OR "Haemophilus Influenzae Type B Vaccine"	1830970
2	Intervention – Policy & Program level	"Immunization Programs" [Mesh] OR "Mass Vaccination" [Mesh] OR "Immunization Schedule" [Mesh] OR "Vaccine Policy" OR "Vaccination Policy" OR "Vaccine Program" OR "Vaccination Program" OR "National Technical Advisory Group on Immunization" OR NTAGI OR "Universal Immunization Program" OR "Expanded Program of Immunization" OR EPI OR UIP OR ("Guidelines as Topic" [Mesh] AND "Vaccination" [Mesh]) OR "Guidelines for adult vaccination" OR "Elderly Vaccination" OR "Vaccination for Elderly" OR "Vaccination for Geriatric" OR "Vaccination in Pregnancy" OR "Vaccination for Pregnant Women"	139223
3	#1 OR #2		1863445
4	Population - #3. Filter: Adult 19+ years		289444
5	Outcome - Quantitative	"Vaccination Coverage" [Mesh] OR "Quality-Adjusted Life Years" [Mesh] OR "Life Expectancy" [Mesh] OR "Health Expenditures" [Mesh] OR Reach OR Coverage OR "Vaccine uptake" OR "Life Saved" OR "Complications Avoided" OR "Complications Averted" OR "Life Expectancy" OR "Economic Loss" OR DALY OR QALY OR "Out-of-pocket Expense*" OR "Out of Pocket Expense*"	1037129
6	Outcome - Qualitative	"Vaccination Hesitancy" [Mesh] OR "Vaccination Refusal" [Mesh] OR "Anxiety" [Mesh] OR Hesitancy OR Anxiety OR Denial OR Antivaxxer OR "Anti-vaccinationism" OR "Anti-vaccinationist" OR (("Cost of Illness" [Mesh] OR "Mortality" [Mesh] OR "Morbidity" [Mesh]) AND reduced) OR "Reduced Mortality" OR "Reduced Morbidity" OR "Reduced Burden of Disease" OR "Reduced Disease Burden" OR "Vaccination Refusal"	526209
7	#5 OR #6		1534897
8	Setting – Country level	India	838561
9	Setting – States / UT level	"Andhra Pradesh" OR "Arunachal Pradesh" OR Assam OR Bihar OR Chhattisgarh OR Goa OR Gujarat OR Haryana OR "Himachal Pradesh" OR Jharkhand OR Karnataka OR Kerala OR "Madhya Pradesh" OR Maharashtra OR Manipur OR Meghalaya OR Mizoram OR Nagaland OR Odisha OR Orissa OR Punjab OR Rajasthan OR Sikkim OR "Tamil Nadu" OR Telangana OR Tripura OR Uttarakhand OR "Uttar Pradesh" OR "West Bengal" OR "Andaman and Nicobar Islands" OR "Dadar and Nagar Haveli" OR "Daman & Diu" OR Chandigarh OR Jammu OR Kashmir OR Ladakh OR Lakshadweep OR Pondicherry OR Puducherry OR Delhi	503657
10	#8 OR #9		864363
11	#4 AND #7 AND #10		517