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REVIEW

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Drivers of and barriers to routine adult vaccination: A systematic literature review

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ABSTRACT

We performed a systematic literature review in PubMed and Embase (2016–2021) to investigate the drivers of and barriers to routine vaccination in adults aged 50 and older globally. A thematic assessment identified three categories across 61 publications: sociodemographic, health-related, and attitudinal. The most common sociodemographic determinants (factors identified in studies; n = 47) associated with vaccination uptake were economic status, age, education, and household composition, which had mixed effects on vaccine uptake. For health-related determinants (n = 27), individuals with comorbidities and health care consumption were the most common factors, both increased vaccine uptake. The most common attitudinal factors (n = 42) were self-efficacy, provider or other's recommendations, and vaccine-preventable disease awareness; across studies, all attitude factors had a positive effect, unlike the socio-demographic and health status categories. Findings suggest that patient and provider awareness and education campaigns are effective ways to increase uptake of routine vaccinations in older adults.

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Introduction

Older adults (65 years or older) constitute a large and growing proportion of the world's population.[1] The World Health Organization (WHO) estimates that between 2015 and 2050, the population aged ≥60 years will nearly double globally.[2] With age comes immunosenescence, leading to increased vulnerability to infectious diseases and a need to boost immunity in this population.[3,4] Vaccination is one of the most life-saving and cost-saving interventions in the history of health care.[5] Each year in the United States, influenza vaccination prevents more than 7 million illnesses and 90,000 hospitalizations, the latter mostly in older adults (ages ≥65).[6] Vaccines also provide economic benefits; one review estimated that for every euro spent on influenza vaccination for older adults in the United Kingdom, €1.35 was saved by reduced medical spending elsewhere in the health care system.[7]

The United States Centers for Disease Control and Prevention (CDC) recommends routine vaccination against tetanus/diphtheria/pertussis (Tdap) and seasonal influenza for adults of all ages, herpes zoster for adults aged 50 years and older, and pneumococcus for adults aged 65 years and older.[8] However, there is much variation globally in recommendations for adult vaccination. For example in January 2022, of the 30 nations in the European Union/European Economic Area, 29 officially recommend influenza vaccine, 21 recommend pneumococcal vaccine, 19 recommend tetanus vaccine, and 7 recommend herpes zoster vaccine.[9] Additionally, the situation in low- and middle-income countries (LMICs) is unique, because public health policies, medical conditions and costs, health awareness, and vaccine availability differ from high income countries. There is a lack of epidemiologic information in many LMICs,[10] which precludes robust estimations of cost-effectiveness of vaccination,[11] leading to a lack of concrete guidance on vaccination practices.[12–14] However, available data indicate that some vaccine-preventable diseases have a greater burden in LMICs,[10,14] creating an impetus for developing vaccine delivery systems in these countries. Ortiz and Neuzil offer several suggestions for facilitating the implementation of influenza vaccination programs in LMICs, including development of vaccines that require fewer healthcare resources to administer, conducting clinical trials in LMIC settings to evaluate vaccine efficacy in terms of locally relevant outcomes, and integration of vaccine administration into current systems of primary care.[15]

Despite the demonstrated value of vaccines, adult vaccination rates in many countries remain suboptimal, even where there are publicly funded programs. For example, in the United States, the Healthy People 2020 goals for adult vaccination rates were 80% for influenza (for ages 18–64 years; 90% in adults over 65 years), 30% for herpes zoster, and 60% for pneumococcus (for ages 18–64 years at increased risk; 90% in adults over 65 years).[16] However, despite vaccination rate goals, based on data from the 2017–2018 National Health Interview Survey in the United States, influenza vaccination coverage among adults aged 50–64 years and those 65 years and over was 48% and 72%, respectively.[17] Only 23% of adults aged 19–64 years at increased risk and 69% of adults aged 65 years and over received the pneumococcal vaccine.[17] The goal for herpes zoster vaccine was met, with 35% of adults aged 60 years and over vaccinated.[17]

The goal set by the WHO resolution WHA56.19 for countries in the European region was 75% influenza vaccination coverage by 2010,[18] and this goal was adopted by the European

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Union for the 2014–2015 season.[19] In surveys conducted by the Vaccine European New Integrated Collaboration Effort (VENICE) consortium, the Netherlands was the only European country to meet the WHO goal for influenza vaccination by 2010. Vaccination rates for influenza in the 33 countries reporting coverage data for older adults in 2014–2015 ranged from 0.03% to 76.3%, with a median of 34%.[20] A slight improvement was observed during the 2016–2017 season, with a median coverage rate of 47%.[21] Studies from other countries report influenza vaccine coverage rates of less than 50% in adults aged 60 years and older in Australia,[22] China,[23] and Iran.[24] Over the past two years, the COVID-19 pandemic has adversely affected adult vaccination uptake, as indicated by a survey of 28,400 respondents from 26 middle- and high-income countries.[25]

To narrow the gap between vaccination rate targets and actual vaccination rates, a better understanding of the factors influencing vaccination uptake in older adults is needed. Recent systematic reviews of the factors affecting adult vaccination rates have covered specific interventions,[26,27] health care settings,[28] and world regions.[29] A comprehensive overview of adult vaccination barriers and drivers is lacking. Thus, we performed a systematic review of the literature on routine adult vaccinations, limited only by age (50 years or older), with the goal of identifying the drivers of and barriers to vaccine uptake in this population.

Methods

The review was conducted in accordance with the principles of narrative synthesis in systematic reviews[30] and is presented in accordance with the extension of the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines on scoping reviews.[31]

We conducted an electronic search on 1 February 2021, going back to 1 January 2016, using PubMed and Embase. The search algorithms are shown in Supplementary Table S1. We compiled all identified articles into a screening file, removed duplicates, and screened the remaining articles for eligibility using the inclusion and exclusion criteria outlined in Table 1. The primary inclusion criterion was the reporting of determinants (either drivers or barriers) of routine adult vaccination uptake. Article selection is illustrated in Figure 1. We selected articles based on their titles and abstracts during the first phase of screening; we then read each selected publication

Table 1. Inclusion and exclusion criteria for literature review study selection[a].

	Inclusion criteria	Exclusion criteria
Population	Human population over 50 years	Less than 50 years of age; populations out of scope (e.g., pregnant women and health care professionals)
Intervention	Routine vaccination programs	Vaccines out of scope (e.g., travel vaccines)
Comparator	Not applicable	Not applicable
Outcomes	Barriers and drivers (e.g., accessibility, behaviors and beliefs, availability of information, affordability, advocacy, policy[b])	Outcomes out of scope (e.g., studies investigating vaccine immunogenicity, efficacy, effectiveness); not about vaccines/vaccination, secondary outcomes
Study design	Any (except editorial or commentary paper)	Secondary research; editorial or commentary
Other	Written in English; published January 1, 2016, to January 31, 2021	

[a]Criteria are presented within the PICOS framework.
[b]Although this was included in the literature search, policy-related articles were not the subject of the current review.

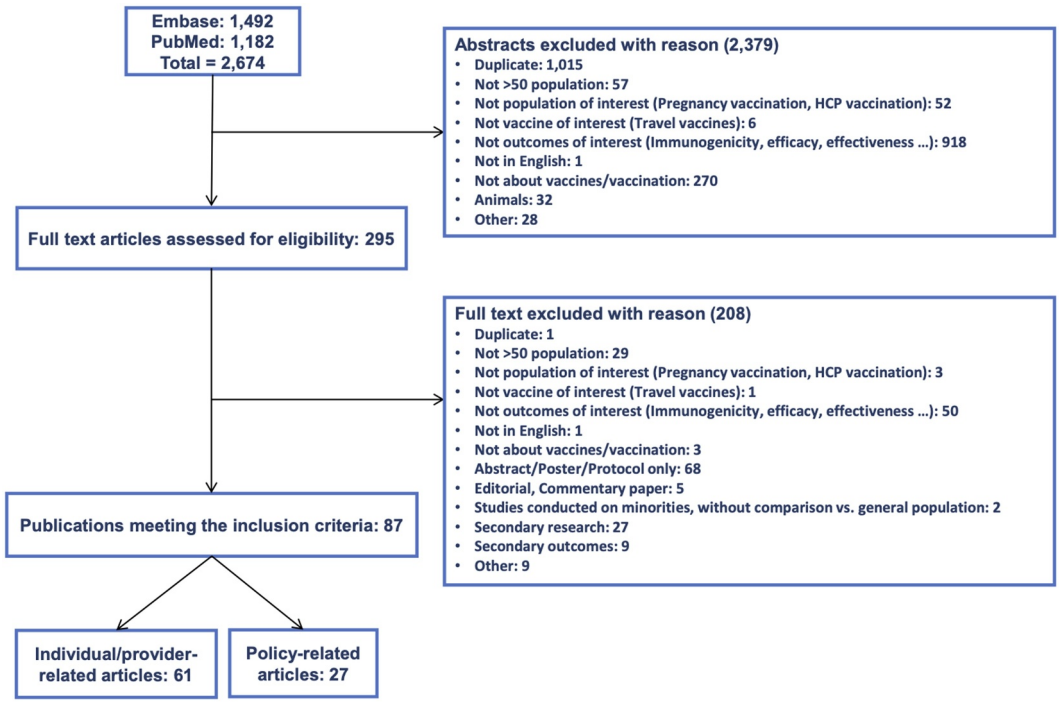

Figure 1. Flowchart of study selection process. One article fit into both final categories. Individual/provider-related articles (n = 61) were the subject of the current review.

in a second phase of screening, and articles were included or excluded based on the full text. All selections and rejections were confirmed by two different reviewers.

Items extracted from each selected article were as follows: title, authors, country/countries of origin, study design, study setting, number of subjects, and analysis type. Additional items of particular interest for this review were the vaccine(s) type being studied and the outcomes reported, including quantitative data on vaccination uptake and qualitative data on patient attitudes and experiences. Data were extracted into an Excel spreadsheet by one reviewer and checked for accuracy by a second reviewer.

We grouped determinants of routine adult vaccination into three categories: sociodemographic factors, health-related factors, and attitudinal factors (Table 2). Sociodemographic factors included items such as age, gender, ethnicity, education level, employment status, and health insurance coverage. Health-related factors included habits such as smoking, alcohol intake, and physical activity, as well as general functional status, the presence of comorbidities, and use of health care services. Attitudinal factors encompassed individual perceptions of the risk of disease and the benefits and risks of vaccination, as well as measures of self-efficacy (the ability to exercise control over one's own health) and social interactions with friends, family, and health care providers (HCPs) regarding vaccines.

Results

The search and screening process identified 87 publications (Figure 1), which we grouped according to whether they reported individual/provider-related determinants (n = 61) or policy/programmatic-related determinants of vaccination uptake (n = 27). Articles describing the individual/provider-related determinants are the subject of this manuscript.

The summary characteristics of the 61 studies included in this review are listed in Supplementary Table S2, including the author, study location, vaccines investigated, study population, study design, analysis type, and a summary of the results for each factor affecting vaccination. The majority of studies had a cross-sectional design (n = 46), while 14 were database analyses or medical records reviews, and one used mixed methods (cross-sectional and prospective components). Among these studies, 22 categories of factors affecting vaccine uptake were identified, which were organized into the three thematic categories shown in Table 2. Some studies contained multiple factors, with 47 studies reporting on sociodemographic factors,[32–78] 27 reporting on health-related factors,[32–34,36,37,40–42,45,46,48,50,53,54,57,61,62,72-81] and [42] reporting on attitudinal factors.[33,34,36,37-39,40,43–45,47,53-55,57,59,61,66–76,78–92] Four studies gathered data from HCPs, as opposed to individual adults.[54,59,82,91] Descriptive statistics for the 61 studies are shown in Figure 2. Most studies reported determinants of influenza vaccination (n = 49), and most originated in European countries (Italy had 13 publications), through the Middle East, the Far East, and North and South America were also represented. Ten studies were from LMICs: Brazil,[40,77] China,[38,39,72,78] Columbia,[32] Thailand,[47] and Turkey.[55,90]

Table 2. Categorization of themes and associated factors influencing routine adult vaccination.

Factor	Description (examples)
Sociodemographic	
Age	Age of individuals (not HCPs), included ages 50 and older
Gender	Male/female
Education levels	Highest achieved educational level (primary school, no education, university, etc.)
Household composition	Number and marital status of cohabitants (living alone, married, divorced, etc.)
Select population groups and communities	Variables related to the geopolitical or genetic origins of people (citizen, migrant, ethnic group, etc.)
Economic status	Income, socioeconomic status (deprivation score, social class, etc.)
Employment status	Variables related to paid work (unemployment, retirement, etc.)
Ease of access	Geographical setting (urban/rural), convenience of access (distance, logistics, availability)
Affordability	Cost of vaccine
Health insurance coverage	Variables related to health insurance (insured vs. uninsured, insurance plan subsidies, etc.)
Health status	
Smoking status	Current or past tobacco consumption (current, former, never a smoker)
Alcohol intake	Level of alcohol intake (abstention, use, abuse)
Physical activity	Participation in activities that require movement (level of physical activity, frequency of physical activity or sport, etc.)
Functional status	Variables related to the level of independence or disability (dependency, disability type and/or severity, impairment in daily activities, etc.)
Comorbidities	Co-existing chronic diseases and conditions (number or type of chronic diseases, Charlson comorbidity index, etc.)
Self-rated health	Individual-reported level of health (feeling healthy, feeling in poor health, etc.)
Health care consumption	Use of the health care system resources (number of GP visits, outpatient visits, etc.)
Attitude	
Perceived benefit	Benefits derived from vaccination (effectiveness, good benefit-risk ratio)
Perceived barriers	Perceived reasons not to get vaccinated (previous experience of side effects, fear of side effects after vaccination)
Perceived individual risk	Perceived susceptibility to disease and disease severity, leading to recognition of the value of vaccination (feeling at risk, feeling the vaccine is unnecessary)
Vaccine and disease awareness	Knowledge of the vaccine or the disease (knowing vaccine recommendations, being exposed to information on the media, forgetting about the vaccine, knowing other vaccinated individuals, receiving mail notification)
Self-efficacy	Beliefs a person holds regarding their power to affect situations and engagement in preventive behavior (previous vaccination, positive attitude toward vaccine, having a vaccination record, attending health screenings)
Recommendations to vaccinate	Advice on vaccination from health care professionals, family, or friends

The determinants of routine older adult vaccination were categorized as sociodemographic, health-related factors, and attitudinal factors (Figure 3). Economic status was the most frequently reported sociodemographic factor (in terms of the number of studies), while having a comorbidity and health care consumption were the most often reported health-related factors. Self-efficacy and recommendations about vaccination were the most frequent attitudinal factors documented in our review.

The heterogeneity of the studies in terms of designs, populations, and analyses precluded a quantitative meta-analysis. For

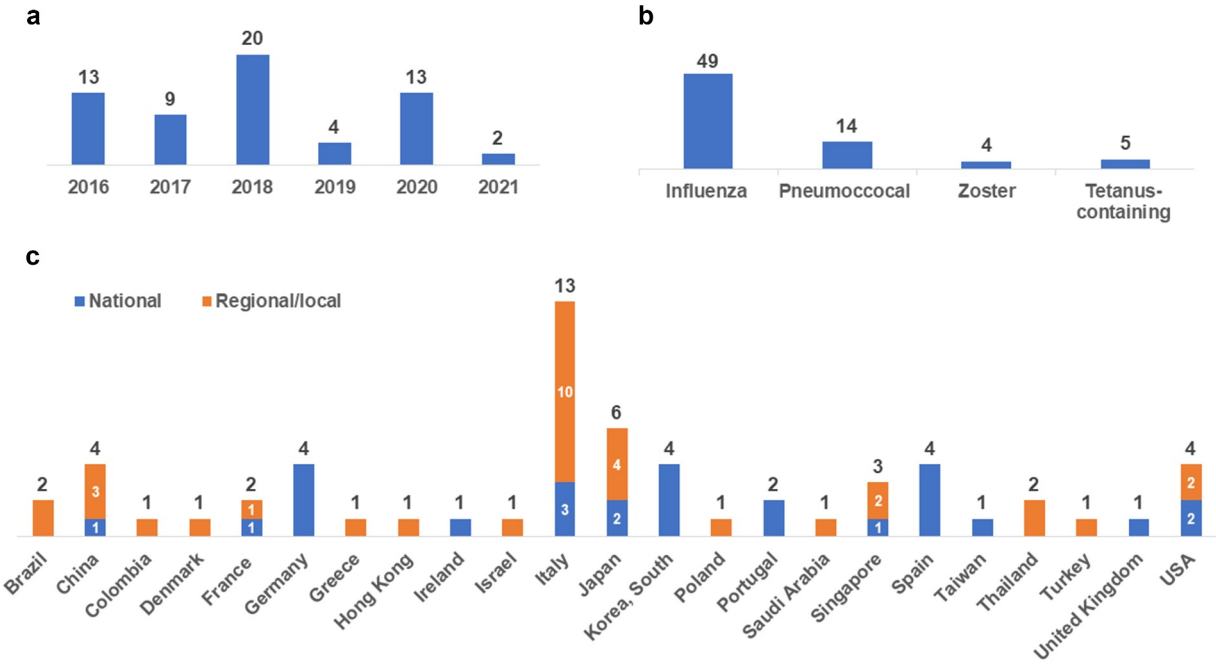

Figure 2. Descriptive statistics of included studies by (a) year, (b) vaccine, and (c) geographic location. Categories in panel B were not mutually exclusive, so the sum is >61.

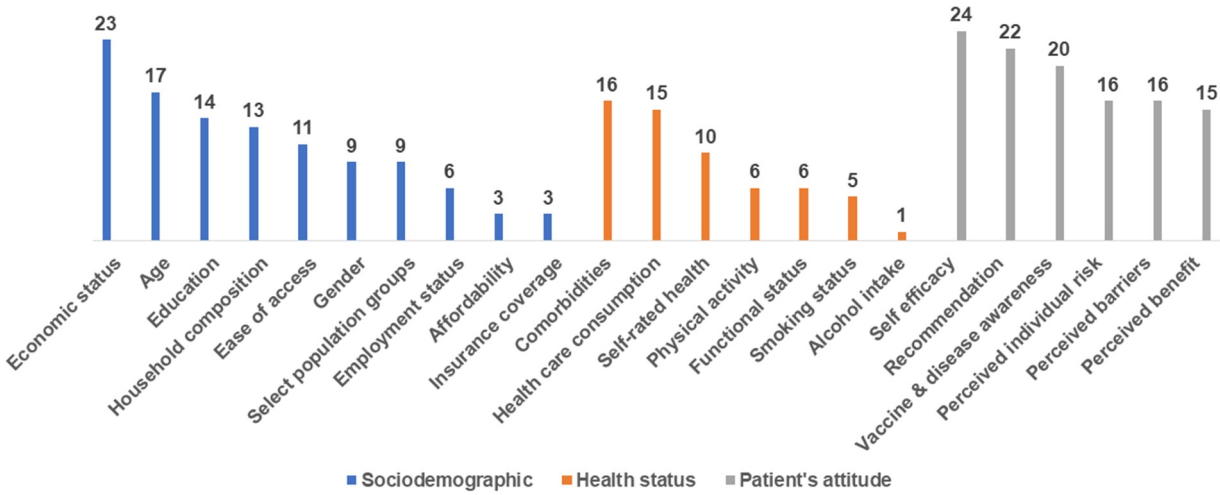

Figure 3. Distribution of studies by the factors impacting routine adult vaccination. The factors correspond to those listed in Table 2.

this reason, a narrative synthesis of findings is reported for each factor category. In each synthesis, the primary focus is on data from individual subjects, and data from HCPs is highlighted separately.

Sociodemographic factors

In studies assessing age and vaccination status, the association between age and vaccination varied by vaccine type. All influenza vaccination studies except one[45] found that older age was statistically significantly associated with greater vaccination uptake.[32,37,38,41,46,48,62,67-70,73,76] Self-reported pneumococcal vaccination was positively correlated with increasing age in two studies.[32,67] However, herpes zoster vaccine acceptability (i.e., being "in favor" of vaccination) was associated with younger age among individuals 50 or older,[43] and findings for tetanus vaccines were mixed.[32,67]

The association between gender and vaccination is unclear. Four studies found that being male was associated with higher influenza vaccination rates,[39,44,61,70] while two studies found that females were more likely to be vaccinated against influenza.[62,73] The latter studies were corroborated by two studies reporting that females had higher influenza vaccination rates than males.[57,74] Del Signore *et al.* 2020 found being a male to be positively associated with herpes zoster vaccination in France.[71]

Studies of select population groups and communities (terms to present results for these groups are derived from the original studies) generally found that immigrant populations, resident foreigners, and ethnic minority groups had lower vaccination uptake than native-born citizens or ethnic majority

groups.[33,35,49,51,56,60,65,70,74] A series of four studies from Italy found that the percentage of "foreigners and stateless persons" residing in a census district was associated with lower influenza vaccine coverage among adults aged 65 or older.[51,56,60,65] A national-level study from Italy found that African immigrants (but not immigrants from Europe, Asia and Oceania, or America) had a lower influenza vaccine coverage ratio than Italian citizens.[35] Similarly, among adults aged 65 or older in Spain, the "foreigner" population was less likely than those of Spanish nationality to be vaccinated against influenza.[70] A comparison of influenza vaccination in Medicare recipients (aged 65 or older) in the United States highlighted racial disparities, with vaccination rates of 49% for Whites, 48% for Asians, 33% for Blacks, and 29% for Hispanics.[74] Racial disparities were also seen in individuals aged 70 in England, where White-British, Indian, and Bangladeshi individuals received the zoster vaccine at rates of 55–61%, while vaccination rates were significantly lower in Black and mixed White/Black or White/Asian individuals.[49] Among older people (aged 65 or older) with disabilities in Taiwan, aboriginal descent was a significant predictor of non-vaccination against influenza.[33]

In assessments of household composition, most studies (11 of 13) showed that being married or living in a larger household (more than two people), compared with living alone, was associated with being vaccinated against influenza.[33,34-37,46-51,53-56,60-65,77] However, two studies from Singapore found that being married was negatively associated with influenza vaccination and that having previously been married (i.e., currently separated, divorced, or widowed) was positively associated with pneumococcal vaccination.[41,50]

Findings were also mixed with regard to education levels. Education was defined in a variety of ways across the studies in this group, and what was considered a "high" level of education differed by local context. Ten studies demonstrated a positive association between higher levels of education and vaccination.[33,37,38,47,50,55,66,72,73,78] Of these, seven were conducted in Asian countries.[33,37,38,47,50,72,78] In contrast, four studies found a negative relationship between higher levels of education and vaccination.[44,53,61,65] In South Korea, a high school or college-level education (vs. middle school) was negatively associated with influenza vaccination for individuals aged 50–64.[53] In Spain, lower levels of education (none vs. any primary, secondary, or university education) were positively associated with vaccination,[44] and in France, having a bachelor's degree (but not a master's or higher degree, and not a high school education) was positively associated with vaccine hesitancy (hesitancy was defined as refusal or delay of vaccination, or vaccination despite having doubts about efficacy).[61]

Four studies found an association between employment status, specifically unemployment or retirement, and higher vaccination rates.[40,41,53,73] Conversely, two studies conducted at a local level in Italy found a negative correlation between living in an area with an increasing unemployment rate and vaccination rates of individuals aged ≥65.[52,65] One study from Korea noted a negative association of vaccination with blue-collar vs. white-collar positions.[53]

Economic status was the most frequently identified sociodemographic factor, but the results regarding its association with vaccination were mixed. Ten studies reported a positive relationship between higher income status or socioeconomic class and vaccination (or, conversely, a negative relationship between greater deprivation or lower income and vaccination).[36,40,41,49,50,54–56,60,75,78] Seven studies found the opposite – that higher economic status was associated with decreased likelihood of vaccination.[32,38,39,44,51,52,65] One study analyzed data separately for men and women of different age groups (50–64 and ≥65)[53] and found that, among men aged 50–64, moderate-high (vs. low) family income had a statistically significant negative association with influenza vaccination. The results in women differed by age group, with moderate-high (vs. low) family income being negatively associated with influenza vaccination among women aged 50–64, but high family income (vs. low) having a positive association with vaccination among women aged ≥65.[53]

Three studies conducted in various municipalities in Italy found that vaccination coverage was lowest at the two extremes of the socioeconomic and health deprivation index, a 5-tier classification system that defines socioeconomic status based on factors such as demographics, housing conditions, and occupational status.[58,63,64] The authors explained this phenomenon as potentially the result of anti-vaccination campaigns, which may have produced an exaggerated perception of potential vaccine risks in the higher socioeconomic classes,[64] or as the effect of different responses to recommendations on disease prevention, probably due to different cultural norms.[58] However, several similarly designed Italian studies observed linear trends of higher vaccination with higher deprivation[52,65] or lower vaccination with higher deprivation,[56,60] as noted above.

A positive association between insurance coverage and vaccination against influenza, pneumococcus, and tetanus was established in three studies.[32,42,78] Affordability was also influential in increasing vaccination uptake, as high cost was given as a reason for non-vaccination among individuals in Poland,[45] and no-cost vaccination access was shown to be a facilitator of vaccination in Ireland.[36] From the HCP perspective, free vaccination was noted by nurses in Israel as a facilitator of influenza vaccination.[54]

There was no clear trend in vaccination uptake between rural and urban areas. Studies from Poland, the United States, and Turkey reported higher vaccination rates in individuals in urban centers compared to rural areas,[45,55,74] while individuals in rural areas had greater vaccination uptake in China, South Korea, and Portugal.[38,39,62,76] For studies looking at overall ease of access, convenience was found to be positively related to vaccination in adult individuals,[45,47,54,59,71] with nurses mentioning on-site vaccination and priority lines as facilitators and difficulty going to the clinic and lack of vaccine availability as barriers to vaccination.[54]

Health-related factors

Among health-related factor studies, a positive relationship between influenza vaccine uptake and the presence of comorbidities (vs. the absence of comorbidities) was observed in 13 out of 15 studies.[34,40,41,45,46,62,70,73–76,78] Three studies found a proportional correlation between the absolute number of

comorbidities and the likelihood of vaccination.[32,62,70] Individuals with specific comorbidities including chronic lung disease,[72,73] cardiovascular disease,[73,78] metabolic disorders,[73] cancer,[73] and mental health diagnoses[75] were more likely to receive influenza vaccination. In contrast, two studies from the United States reported a negative association between the presence of comorbidities and influenza vaccination.[42,75] Regarding other vaccines, Cano Gutierrez *et al.* 2016 established that individuals with comorbidities were more likely to self-report pneumococcal vaccination in Colombia, but the results were inconclusive for tetanus vaccination.[32] Watanabe *et al.* 2020 found the presence of chronic respiratory diseases to be positively associated with pneumococcal vaccination in Japan.[81]

Studies evaluating the association between health care consumption and adult vaccination unanimously reported a positive relationship for both influenza (n = 12) and pneumococcal (n = 2) vaccination.[33,34,40,41,46,48,50,57,68,74-77,79] Seven studies showed that vaccination was significantly positively associated with increased general practitioner (GP)/doctor visits, increased contacts with primary care, or having a regular GP to consult.[34,41,48,50,68,75,79] One study reported this positive association specifically in patients with chronic obstructive pulmonary disease,[48] while another reported a positive association of vaccination with outpatient visits in a disabled population aged 65 and older.[33] Two studies confirmed an increased frequency of vaccination when there was an increase in physician visits and government-subsidized prescriptions[74] or when contact with a GP increased via telephone consultations and office or home visits.[57]

Self-rated health was found to influence vaccination status in different ways. Five studies found a positive association with vaccination when individuals perceived their health as poor,[70,73,80] or a negative association when it was perceived as good.[37,53] Machado *et al.* 2020 showed that Portuguese women with poor self-rated health presented higher vaccination prevalence than those with good self-rated health.[76] From the HCP perspective, nurses interviewed in Israel reported that an individual's feeling of general good health was associated with an unwillingness to get vaccinated.[54] Three studies found contrasting results in adult individuals, where poor perceived health levels were negatively associated with vaccination or were associated with increased vaccine hesitancy.[41,50,61]

A positive relationship between influenza vaccination and physical activity was observed in five out of six studies.[37,40,41,53,77] Physical activity was most often defined as being active at least 150 minutes per week in the reviewed studies.[40,41,77] Byeon *et al.* 2018 (Korea) observed a stronger association between influenza vaccination and physical activity as individuals' age increased.[53] Regarding activity frequency, Kwon *et al.* 2016 (Korea) found moderate activity (self-defined physical activity at least once per week) to be significantly associated with vaccination while everyday activity was not significant.[37] In contrast, Hellfritzsch *et al.* 2017 (Denmark) found that physical activity was less common among vaccinated people in comparison to unvaccinated people.[46]

Five studies found a positive relationship between vaccination and increased independence and functional status.[32–34,73,79] A variety of measures were used to quantify independence and functional status: the Lawton scale, which assigns a score from 0 to 8 based on the ability to accomplish activities of daily living such as using the telephone, taking medications, managing finances, preparing meals, etc.;[32] the Barthel index, which assigns a score ranging from 0 (complete dependence) to 100 (complete independence);[34,79] and some categorical measures based on type and severity of disability[33] or living in a nursing home.[73] However, Hellfritzsch *et al.* 2017 found that increased dependence and support was more frequent among vaccinated individuals in Denmark.[46] Along with these findings, the authors noted that in Denmark there are policies including no-cost in-house vaccination for providers or patients.

A negative relationship between influenza vaccination and current smoking (vs. never or former smoking) was observed in four studies,[37,40,53,76] but no association was observed in one study.[46] One study from Korea reported a negative impact of alcohol use on vaccination, with an 11–16% reduction in influenza vaccination in women aged ≥50 who drank alcohol (compared to those who did not, amount unspecified in study) and a 19% reduction in men aged 50–64.[53]

Attitudinal factors

Among all the factors included in this review, the most frequently studied was self-efficacy, i.e., a person's belief that they have power over their own health. Manifestations of self-efficacy included previous acceptance of vaccines and preventive health behaviors such as completing health screenings. Twenty-four studies demonstrated that a history of previous vaccination,[33,34,54,57,72,74-75,79,80,83-87,89-91] having a positive attitude toward vaccination,[43,45,61,68,71,92] and adopting preventive behaviors[37,53,70,76] were associated with a positive influence on vaccine uptake. Regarding previous vaccination, seven studies showed that having a vaccine record and/or previous vaccination had a positive association with vaccination in the future against the same or a different vaccine-preventable disease.[33,34,75,79,80,87,91] In two studies conducted in the United States and China, individuals with previous pneumococcal vaccination presented higher influenza vaccination coverage rates than those without.[72,74] A study in the Netherlands showed that vaccination in the previous year had the strongest impact on predicting influenza vaccination uptake[83] Among studies of attitudes toward vaccination, results showed that willingness or intent to receive the influenza vaccine, or a generally positive/confident attitude toward vaccination, was positively associated with vaccination against influenza,[45,68] herpes zoster,[43,71] and pneumococcus.[92] Consistent with these findings, one study found that being vaccine hesitant was negatively associated with influenza vaccination uptake.[61] Finally, studies of preventive behaviors all found that the practice of having health screenings had a positive association with vaccination.[37,53,70,76] Health screenings varied across studies and included clinical and laboratory measurements of blood pressure, cholesterol, and glucose as well as colonoscopy, prostate, and breast exams.

Among the 22 studies examining the impact of a recommendation to vaccinate by a HCP, 17 found a positive effect.[36,39,40,43-45,54,68,69,80,82,84,85,87,89-91] Eight of the studies found

that recommendations from relatives had a positive influence on vaccination.[45,54,68,78,88,89,91,92] Conversely, five studies indicated lack of recommendation from HCPs[35,81,85] had a negative correlation with vaccination and two studies found discouragement from an HCP was the main reason for not vaccinating.[67,90] From the HCP perspective, three studies surveyed HCPs on providing recommendations for vaccinations;[54,82,91] among them it was found that doctors who regularly prescribed pneumococcal vaccination also encouraged revaccination[91] in Japan, where there are guidelines for HCPs to revaccinate adults aged 65 years and older.[93] Additionally, non-vaccination of patients was associated with providers not regularly advising vaccination (i.e., at the first visit within an accounting period) or when the provider reported neutral (as opposed to positive or negative) feelings about vaccination counseling.[82]

Twenty studies showed that awareness of the vaccine and associated disease were positively associated with vaccination uptake.[36,39,40,43,45,47,54,55,59,66,67,73,78,80-82,85,89,91,92] Four studies showed that being knowledgeable about the vaccine or the infectious disease had a positive association with vaccination.[80,85,91,92] Seven studies described the reasons why people did not get vaccinated; these included forgetting about the vaccine,[36,40] not being aware of an existing vaccine,[43] and lack of knowledge/understanding of the vaccine or the disease.[45,66,78,85] Six studies [39,47,67,80,81,92] found that being exposed to vaccine-related information through television, social media, leaflets, or mail notifications was positively associated or correlated with vaccination. However, in one study from the HCP perspective, nurses expressed that bad media coverage related to the vaccine could also be a barrier to vaccination.[54] From the individual perspective, personal knowledge of someone who was at risk for a vaccine-preventable disease[73] or who had the disease[43] was positively associated with vaccination. From the provider perspective, a lack of clear information on a vaccination campaign or on official recommendations was reported to hinder trust and limit vaccination promotion to patients.[59,82]

Perceived individual risk of the infectious disease or its severity was positively associated with vaccine uptake.[36,39,40,43,55,59,78,80,82,84-89,92] The perceived risk of disease was associated with increased vaccination in three studies.[43,89,92] Conversely, when individuals did not consider themselves at risk for the disease, it was associated with non-vaccination.[36,43,84,89] Perceptions of the severity of pneumonia were associated with pneumococcal vaccination,[87] while perceptions that shingles or influenza infections were mild correlated with non-vaccination.[43,89] As expected, believing vaccination to be "important" was associated with uptake,[80] whereas those who did not believe in vaccines was associated with non-vaccination.[86] Feeling healthy, feeling too old, or believing that illness is inevitable were included as reasons for not seeing the necessity of vaccination.[39,55,89] From the provider perspective, a study of German HCPs found that they may not recommend vaccination if they think patients are not at risk,[82] and in Italy, only half of surveyed GPs felt influenza vaccination was a priority.[59]

A primary perceived barrier to vaccination is the experience or expectation of side effects. Across 16 studies, previous experience of vaccine-related side effects or fear of vaccines was shown to negatively influence a patient's vaccination status.[39,40,43,45,54,55,61,66,69,82-86,89,92] Fear of side effects or the belief that the vaccine had an unfavorable risk-benefit balance was associated with non-vaccination in 10 studies.[39,43,45,55,61,69,85,86,89,92] In three studies, individuals reported a previous adverse reaction to a vaccine, and in each case this was shown to impact influenza vaccination uptake.[40,45,83] From the provider perspective, GPs in Germany who did not perceive that the "benefit of officially recommended pneumococcal vaccine exceeds its potential harms" were statistically less likely to advise vaccination.[82] Also from the provider perspective, patients' fear of a vaccine's side effects was identified by nurses in Israel as a barrier to vaccination.[54]

Unsurprisingly, perceived benefits of vaccination were associated with higher vaccination uptake in 15 studies.[43,45,47,54,66,69,71,78,82,83,85,86,88,91,92] Several studies demonstrated that a perception of benefit for oneself or for others,[47,92] perceived effectiveness,[69,85] and thinking that vaccination is a good prevention tool[71] had a positive influence on vaccination rates. In contrast, doubts about a vaccine's effectiveness discouraged patients from being vaccinated.[86] Effectiveness or lack of effectiveness was stated as a main reason for getting vaccinated or not getting vaccinated, respectively, in several analyses of patient-reported data.[45,78,88] Several studies reported the provider perspective on this factor. Among HCPs in Japan, belief that the benefits of pneumococcal revaccination exceed the risks caused them to administer the second dose of the vaccine to their adult patients.[91] Conversely, a common explanation given by German GPs for not advising vaccination was "doubts on its effectiveness."[82] A similar lack of faith in the effectiveness of vaccination hindered patient vaccination, as reported by nurses in Israel.[54]

Discussion

Based on 61 included studies, we found that sociodemographic factors (economic status, age, education, and household composition), health-related factors (comorbidities and health care consumption), and attitudinal factors (self-efficacy, provider or other recommendation, and awareness of the disease and respective vaccination) all played a part in routine adult vaccination uptake.

Among the determinants covered in this review, several stood out as being consistent drivers of or barriers to vaccination. Attitudinal factors, regardless of study design and setting, were the most consistent factor category that demonstrated an association with higher vaccine uptake. Self-efficacy, a recommendation to vaccinate, awareness of the vaccine and the disease it prevents, understanding the importance of vaccination based on disease severity, and understanding the benefits of vaccination were all associated with increased vaccination uptake. Discrete choice experiments like the one described by de Bekker-Grob *et al.* 2018 have shown that individual attitudinal factors influence vaccine acceptance even more than vaccine characteristics.[83] The impact of such factors can be maximized by HCPs focusing on educating individuals who have not been previously vaccinated or who have experienced side effects. Recommendations to vaccinate

from HCPs have consistently been found to be important across the reviewed literature. To help increase provider recommendations, educational initiatives targeting HCPs both practicing and during academic studies prior to practice could help them understand how important their role is in vaccination and could be used to improve communication tactics with patients to increase vaccine confidence.[94] Simplification of vaccination guidelines may also facilitate recommendations to vaccinate, as described in an analysis of the cost-effectiveness of pneumococcal vaccination of adults aged 50–64 years under different scenarios, including universal vaccination based on age regardless of comorbidity status.[95]

Within the health status category, health care consumption consistently had a positive impact on vaccination, which is important because increased interactions with HCPs may result in more consistent recommendations. Studies of individuals with comorbidities commonly attributed higher vaccination uptake in this group to increased health care consumption and thus increased opportunities for both recommendation and actual vaccination.[32,33,40,70,74]

For the sociodemographic factors, affordability and insurance coverage consistently had a positive impact on vaccination. Increasing access to vaccination by ensuring affordability, either through insurance coverage or by publicly funding national immunization programs, will remove at least some of the cost barriers. Nationwide, government-subsidized vaccination policies have been shown to increase adult vaccine uptake in the United Kingdom and Spain.[96] However, public programs are lacking in many countries for older adults.

Studies on ease of access found that convenience, as described by both individual adults and HCPs, was a consistent facilitator of vaccination uptake. Measures of convenience included geographical proximity (e.g., in-house vaccine administration, a vaccine clinic close to home) and procedural simplicity (e.g., priority waiting lines, ready vaccine availability, ambulatory vs. inpatient setting). Policy makers can maximize convenience for vaccine recipients by expanding the scope of practice laws to allow for a broader range of vaccinators, such as pharmacists, which has been found to increase vaccination coverage rates, in part due to increased convenience with longer hours of operation.[97–99] Geographical proximity of local pharmacies should also be considered, as it may explain why some studies found vaccination rates to be higher in urban areas.

Our review consistently highlighted that there is an important need for targeted vaccination campaigns for older adults from select population groups, specifically racial or ethnic minority groups and foreign-born persons. Undervaccination of the older adults in these groups has been documented in other reviews at both national (United States)[100] and global levels.[96,101,102] Reaching these groups with COVID-19 vaccines has also been a challenge,[103] and although this was out of scope for the current review, it highlights the importance of increased support for different types of communities. Strategies proposed for reaching individuals in these types of communities include: (i) at the individual level, HCP efforts to provide accurate information and correct misconceptions around vaccines, establishing long-term trusted relationships with HCPs, and having tailored conversations the include a sympathetic exploration of patient-related health beliefs; (ii) at the health care system level, implementing vaccination reminders and providing translated written information; and (iii) at the policy/governance level, addressing issues of access including proximity, convenience, and cost.[102]

Many other factors reviewed in this study showed mixed results, in that they sometimes had a positive association with vaccination uptake and other times a negative association. Sociodemographic factors with mixed findings included economic status, age, education level, household composition, and employment status. Across these factor categories there was much heterogeneity in the studies, limiting the comparability, and both local context and individual study definitions must be considered to further understand the mixed results. For example, two employment status studies found lower vaccination rates in regions with higher unemployment rates,[52,65] while other studies in this category found higher vaccination rates in those labeled unemployed. These findings must be considered in light of the fact that individuals in the included studies are at an age where retirement comes into play, so employment status may not be as important as in younger adults. Also, employment status is closely linked with educational levels and thus socioeconomic status, so it may be difficult to obtain clear findings on each of these individual factors in the absence of studies designed to mitigate the confounding among them. For example, current income may not reflect the previous earning potential of retirement age subjects,[104] and thus their actual socioeconomic status may differ from their status as defined by current employment or income level.

Similarly, educational level is determined at a much earlier stage of life than that being assessed in this review,[40] meaning that its effects on health care decisions such as vaccination may be indirect. In addition, as noted by Kwon *et al.*, although higher education and household income ensure greater access to health services, greater wealth also allows individuals in this socioeconomic class to live alone more frequently, which introduces the role of household composition.[37] At the same time, educational attainment is often associated with greater health literacy and greater participation in technical occupations,[72,104] both of which tend to ensure that people with more education are exposed to information about and opportunities for vaccination. In the case of pneumococcal disease, one concern that has been raised is that in communities with lower educational attainment, and correspondingly low vaccine coverage rates, individuals tend to also have increased risk of disease or disease complications.[105] Also in these communities, pediatric pneumococcal vaccine coverage may be lower, and in the context of a known protective community benefit for older adults,[106] this can create infection "reservoirs" leading to some of the health disparities commonly linked to socioeconomic status.

Studies of economic status (i.e., income level, social class, and deprivation status) showed a mixed effect with both positive and negative associations with vaccination uptake. These variations existed even within different studies conducted in the same country but in different regions; for example, in both China and Italy, different studies in our review concluded that having a higher income status was associated with increased vaccination uptake in some studies and low uptake in other studies. There are several possible confounding variables that may affect economic status associations. For example, higher income groups

may have greater exposure to anti-vaccination campaigns that result in lower uptake or greater access to health care resources (more HCP recommendations to vaccinate) that result in higher uptake. On the other hand, low-income groups may more readily qualify for state-subsidized insurance or be more likely to take advantage of government funded vaccination programs, both of which were found in this review to lead to better vaccination uptake. Ang *et al.* 2017 described conflicting evidence on economic status from various parts of the world and concluded that the association between income and vaccination has to be examined in the context of "financing policy," i.e., how the cost of vaccination is covered.[41] Free (government-subsidized) vaccination or free access to vaccination via insurance should offset the effects of income. However, McLaughlin *et al.* 2019 point out the clear relationship between higher pneumococcal vaccination uptake and increasing household income in the United States, despite the fact that all US adults aged ≥65 have access to the vaccine with zero out-of-pocket costs due to Medicare coverage.[105] They conclude, along with Abbas *et al.* 2018, that the relationship between local socioeconomic measures and vaccination outcomes is complex, encompassing not only the cost of vaccination but also factors such as transportation and the ability to take time off from work.[105,107]

The impact of age on the uptake rate of vaccinations was found to be somewhat dependent upon the vaccine, with both influenza and pneumococcal vaccines having increased uptake in individuals of more advanced age within the older adult age groups (e.g., adults 70 to 75 years old demonstrated higher uptake than adults aged 65 to 69 years old). Of the vaccine-preventable diseases in older adults, pneumococcal disease and influenza have been found to cause the highest disease burden compared to herpes zoster and pertussis,[108] which may be prompting stronger recommendations from HCPs and greater overall disease awareness for individuals, which were factors our review found to be consistently associated with increasing vaccination uptake.

Among the factors related to health status, comorbidities and self-rated health were found to have mixed effects on vaccination uptake. Comorbidities (i.e., higher comorbidity score or a greater number of comorbidities) were found to be associated with greater vaccination uptake in 13 out of 15 studies. Of the two studies presenting the opposing results, one reported a small effect size (5% decrease in odds of influenza vaccination per unit increase in comorbidity score)[75] and the other was confined to a single comorbidity, asthma.[42] Thus, while there were some outliers among the results, comorbidities might be expected to be positively associated with vaccination, as studies have found that individuals with comorbidities may be disproportionately affected by influenza and pneumococcal infections;[109,110] additionally, care for their conditions may result in higher healthcare consumption, which our review found to be consistently independently positively associated with vaccination uptake.

With regard to self-rated health, the mixed findings were observed across different world regions, suggesting that attitudes about personal health and the need for vaccination are not based in individual cultures. When poor self-rated health predicted vaccination uptake, study authors attributed it to the presence of comorbidities, which would prompt an older individual to be vaccinated,[70] or conversely, to older adults who regarded themselves as healthy lacking the motivation to receive a vaccination.[37] When good self-rated health predicted vaccination uptake, it was attributed to a positive attitude toward preventive health services and/or a greater inclination to maintain physical well-being.[41,50]

The factors that exhibited mixed results in our review highlight some of the gaps in evidence regarding adult vaccination. One that was alluded to above is the need for studies that analyze individual factors simultaneously in a way that addresses the confounding among them. Such studies can help to dissect the interplay between factors such as age and employment status, and socioeconomic status and education level. Another need is for studies that examine regional context more closely, i.e., geographical and cultural specificities, as well as features of local and national health care systems that either promote or discourage adult vaccination. An example of this is an analysis by La et al., who assessed vaccination by state within the United States and found that state-level variations in vaccination coverage persisted even after adjusting for individual-level factors associated with vaccination.[111] Finally, there is a lack of interventional data on many of the factors assessed in this review. The included studies were all observational, and there is a need for more information on implementation strategies that will effectively maximize adult vaccination rates.

This study has several limitations related to its design. The field of adult vaccination is a broad one, and only studies identified by our search terms (see Supplementary Table S1) were included; other studies that reported on drivers of and barriers to adult vaccination may be present in the literature and offer additional insights into this topic. Because the majority of included studies reported on influenza vaccination, the findings on influenza are more robust than for pneumococcal, herpes zoster, and tetanus vaccination. Heterogeneity of the study designs and settings, in terms of scope (local vs. national), national economic status, and national vaccination practices, precluded a meta-analysis and presents a caveat when grouping the results of different studies. In addition, data on adult vaccination rates are lacking in many parts of the world, so the current literature is, by definition, an incomplete dataset. Finally, the determinants of uptake of routine older adult vaccines are multifactorial and interrelated, so causality of individual factors cannot be inferred from a topical synthesis such as this one.

In conclusion, adult vaccination is becoming a cornerstone of preventive care in an aging global population.[112,113] This narrative synthesis of the literature on factors affecting vaccination uptake in older adults provides insights into the best ways to improve vaccination coverage. Attitudinal factors were the factors most consistently associated with vaccination status, which suggests that awareness and education campaigns for both individuals and HCPs might be important initiatives to increase vaccination coverage. However, there is still a need for increased understanding of factors that impact vaccine uptake, which is critical for guiding decision makers toward using their resources for evidence-based practices to increase vaccine uptake in older adult populations.

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ALE is currently an employee at Merck Sharp & Dohme LLC, a subsidiary of Merck & Co, Inc., Rahway, NJ, USA and a shareholder in Merck & Co., Inc., Rahway, NJ, USA. The company manufactures and sells vaccines used in routine immunization programs globally. MN was an employee at Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA and a shareholder in Merck & Co., Inc., Rahway, NJ, USA when the study was performed. JB reported that the International Federation on Aging has agreements with Bayer, AbbVie, BioGen, Pfizer Inc., GSK, Seqirus, and Merck & Co., Inc.

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