

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Vaccine 39 (2021) 5240-5250



Contents lists available at ScienceDirect

Vaccine



journal homepage: www.elsevier.com/locate/vaccine

Conference report

A global agenda for older adult immunization in the COVID-19 era: A roadmap for action

Lois A. Privor-Dumm^{a,*}, Gregory A. Poland^b, Jane Barratt^c, David N. Durrheim^d, Maria Deloria Knoll^a, Prarthana Vasudevan^a, Mark Jit^e, Pablo E. Bonvehí^f, Paolo Bonanni^g, on behalf of the International Council on Adult Immunization¹

^a International Vaccine Access Center, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

^b Mayo Vaccine Research Group, Mayo Clinic and Foundation, Rochester, MN, USA

^c International Federation on Ageing, Toronto, Canada

^d Public Health Medicine, University of Newcastle, Wallsend, NSW, Australia

^e Department of Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, England, United Kingdom

^fEMIC, Buenos Aires, Argentina

^g Department of Health Sciences, University of Florence, Florence, Italy

ARTICLE INFO

Article history: Received 29 April 2020 Received in revised form 26 June 2020 Accepted 29 June 2020 Available online 3 July 2020

Keywords: Adult immunization Policy Vaccines Aging Older adults COVID-19

ABSTRACT

Given our global interconnectedness, the COVID-19 pandemic highlights the urgency of building a global system that can support both routine and pandemic/epidemic adult immunization. As such, a framework to recommend vaccines and build robust platforms to deliver them to protect the rapidly expanding demographic of older adults is needed. Adult immunization as a strategy has the broad potential to preserve and improve medical, social, and economic outcomes, including maintaining functional ability that benefits older adults, their families, communities, and countries. While we will soon have multiple vaccines against COVID-19, we must recognize that we already have a variety of vaccines against other pathogens that can keep adults healthier. They can prevent simultaneous co-infection with COVID-19, and may favorably impact- the outcome of a COVID-19 illness. Further, administering a vaccine against COVID-19 requires planning now to determine delivery strategies impacting how older adults will be immunized in a timely manner. A group of international experts with various backgrounds from health and aging disciplines met to discuss the evidence case for adult immunization and crucial knowledge gaps that must be filled in order to implement effective policies and programs for older adult immunization. This group, coming together as the International Council on Adult Immunization (ICAI), outlined a high-level roadmap to catalyze action, provide policy guidance, and envision a global adult immunization platform that can be adapted by countries to fit their local contexts. Further meetings centered around the value of adult immunization, particularly in the context of COVID-19. There was agreement that programs to deliver existing influenza, pneumococcal, herpes zoster vaccines, and future COVID-19 vaccines to over a billion older adults who are at substantially higher risk of death and disability due to vaccinepreventable diseases are more urgent than ever before. Here we present a proposed framework for delivering routine and pandemic vaccines. We call upon the global community and governments to prioritize action for integrating robust adult immunization programs into the public health agenda.

^{*} Corresponding author.

¹ International Council on Adult Immunization: Narendra Arora, INCLEN Trust, India; Jane Barratt, International Federation on Ageing, Canada; Paolo Bonanni, University of Florence, Italy; Pablo Bonvehi, CEMIC, Argentina; David Durrheim, University of Newcastle, Australia; Laura Hammitt, Johns Hopkins Bloomberg School of Public Health, USA; Heidi Larson, London School of Hygiene & Tropical Medicine, UK; Poh Lian Lim, National Centre for Infectious Diseases, and Lee Kong Chian School of Medicine, Singapore; Janet McElhaney, Health Sciences North Research Institute, Canada; David Murdoch, University of Otago, NZ, Justin Ortiz, University of MD, USA; Lois Privor-Dumm, Johns Hopkins Bloomberg School of Public Health, USA (Secretariat Director); Gregory Poland, Mayo Clinic & Foundation, USA (ICAI Chair), David Sinclair International Longevity Centre, UK. MArtin Friede (WHO) and Mark Jit (London School of Hygiene & Tropical Medicine are advisors. Katherine O'Brien (WHO) was a member of ICAI while at Johns Hopkins Bloomberg School of Public Health.

1. The need for a global adult immunization effort

Vaccine preventable diseases (VPDs) cause significant health, economic, and social impact in older adults, yet vaccines are underutilized in this population around the world [1–3]. At the same time, the world's population is aging at an unprecedented rate. One in six people worldwide, and one in four in Europe and North America, will be 65 years of age or older by 2050 [4]. The population of older adults is expected to double between 2019 and 2050 in every region except Sub-Saharan Africa [4]. This growing population of older adults not only leads to moral and ethical questions about the need to prioritize resources to address more severe health outcomes in older adults, but also demands consideration regarding the economic and social impacts that disease brings. Older people are not all frail and dependent upon care but rather contributors to the rich fabric of community and society in all countries.

In late 2018 an international group of vaccine and aging experts, along with social scientists, economists and a designer, came together as the International Council on Adult Immunization (ICAI) to discuss the need for creating a platform and a culture around immunization for older adults. Although policy makers often define older adults by an age cut-off, for example over age 60 or 65 years, older adults are a heterogeneous group whose health status and strength of immune system can vary substantially from country to country and amongst people within a country [5]. Here, we define older adults over the age of 50 years, and more likely to have underlying comorbidities. ICAI recognized the need for greater emphasis on older adult vaccination, including in low-and middle-income countries (LMICs), and developed a framework to catalyze action across the global community.

1.1. Meeting objectives

The goal of the initial ICAI meeting was to define a high-level roadmap to guide efforts to prioritize adult immunization decision-making and implementation globally. We defined our vision as a world where all adults can age in wellness and dignity without health, economic, or social consequences of VPDs. This mission brings together global experts, spanning a wide range of disciplines, perspectives and geographies to accelerate immunization as a key strategy to maintain health and well-being for adults and to call upon various stakeholders to establish, expand and implement evidence-based adult immunization policies and programs. COVID-19 further and dramatically highlights an urgent need to build a system that can fully support adult immunization. This includes a broader understanding of the value of immunization of older adults and steps needed to put in place infrastructure and programs that can protect this growing demographic. Below we provide an overview of the discussions supporting ICAI's mission in making the case for adult immunization in order to build political support and the platforms necessary to enable protection, particularly in the time of COVID-19.

1.2. Defining a metanarrative

It is critical that older adults, their families, health providers and policy makers understand the value of adult immunization. To achieve this, clearer messages must be crafted and become the language of health officials, providers, older adults and their families. We defined a metanarrative to succinctly describe what is needed. (Fig. 1) Particularly in the current context of COVID-19, it will be imperative to widely communicate the value of adult immunizations and the need to build platforms (the people, institutions, systems and resources) to deliver vaccines in order to save lives, help prevent costly outcomes due to COVID-19 in the older population, and ensure prioritization considers the rights and contributions of older adults as challenging decisions regarding the allocation of COVID-19 vaccines are faced [6].

2. Development of a framework for action on adult vaccines

The group used a framework method to evaluate persons, ideas, context, and issue characteristics, each of which has been shown to influence the success of global initiatives [7] (Table 1). Within the analysis of each element of the framework, we were able to develop a roadmap that defines how best to prioritize adult immunization nationally and globally.

2.1. Refining the framework given the current COVID-19 context

Adult immunization alone is an important issue, but COVID-19 has dramatically prioritized the needs of older adults. A COVID-19 vaccine against SARS-CoV-2, the virus causing the disease, is likely to be available in the next months [8], but many questions need to be addressed and preparations made before it can be delivered effectively. COVID-19 disproportionately impacts older adults in both morbidity and mortality, [9,10] and a safe and effective vaccine for that population could provide protection against death and hospitalizations. In addition to mortality, there are also downstream effects including persistent cardiovascular, neurologic, and lung morbidity among COVID-19 survivors [11,12]. Vaccination strategies to protect older people against both existing and emerging threats will be needed and may help mitigate the impact of COVID-19 (Fig. 2). Even if there is a successful vaccine, unless COVID-19 is eliminated, the need for immunization of older adults is expected to persist along with the importance of developing stronger platforms for other existing or new vaccines for older adults. A COVID-19 vaccine provides an opportunity to ensure that once available, it and other vaccines can be delivered successfully to the older adult population. The emphasis on COVID-19 vaccine may potentially boost immunization rates of other vaccines due

Older adults, a rapidly growing demographic worldwide, should live healthy, full productive lives, free of the burdens and complications of vaccine preventable disease no matter where they are. They are at the highest risk for complications from infectious diseases, but vaccines can help prevent consequences of hospitalizations, loss of paid or volunteer work, or a downward spiral with concomitant illness which may lead to premature loss of independence. Vaccines are important across the life-course, but have not received adequate attention for older adults. Vaccines for older adults provide an excellent return on investment for both the individual and society when considering the whole spectrum of costs: medical, loss of daily function and independence, impact on caregivers, lost productivity, and exacerbation of poverty and inequities. We call on WHO, healthy aging organizations, civil societies, and governments to approve national vaccine recommendations for older adults, and to promote evidence-based policies, and overcome barriers to equitable access and high coverage with key vaccinations across all populations.

5242

Table 1

	Description	Need
Actor (Stakeholder) Power	The strength of the individuals and networks concerned with the issue	Broader group of stakeholders and champions to call for adult recommendations. Stakeholder mapping (visually assessing groups or individuals with the power and interest to influence adult immunization as a political priority).
Ideas	The ways in which those involved with the issue understand and portray it	To understand the action drivers of the actors with resources and how they perceive the issue. Evaluate meta-narrative (coming from a person-centered design process) to see if messages move people to acceptance or action.
Context	The environment in which actors operate	Consider positioning adult immunization within other initiatives and messaging, e.g., G20 (Japan's focus on aging), Global Vaccine Action Plan (GVAP), Decade of Healthy Aging, UHC, primary health care, NCD burden, health security, urbanization, migration, demographic shift. May need to address the increasing cultural distrust of public & officials.
Issues	Features of the problem	Data that demonstrate disease burden and broader economic impact particularly in LMICs, which may have higher burden than recognized. Also need to have metrics to look through an equity lens. The economic cost will bring further importance and global health security will help establish necessity.

Based on Shiffman & Smith et. al, Lancet 2007.

to an increased focus on the value of immunization for older adults as well as enhance efforts to ensure ease of vaccine access for this group. The planning and development of vaccines for older adults should also include defining attributes as part of the target product profile needed to address the specific needs of older populations; global guidance for countries to develop policies for vaccine usage of COVID-19 in older populations; and guidance that highlights the systems that are needed to ensure robust decision-making, delivery of vaccines, and monitoring efficacy, safety, vaccine coverage and impact of immunization programs in older adults.

3. The evidence supporting the need for adult immunization

Initial discussions centered around the framework by defining the problem – something that has not been well-articulated previously and that will be needed to support an evidence case for investment in adult immunization. Those investments can support development of vaccines that meet the needs of older adults, prioritize action to adopt and recommend vaccines, and redesign delivery strategies to help ensure high uptake.

3.1. Burden of disease

VPDs, including influenza, pneumococcal disease, and herpes zoster, are a significant concern in older adults. Influenza although not as contagious or deadly as COVID-19 - is estimated to have caused 39 million cases and killed 24,000 Americans in the USA as of the end of March 2020 in the current influenza season [13]. Globally, respiratory infections (including influenza and pneumonia) resulted in more than 1.5 million deaths in adults 50 years or older in 2017, and accounted for 23 million years of life lost due to premature mortality [14]. The highest incidence was in low-income countries (LICs) where access to vaccines for adults is almost nonexistent. Other VPDs including pneumococcal disease, a major cause of pneumonia, and herpes zoster (shingles) place a substantial burden on older adults [14]. Pneumococcal disease has a high case fatality rate in older adults, killing an estimated 1 in 20 adults with pneumococcal pneumonia and 1 in 6 with pneumococcal bacteremia [15]. Almost a third of adults will develop herpes zoster in their lifetime [16], and although rarely fatal, it can be debilitating, causing chronic pain, suffering, elevated medical costs, reduced productivity, and loss of independence [17].

3.2. The broader health impact of adult immunization

Health policy needs to consider the heterogeneity of older people across countries in terms of demographics, VPD burden, existing systems serving older adults, available public health resources and disease priorities. Where immunization policies exist, they often target a specific age group, largely to ensure that the population targets for those policies are clear and implementable. The World Health Organization (WHO) has provided a policy framework on healthy aging that acknowledges that older people are not a homogenous group, and should not be defined by chronological age [5], While we agree with that premise, it is important to set a practical global mantra that fits with current healthcare and policy-maker thinking; while efforts continue in parallel to establish practical definitions of older age, we consider adults over the age 50 due to increasing prevalence of comorbidity.

VPDs can increase the risk for non-communicable disease (NCD) events and exacerbate existing chronic diseases [10]. Influenza, pneumococcal pneumonia, and shingles may increase the risk of myocardial infarction or stroke [18-20] and exacerbate chronic obstructive lung disease [21] and cardiovascular disease [22,23], potentially leading to a decline in functional ability, loss of independence, or even premature death (Fig. 2). There is also evidence of a complex indirect relationship between VPDs and frailty [24,25], cognitive decline [26] and depression [17,27]. Disease burden estimates of the value of vaccines generally do not include the benefits of preventing these downstream conditions [28] or resulting events such as falls caused by weakness following a VPD episode, suggesting that the true impact is underestimated [29]. The role of vaccines in preventing NCD events is also underappreciated in clinical settings and should have more prominence in the management and prevention of those diseases [24,30].

For optimal health benefits of adult immunization to be realized, adult vaccines must be perceived to be effective by the public, payers, and health professionals [1]. Progress is being made with new strategies to address the context of immunosenescence, which can reduce effectiveness of vaccines as well as impact susceptibility to new infections in older adults [30]. Specific high-dose, adjuvanted, and recombinant influenza vaccines, conjugated pneumococcal vaccines, and a recombinant adjuvanted shingles vaccine have demonstrated improved efficacy and effectiveness in older adults [31–33]. Such strategies or others aimed to overcome the negative effect of immunosenescence, should be considered now for COVID-19 and other vaccines either available for all or targeted to the older population.

3.3. Social benefits of older adult immunization and equitable vaccine access

Immunizing older adults has important social benefits for families, individuals, communities, and society overall since prevention



Fig. 2. Illustration of the potential mitigating effects of VPD immunization on the severity and outcomes of COVID-19 in older adults. Source/Notes: Authors' visualization based on the following: McElhaney JE, Kuchel GA, Zhou X, Swain SL, Haynes L. T-Cell Immunity to Influenza in Older Adults: A Pathophysiological Framework for Development of More Effective Vaccines. Front Immunol. 2016;7:41. Wedzicha JA, Seemungal TAR. COPD exacerbations: defining their cause and prevention. The Lancet. 2007;370(9589):786-96. Pickering G, Marcoux M, Chapiro S, David L, Rat P, Michel M, et al. An Algorithm for Neuropathic Pain Management in Older People. Drugs Aging. 2016;33(8):575-83. Bula CJ, Ghilardi G, Wietlisbach V, Petignat C, Francioli P. Infections and functional impairment in nursing home residents: a reciprocal relationship. J Am Geriatr Soc. 2004;52(5):700-6. Warren-Gash C, Smeeth L, Hayward AC. Influenza as a trigger for acute myocardial infarction or death from cardiovascular disease: a systematic review. Lancet Infect Dis. 2009;9(10):601-10. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020. Notes: Older adults start off at different baselines of health: As they age, older adults will encounter VPDs and the outcomes will depend on individual resiliency. Vaccines have been shown to play a role in reducing the severity and length of events following an episode of VPD, as well as in impacting other outcomes like cardiovascular disease and stroke. The severity of outcomes at the right that occur following an infection with a VPD represent the increasing likelihood of worse outcomes if baseline health status is worse or if another health threat such as COVID-19.

of VPDs is central to healthy aging. Healthy older adults are often pillars for their families and perform various valuable functions in an informal economy, including childcare and providing financial and emotional support. They volunteer and participate actively in their communities [34] or work into older age, contributing to a nation's social and economic development [5]. Quality of life, valued by older adults [35], can be adversely impacted by VPDs, which can cause symptoms of distress and depression [34], sleep deprivation, and loss of enjoyment of life [36]. Social isolation due to disease and/or disability further perpetuates health problems [37], creating a perverse cycle that further magnifies these adverse impacts.

Equity is an important consideration for vaccine policies and programs and involves some tension between leveraging existing systems to strategically increase equitable uptake without overburdening them [38]. Higher rates, earlier onset, and the greater severity of influenza and pneumococcal disease in Aboriginal and Torres Strait Islander populations prompted Australia to provide this population with pneumococcal and influenza vaccines at an earlier age [39], and Canada to prioritize funding for influenza vaccines for First Nations peoples [40]. Gaps in vaccine coverage among specific groups of older adults (by age, gender, or socioeconomic status) should be identified and assessed so that policies and programs address potential inequities. Groups who are not immunized are also less likely to access other healthcare services [41]; therefore, immunization could support broader significant public health benefits.

3.4. Economic benefits of older adult immunization

Billions of dollars have and will continue to be invested in the development of COVID-19 vaccines, by companies, governments and international coalitions not only for product development, but also for manufacturing hundreds of millions to billions of doses [8,42,43]. Although current indications are that the manufacturers will commit to a supply of an affordable product, the cost of a vaccine is still likely to be substantial. It will be important that a full economic analysis include older age groups.

Many studies have shown that vaccines against influenza [44,45], pneumococcus [46-49] and herpes zoster [50-52] are cost-effective when given to older adults in a range of settings [53]. Notwithstanding this, the corresponding global economic burden offset by these adult VPD vaccines has not been fully calculated. Estimated costs of influenza, pneumococcal disease, and herpes zoster in US adults over 50 years of age range from \$6.9B (2015) to \$26.5B (2013) [54,55]. Sometimes these costs incorporate lost productivity of working adults, but not unpaid labor and other important ways that older adults contribute to society [34]. They also do not consider the impact on caregiver productivity, and health and social service system savings [56]. Estimates also generally limit health-related costs to the acute episode of the VPD, and do not include costs associated with exacerbated underlying illness and co-morbid conditions or antimicrobial resistance rates [57]. In order to fully capture both direct and indirect costs, many have argued for a broader definition beyond direct costs of illness and lost productivity of working adults and their caregivers, allowing these costs and benefits to inform decisions about adult immunization policies [58].

The economic burden of VPDs disproportionately affects those who are the most vulnerable. The poor who are at higher risk of disease may be the most impacted and potentially suffer loss of financial security or impoverishment [59]. This is certainly evident in the current COVID-19 pandemic, which has targeted the poor, older adults, and those with underlying conditions. Although the economic consequences are not solely related to disease in adults, the evaluation of adult immunization strategies, either through direct immunization or indirect protection through immunization of younger generations who can transmit disease, must be carefully considered. Different strategies are likely to achieve different outcomes and may impact the ultimate severity of disease in older patients, which in turn has an impact on caregivers, families, and the broader economy. It is estimated that this current pandemic could cost the global economy \$1 trillion to \$2 trillion in 2020 [60], so immunization strategies and actions to avert future costs are critical. Modeling of influenza pandemics of the severity of the 1918 Spanish Influenza pandemic suggested an economic impact in the hundreds of billions of dollars [61]. Many countries do not have adequate health systems to provide emergency care in the context of epidemics [62] and effects can be crippling and destabilizing, as seen already with COVID-19 in many countries [63–65]. The impact of the disease is overwhelming primary healthcare, leading to additional indirect deaths and exacerbation of illness [66]. Additional resources will be needed to address the immediate needs of emergencies and also for ongoing primary healthcare system strengthening [67].

3.5. Life-course immunization strategies for adults

Vaccine programs have traditionally been focused on childhood diseases, but there is increasing emphasis on the value of immunization at all ages [68]. Life-course immunization prevents diseases later in life. High uptake of some childhood vaccines can reduce the population spread of disease providing substantial indirect community protection of unimmunized persons [30]. As an example, childhood immunization has been shown in some settings to be an effective strategy for reducing the adult incidence of seasonal influenza [69,70] and pneumococcal disease [71,72]. Hence adult and child immunization programs need to be seen as complementary approaches to prevent infectious disease and promote better health for adults.

3.6. Adult immunization and antimicrobial resistance

Adult vaccines can also help in the fight against antimicrobial resistance (AMR). Viral pneumonias may be followed by secondary bacterial infections, worsening their outcomes and increasing the risk of death [73]. These diseases are often treated with antibiotics, contributing to AMR. WHO considers AMR to be one of the ten global health threats and prevention of disease through immunization is an important strategy to prevent the burgeoning problem [57]. Influenza immunization has been associated with reductions in antibiotic prescriptions, including in older adults [74]. Pneumococcal vaccines have been shown to have a more direct effect by reducing carriage and transmission of antimicrobial resistant strains of pneumococcus [75].

4. Functional ability

Functional ability is made up of an individual's intrinsic capacity (a composite of physical and mental capacities that a person has developed over time and can draw upon in older age), the environment, and how they interact. WHO further describes functional ability as health attributes that enable people to do the things they value in their daily lives [5].

The group discussed the importance of maintaining functional ability in order to continue to lead healthy lives and focused on the concept of "vaccine-preventable disability." The metric of functional ability needs to become part of the goal of vaccine policy and a lens through which various strategies are evaluated. The objective must be to add "life to years" rather than years to life, although participants recognized that this is not necessarily how physicians are trained to act. Often declines in frailty are gradual, so many older adults may not realize they are at higher degree of risk for various health threats. Functional ability can be positively impacted by multiple strategies, including protection against VPDs along with other healthy behaviors including exercise, diet and smoking cessation.

Preventing influenza, pneumonia and other VPDs in older adults with the vaccines we have on hand may also help mitigate the outcomes of COVID-19 and other future health threats (Fig. 2). This is because weakened immune systems and deteriorating health status following VPDs are likely to leave the recovering patients more vulnerable than their immunized counterparts. Because COVID-19 outcomes are worse in older people and particularly those with comorbid conditions [10,76,77], prevention of preceding VPDs may dampen its impact. Notably, one small study demonstrated that 20% of COVID-19 patients are co-infected with another respiratory pathogen [78]. However, adult immunization is not wide-spread globally and is underutilized where it is available.

5. Delivering older adult immunization programs: Current challenges & potential approaches

5.1. Decision-making and delivery capacity needed,

Many factors influence successful implementation of adult immunization including the availability of evidence and policies, political and public health will, funding, monitoring, ease of access, and communication [79]. Many countries do not have the data and capacity for evidence-based decision-making around adult immunization, lacking data, policies, expertise on issues impacting older adults, and political will and resources [79]. Others may not have systems to reach older adults with vaccines or have systems that are so fragmented that opportunities are missed to recommend vaccines [79,80]. To improve patient access, making systems less complicated, improving convenience and expanding the groups who can immunize (for example, through pharmacists [81], direct delivery or mobile services) should be considered. Programs that build upon existing primary healthcare (PHC) systems can encourage "diagonal" programs that serve as a gateway to other health services [82].

5.2. Strategies to address hesitancy and identifying low coverage

Strategies to address determinants of vaccine reluctance or refusal, and concomitant education and engagement of health care providers in making a strong vaccine recommendation can help build confidence and demand [83–85]. The issue of vaccine hesitancy may also arise with COVID-19 once a vaccine is available, and a plan to address that should be developed early. In 2019 WHO listed vaccine hesitancy and vaccine rejection as a top ten global health threat [86]. Countries should be able to identify gaps in coverage, and immunization registries can help manage program performance. Yet, registries are not widely implemented for adults given the fragmentation of providers and health systems, L.A. Privor-Dumm et al. / Vaccine 39 (2021) 5240-5250

Table 2 Adoption of three key older adult vaccines in 34 high and middle-income countries, as of October 2018.

				Status	of vaccin	e for older ad	ults (2018)	d	
	-65 (6) ^a	atus	that Aging 2018)⁰	Influer	ıza	Pneumoco	ccus	Herpes z	oster
Country	% of population >65 years of age (2016) ^a	Country Aging Status (2016) ^b	Policies Created that Support Healthy Aging and/or Services (2018) ^c	Recommended	Financed by Government	Recommended	Financed by Government	Recommended	Financed by Government
Argentina	10.9	Aging					OOP		OOP
Australia	15.3	Aged							
Belgium	18.2	Aged							OOP
Brazil	8.2	Aging					0		OOP
Canada	16.5	Aged			S				
China	10.0	Aging							OOP
Colombia	7.7	Aging					0.0.0		OOP
Denmark	18.8	Aged					OOP	8	OOP
France	18.8	Aged						, in the second se	OOP
Germany	21.1	Super-							
Crease	21.3	Aged Super-							
Greece	21.3	Super- Aged	-						OOP
Hong Kong	15.9	Aged			OOP				OOP
India	5.8	N/A	-		UUF		OOP		OOP
Ireland	13.2	Aging					001 00P		OOP
Italy	22.0	Super-					001		001
italy	22.0	Aged			s		s		s
Japan	27.3	Super- Aged							OOP
Korea	13.2	Aging	-		OOP		OOP		OOP
Malaysia	6.0	N/A					OOP		OOP
Mexico	7.0	Aging							OOP
Netherlands	18.2	Aged					OOP		OOP
New Zealand	14.9	Aged							
Norway	16.4	Aged			OOP				OOP
Peru	6.7	N/A					OOP		OOP
Philippines	4.9	N/A			OOP				OOP
Russia	14.2	Aged					OOP		OOP
Saudi Arabia	3.2	N/A		s	S		OOP		OOP
Spain	18.7	Aged					S		OOP
Sweden	19.8	Aged							OOP
Switzerland	18.0	Aged					OOP		OOP
Taiwan	13.2	Aging					OOP		OOP
Turkey	8.2	Aging							OOP
UAE	1.1	N/A					S	l l	
UK	17.9	Aged							
USA	15.2	Aged							

Results derived from quantitative and qualitative data collected from January 2018 through October 2018 through a series of qualitative interviews and a landscape review on older adult immunization decision-making and implementation in 34 high and middle-income countries

Key:

recommended; mixed system); mixed system);

OOP=out of pocket/privately paid; s subnational/regional tenders; N/A not applicable; *Germany's Herpes Zoster recommendation was updated after October 2018; blank boxes: data unavailable

Sources:

^a World Bank Data: Populations 65 and above

https://data.worldbank.org/indicator/sp.pop.65up.to.zs?end=2016&start=1960

^b WHO's convention for categorizing countries by aging (based upon percent of adults ≥65 years of age in the total population): 7-14%= Ageing; 15-19%= Aged; 20%+= Super-Aged.

^c UN/WHO/World Bank/ UNICEF/ Gavi websites; countries' Ministry of Health websites/ reports/white papers, and peer-reviewed papers.

^d Countries' Ministry of Health websites/ reports/white papers; peer-reviewed papers; media articles; and personal communications with in-country experts.

and lack of government prioritization [79]. Nonetheless there are opportunities to leverage existing country initiatives, including in LMICs . India, for example, established health and wellness centers and registries for adults over 60 years of age, a program that could be leveraged to deliver vaccines and monitor immunization of older adults [87].

5.3. Integration with other priorities

Integration with other country priorities, including emergency preparedness for infectious diseases, is also important. While influenza surveillance amongst adults is in place in some countries, significant gaps remain globally, particularly in LICs [80]. COVID-19 underlines the urgent need to integrate PHC platforms for older adults into emergency preparedness plans [88]. Providers of healthcare play an important role in ensuring their patients are up-to-date with all recommended vaccines and communicating the need for vaccination, including ensuring patients understand some of the more severe downstream risks of disease even when they recover from an initial VPD. The ideal system would integrate individual-level immunization history and timely population-level data collection, similar to the United Kingdom (UK) or Australian models [89,90]. General practitioners from the UK reach out directly to their patients to ensure they are immunized. Immunization registries in Australia have been used as an important tool in Australia's decentralized health system. Both countries have centralized review of immunization data [79]. Review of data, identifying gaps, and devising new strategies can be contributors to higher uptake, including in decentralized systems, but most countries are far from achieving that goal [79].

5.4. Research & innovation

ICAI discussed several research gaps for adult immunization, including disease burden studies, especially in LMICs, as modelled estimates rely on data from higher income settings. Other needs include understanding vaccine coverage measures including what is measured, availability of data for particular risk groups, analyses of the broader economic value of vaccine, and cost to the patient. User research on facilitators or barriers to adult vaccine acceptance by patients and healthcare providers Is also needed. Discussions about the link between older adult immunization and functional outcomes (including understanding the mechanistic link between influenza, pneumonia and cardiac outcomes, and measuring inflammatory consequences of VPDs on heart disease, stroke and dementia) are also needed to address the downstream impact on future health outcomes of subsequent disease such as COVID-19.

Additionally, operational research would also be helpful to understand how older adults can best be immunized. Now is an opportunity with new COVID-19 vaccines to explore innovative improvements in delivering COVID-19 and other vaccines to older adults. Having to travel to clinics or wait in waiting rooms for immunization may paradoxically put older adults at some level of increased risk during epidemics and pandemics. Considering innovative alternatives that reduce the risk of exposure to the disease, such as formulations allowing self-administration [91], or delivery by mail or by outreach from community members previously exposed to COVID-19, may not only reduce inadvertent transmission but also make vaccines more accessible, potentially boosting immunization rates to all vaccines.

When a COVID-19 vaccine becomes available, it is not clear if the immunity produced by SARS-CoV-2 candidate vaccines will be protective and long lasting in older adults. A strategy to protect a population who may not respond well to available vaccines may be to immunize the younger population and protect older people indirectly if such vaccines turn out to not be efficacious in older adults. Although this may not be sufficient to protect the entire older adult population, particularly in the short-term, it may serve as a bridge until vaccines that are effective in immunosenescent older adults can be developed. Strategies to address immunosenescence and associated potential concerns about efficacy in this population are important early considerations for vaccine developers. Research will be needed to supplement our knowledge about the type of support needed to develop policy and guidance at the country-level.

6. Policy-driven action: Achieving global technical and policy consensus for adult immunization

Various strategies, including the Global Strategy and Action Plan on Aging and Health [92], the Decade of Healthy Aging [93] and the Immunization Agenda 2030 [68] have already called for a life-course approach to immunization policy. The context of COVID-19 specifically raises the urgency and need for an adult immunization platform. Many countries have a sufficient evidence case to support life-course immunization, yet policies and adoption into national programs has been slow [79,80] and funding for existing vaccines is not yet available (Table 2). Levine et al. provide the global health community with a framework to move from evidence to vaccine access [94]; data gaps, particularly in LMICs, must be considered [95], but should not unnecessarily delay action and implementation. Technical consensus, champions, and an appreciation of value and impact are needed to catalyze progress [7]. Additionally, the ideas and interests intersecting with healthy aging - such as creating specific strategies to immunize older adults in the face of an emergency; articulating an evidencebased narrative about the benefits of adult immunization both to improve uptake and to show an economic benefit; demonstrating immunization benefits in the fight against NCDs and AMR; showing how immunization can help address equity on the basis of gender, medical, social or financial vulnerability – can all help build political support for immunization [7].

In order to make progress with this mandate, plans will need to identify partners to engage. Discussion regarding who would be responsible and accountable for particular actions was robust (Tables 3 and 4). The global technical community – including

Table 3 Priority stakeholders to engage.

- Key Stakeholders (to engage first): The global technical community vaccine, healthy aging organizations
 - Governments (Ministry of Health), policy makers
 - Funders, vaccine agencies such as US Centers for Disease Control and Prevention, European Centre for Disease prevention and Control, The World Health Organization, UN agencies, including regional offices
 - Health professional associations Advocacy groups and patient organizations
- Other priorities:
- Private sector
- Economists
- Lay people
- · Marginalized populations, indigenous populations
- Antimicrobial resistance groups or initiatives
- Politicians
- Opportunistic.
- Equity focused organizations, poverty NGOs
- Media, entertainment (ty scripts)
- Those who provide website guidance
- "Statesmen" or high profile figures
- Others:
- Employers, insurers, actuaries, frontline staff that do and don't recommend vaccines,
- Global Fund
- World Bank
- School educators, pediatricians (to provide lessons learned)
- Generations united
- Celebrities

Table 4

High-level strategies and	partners needed to build	l political priori	tv and a	platform for adult immunization.

Strategy	Description	Who
Technical consensus	 Synthesize evidence and assess the broad value of vaccines including impact on functional ability, caregivers, health system and society Quantify the health, social and economic impact and call for prioritizing COVID-19 and existing vaccines Consider the pandemic and what resources are needed postpandemic, including investments in surveillance, immunization registries, etc. Identify data gaps and inform research agendas 	WHO (at the highest levels), experts in vaccines, healthy aging vaccine development, health policy, immune senescence, health systems, emergency preparedness, antimicrobial resistance, economics, financing, social sciences, human rights business, national governments, professional organizations from diverse settings
An organized global effort	 Integrated and coordinated with other health, social justice, and/or environmental initiatives, emergency preparedness, Engages a wide range of country stakeholders to leverage existing health platforms, other existing structures or propose new platforms to reach older adults with immunization programs. A global forum to determine structure, leadership, process with country input 	A coalition of partners and initiatives that intersect with healthy aging and immunization at global, regional and national levels
Political Will & funding	 Political and financial commitment to ensure the immunization needs of older adults in every country are given appropriate priority <i>National leaders prioritize</i>: Identification of vaccine needs and system gaps that might impact equitable deployment of vaccines to older adults Strengthening of decision-making and implementation to ensure equitable access and high coverage of influenza, pneumococcal and herpes zoster vaccines for older adults Improved surveillance and monitoring of vaccine use amongst older adults Global and regional leaders prioritize: Strategies to develop vaccines that are optimized for all populations or specifically targeted to an older population Research to understand country typologies to better leverage learnings and strategies to country needs and context Strategies to support optimization of delivery platforms, surveillance, measurement of vaccine uptake and monitoring of success Funding to support the above <i>Civil society prioritize:</i> Advocacy for the rights of older people in the context of vaccines Identification of champions and providing support for efforts by a guiding institution Rights of older adults and holding leaders accountable to provide immunization for all Communication to ensure the older adults value and seek recommended vaccines Integrated delivery of vaccines to older adults where they would seek care <i>Donors prioritize</i>: Funding vaccine and systems research to address the needs of the most vulnerable Calls for global and national leaders to prioritize vaccines that will address the needs of all, Business and the private sector prioritize: Advocacy & support for vaccination of employees, customers and older community members In-kind contributions to lend their expertise 	Global, regional, national and local champions; governments; donors; civil society; business and the private sector
Strengthened or redesigned primary healthcare platforms	 Vaccines that address the faces of order address (suppliers) Preparedness strategies that include vaccination for older populations and their caregivers in the face of an emergency. Country-driven immunization programs within existing platforms or new platforms. Design processes that specifically address delivery, monitoring and measurement of impact in older adult populations 	Designers, health systems experts, economists, private sector and users of the system WHO and UN institutions to lead the charge of a country-driver approach
Accelerated efforts and support to identify, prioritize and fill key evidence gaps	 Identify and fill evidence gaps specific to the COVID-19 pandemic LMIC disease burden Quantify downstream impacts of VPDs Fully cost impact of VPDs and vaccination Understand drivers of acceptance in older populations 	Researchers, country experts, partners, funders
Redefined intergenerational value of adult immunization	 Onderstand drivers of acceptance in order populations Reshaped narrative around the health, social, and economic impact of vaccines, not only for the person being vaccinated, but for those who are impacted by their well-being Focus on preserving functional capability and independence in addition to prevention of severe illness, hospitalization and death 	Communicators, partners, variety of stakeholders in health, aging, the economy, politicians, etc.
Person-centered innovation	Geath Solutions driven by human-centered design principles including:	Wide variety of stakeholders including, health providers, the (continued on next p

Table 4 (continu	lea)
------------------	------

ine 4 (continued)		
Strategy	Description	Who
	 New technologies (e.g., non-injection) and new ways of deliver- ing those technologies (e.g., self-administration) are needed to address the health, economic and social challenges faced Better understanding of issues impacting acceptance of adult immunization 	public, manufacturers, healthy ageing advocates, economists private sector, public sector, etc.
	 Effective culturally-tailored mechanisms to communicate the investment case for addressing country priorities. 	

WHO, public health experts, economists, social scientists, and aging advocates - has yet to present countries with comprehensive and practical guidance on life-course vaccination; the current situation of COVID-19 increases that urgency. Global and local infectious disease, aging and other experts should use their expert voice to call on WHO and others to move the conversation forward, support development of technical consensus, and help identify research gaps. Evidence must be presented in a compelling, context-specific and human-centered way to encourage the global health, aging, and vaccine communities to unite and make progress in life-course immunization. Engaging a wide variety of partners across perspectives and generations is crucial; for this reason, we call on international and national organizations to consider the broad value of adult immunization and take action within their remit and priorities. To ensure that we were addressing the issues that would lead to political priority, we went through various exercises to identify which stakeholders would respond to particular issues, and sought to define the political context and issue characteristics. We then synthesized those findings into an outline that provided a high-level global roadmap to prioritize older adult immunization.

7. The roadmap

Drawing on collective experience in implementing global health initiatives [7] and building on ongoing and previous efforts to move the agenda forward [96–98], we urge that the strategies outlined be enacted to catalyze progress on evidence-based decisions and policy toward establishing adult immunization programs globally (Table 4).

The roadmap must recognize the broader value of adult immunization and enable country actions to incorporate adult vaccines into policies and programs that are part of an integrated lifecourse approach. ICAI and others have begun to synthesize evidence, including disease burden, health, economic, and social impact of adult VPDs and immunization, country capabilities, and approach to supporting policies and actions, but much more is needed. Researchers and initiatives working on adult immunization are ready to work alongside WHO, partners and countries to identify research and policy gaps (particularly those in LMICs). They can assist in communicating gaps and priorities to relevant stakeholders in order to develop solutions to address vaccine delivery at a multitude of levels. ICAI proposes a broader high-level plan that includes feasible actions to help build political will and broad engagement. A consensus meeting at a global level would supplement ongoing efforts at the national level, gathering key partners to co-create an action plan that would provide more operational detail and outline roles and responsibilities. This meeting, which should cover all parts of the world should be convened by WHO as a follow-up to their previous meeting in 2017 [99]. This plan calls for WHO to establish an life-course immunization working group with attention to older adults and those with underlying conditions to engage with countries and other UN agencies so a more detailed strategy and way forward can be developed. While a huge and difficult issue, through the lens of a pandemic, we have no choice but to act.

The urgency to act comes because strategies for COVID-19 vaccine development and systems to deliver those vaccines will be influenced by the needs of older populations in every country, each with unique public health systems and priorities. We must engage and gain the endorsement of Member States to allocate resources to deliver vaccines to older adults; funders to support efforts for evidence generation and building political will; manufacturers to develop products that better address needs of older adults; and the public, healthcare workers, policy makers and politicians to communicate the importance and potential broad impact of adult immunization. The COVID-19 pandemic is new territory, and while all ages are a priority, older adults clearly suffer disproportionate morbidity and mortality. We should not delay any longer and seize the opportunity to move together to truly implement a plan for the needs of all ages that includes older adult immunization.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Lois Privor-Dumm reports grants from Pfizer, GSK and Merck. Greg Poland reports a grant from NIH and personal fees from Merck, Avianax, Adjuvance, Valneva, Medicago, Sanofi Pasteur, GSK, Emergent Biosolutions, and Dynavax. Maria Knoll reports grants from Merck and Pfizer; personal fees from Merck. Pablo Bonvehi reports personal fees from Sanofi Pasteur, Seqirus, Abbott and Merck. All other authors report no conflicts of interest.

Acknowledgements

The authors are grateful to all ICAI members who provided valuable comments to various versions of this document; Jak Spenser (Helen Hamlyn Centre for Design) for his design advice; Priyanka Das for her help in visualizations; and Sara Carson, MD for her thoughts on the paper. The authors received no funding to write this paper. The International Vaccine Access Center received a Pfizer sponsorship to conduct the meeting. No Pfizer employees were present at the meeting.

References

- [1] Tan L. Adult vaccination: Now is the time to realize an unfulfilled potential. Hum Vaccin Immunother 2015;11:2158–66.
- [2] Bonanni P, Bonaccorsi G, Lorini C, Santomauro F, Tiscione E, Boccalini S, et al. Focusing on the implementation of 21st century vaccines for adults. Vaccine 2018;36:5358–65.
- [3] Doherty TM, Connolly MP, Del Giudice G, Flamaing J, Goronzy JJ, Grubeck-Loebenstein B, et al. Vaccination programs for older adults in an era of demographic change. Eur Geriatr Med 2018;9:289–300.
- [4] United Nations department of economic and social affairs population division. World Population Prospects 2019: Highlights; 2019.
- [5] Beard JR, Officer A, de Carvalho IA, Sadana R, Pot AM, Michel JP, et al. The World report on ageing and health: a policy framework for healthy ageing. Lancet 2016;387:2145–54.

- [6] Institute of Medicine (US). Ethical issues in pandemic planning and response. Ethical and legal considerations in mitigating pandemic disease: workshop summary. Washington (DC); 2007.
- [7] Shiffman J, Smith S. Generation of political priority for global health initiatives: a framework and case study of maternal mortality. Lancet 2007;370:1370–9.
- [8] Coalition for epidemic preparedness innovations. CEPI expands investment in COVID-19 vaccine development. Oslo, Norway2020.
- [9] Novel coronavirus pneumonia emergency response epidemiology team. [The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China]. China CDC Weekly. 2020;41:145–51.
- [10] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020.
- [11] Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. JAMA Cardiol 2020.
- [12] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507–13.
- [13] Centers for Disease Control and Prevention. Weekly U.S. Influenza Surveillance Report; 2020.
- [14] Global burden of disease collaborative network. Global Burden of Disease Study 2017 (GBD 2017) Cause-Specific Mortality 1980-2017. Seatt, United States: Institute of Health Metrics and Evaluation; 2018.
- [15] Centers for Disease Control & Prevention. Pneumococcal Vaccines (PCV13 and PPSV23): Addressing Common Questions about Pneumococcal Vaccination for Adults. 2019.
- [16] Harpaz R, Ortega-Sanchez IR, Seward JF. Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2008;57. 1–30; quiz CE2-4.
- [17] Schmader K, Gnann Jr JW, Watson CP. The epidemiological, clinical, and pathological rationale for the herpes zoster vaccine. J Infect Dis 2008;197 (Suppl 2):S207–15.
- [18] Warren-Gash C, Smeeth L, Hayward AC. Influenza as a trigger for acute myocardial infarction or death from cardiovascular disease: a systematic review. Lancet Infect Dis 2009;9:601–10.
- [19] Sosa Liprandi MI, Sosa Liprandi A, Fernandez A, Stecher D, Bonvehi P, Veron MT. Influenza and pneumococcal immunization in cardiovascular prevention. Medicina (B Aires) 2014;74:245–53.
- [20] Erskine N, Tran H, Levin L, Ulbricht C, Fingeroth J, Kiefe C, et al. A systematic review and meta-analysis on herpes zoster and the risk of cardiac and cerebrovascular events. PLoS ONE 2017;12. e0181565.
- [21] Wedzicha JA, Seemungal TAR. COPD exacerbations: defining their cause and prevention. The Lancet 2007;370:786–96.
- [22] Pickering G, Marcoux M, Chapiro S, David L, Rat P, Michel M, et al. An algorithm for neuropathic pain management in older people. Drugs Aging 2016;33:575–83.
- [23] Bula CJ, Ghilardi G, Wietlisbach V, Petignat C, Francioli P. Infections and functional impairment in nursing home residents: a reciprocal relationship. J Am Geriatr Soc 2004;52:700–6.
- [24] McElhaney JE, Kuchel GA, Zhou X, Swain SL, Haynes L. T-cell immunity to influenza in older adults: a pathophysiological framework for development of more effective vaccines. Front Immunol 2016;7:41.
- [25] Yao X, Hamilton RG, Weng NP, Xue QL, Bream JH, Li H, et al. Frailty is associated with impairment of vaccine-induced antibody response and increase in post-vaccination influenza infection in community-dwelling older adults. Vaccine 2011;29:5015–21.
- [26] Loughlin D, Brown M. Improving surgical outcomes for people with dementia. Nurs Stand 2015;29:50–8.
- [27] Bornand D, Toovey S, Jick SS, Meier CR. The risk of new onset depression in association with influenza-A population-based observational study. Brain Behav Immun 2016;53:131–7.
- [28] Chang AY, Skirbekk VF, Tyrovolas S, Kassebaum NJ, Dieleman JL. Measuring population ageing: an analysis of the global burden of disease study 2017. Lancet Public Health 2019;4:e159–67.
- [29] Cafiero-Fonseca ET, Stawasz A, Johnson ST, Sato R, Bloom DE. The full benefits of adult pneumococcal vaccination: A systematic review. PLoS ONE 2017;12. e0186903.
- [30] Thomas-Crusells J, McElhaney JE, Aguado MT. Report of the ad-hoc consultation on aging and immunization for a future WHO research agenda on life-course immunization. Vaccine 2012;30:6007–12.
- [31] Lee JKH, Lam GKL, Shin T, Kim J, Krishnan A, Greenberg DP, et al. Efficacy and effectiveness of high-dose versus standard-dose influenza vaccination for older adults: a systematic review and meta-analysis. Expert Rev Vaccines 2018;17:435–43.
- [32] McElhaney JE, Beran J, Devaster JM, Esen M, Launay O, Leroux-Roels G, et al. AS03-adjuvanted versus non-adjuvanted inactivated trivalent influenza vaccine against seasonal influenza in elderly people: a phase 3 randomised trial. Lancet Infect Dis 2013;13:485–96.
- [33] Bonten MJ, Huijts SM, Bolkenbaas M, Webber C, Patterson S, Gault S, et al. Polysaccharide conjugate vaccine against pneumococcal pneumonia in adults. N Engl J Med 2015;372:1114–25.
- [34] Postma MJ, Carroll S, Brandao A. The societal role of lifelong vaccination. J Mark Access Health Policy 2015. 3.
- [35] Rappuoli R, Pizza M, Del Giudice G, De Gregorio E. Vaccines, new opportunities for a new society. Proc Natl Acad Sci U S A 2014;111:12288–93.

- [36] Schmader KE, Sloane R, Pieper C, Coplan PM, Nikas A, Saddier P, et al. The impact of acute herpes zoster pain and discomfort on functional status and quality of life in older adults. Clin J Pain 2007;23:490–6.
- [37] Raina MacIntyre C, Menzies R, Kpozehouen E, Chapman M, Travaglia J, Woodward M, et al. Equity in disease prevention: Vaccines for the older adults - a national workshop, Australia 2014. Vaccine 2016;34:5463–9.
- [38] Jit M, Hutubessy R, Png ME, Sundaram N, Audimulam J, Salim S, et al. The broader economic impact of vaccination: reviewing and appraising the strength of evidence. BMC Med 2015;13:209.
- [39] Australian Technical Advisory Group on Immunisation (ATAGI). The Australian Immunisation Handbook 10th Edition. Canberra: Australian Government Department of Health.; 2017.
- [40] Government of Canada. Public Funding for Influenza Vaccination by Province/ Territory (as of September 2017). 2017.
- [41] Lu PJ, O'Halloran A, Williams WW, Lindley MC, Farrall S, Bridges CB. Racial and ethnic disparities in vaccination coverage among adult populations in the U.S. Am J Prev Med 2015;49:S412–25.
- [42] Astra Zeneca. AstraZeneca takes next steps towards broad and equitable access to Oxford University's COVID-19 vaccine; 2020.
- [43] US department of health and human services. Trump administration's operation warp speed accelerates astrazeneca COVID-19 vaccine to be available beginning in October. 2020.
- [44] Peasah SK, Azziz-Baumgartner E, Breese J, Meltzer MI, Widdowson MA. Influenza cost and cost-effectiveness studies globally-a review. Vaccine 2013;31:5339-48.
- [45] Ting EEK, Sander B, Ungar WJ. Systematic review of the cost-effectiveness of influenza immunization programs. Vaccine 2017;35:1828–43.
- [46] Chen C, Beutels P, Wood J, Menzies R, MacIntyre CR, McIntyre P, et al. Retrospective cost-effectiveness of the 23-valent pneumococcal polysaccharide vaccination program in Australia. Vaccine 2018;36:6307–13.
- [47] Jiang Y, Yang X, Taniguchi K, Petigara T, Abe M. A cost-effectiveness analysis of revaccination and catch-up strategies with the 23-valent pneumococcal polysaccharide vaccine (PPV23) in older adults in Japan. J Med Econ 2018;21:687–97.
- [48] Thorrington D, van Rossum L, Knol M, de Melker H, Rumke H, Hak E, et al. Impact and cost-effectiveness of different vaccination strategies to reduce the burden of pneumococcal disease among elderly in the Netherlands. PLoS ONE 2018;13. e0192640.
- [49] Willem L, Blommaert A, Hanquet G, Thiry N, Bilcke J, Theeten H, et al. Economic evaluation of pneumococcal vaccines for adults aged over 50 years in Belgium. Hum Vaccin Immunother 2018;14:1218–29.
- [50] Prosser LA, Harpaz R, Rose AM, Gebremariam A, Guo A, Ortega-Sanchez IR, et al. A cost-effectiveness analysis of vaccination for prevention of herpes zoster and related complications: input for national recommendations. Ann Intern Med 2019;170:380–8.
- [51] Melegaro A, Marziano V, Del Fava E, Poletti P, Tirani M, Rizzo C, et al. The impact of demographic changes, exogenous boosting and new vaccination policies on varicella and herpes zoster in Italy: a modelling and costeffectiveness study. BMC Med 2018;16:117.
- [52] Chiyaka ET, Nghiem VT, Zhang L, Deshpande A, Mullen PD, Le P. Costeffectiveness of herpes zoster vaccination: a systematic review. Pharmacoeconomics 2019;37:169–200.
- [53] Leidner AJ, Murthy N, Chesson HW, Biggerstaff M, Stoecker C, Harris AM, et al. Cost-effectiveness of adult vaccinations: A systematic review. Vaccine 2019;37:226–34.
- [54] Ozawa S, Portnoy A, Getaneh H, Clark S, Knoll M, Bishai D, et al. Modeling the economic burden of adult vaccine-preventable diseases in the United States. Health Aff (Millwood) 2016;35:2124–32.
- [55] McLaughlin JM, McGinnis JJ, Tan L, Mercatante A, Fortuna J. Estimated human and economic burden of four major adult vaccine-preventable diseases in the United States, 2013. J Prim Prev 2015;36:259–73.
- [56] Bonanni P, Picazo JJ. Remy V. The intangible benefits of vaccination what is the true economic value of vaccination? J Mark Access. Health Policy 2015;3.
- [57] Rappuoli R, Bloom DE, Black S. Deploy vaccines to fight superbugs. Nature 2017:552:165-7.
- [58] Bloom DE, Brenzel L, Cadarette D, Sullivan J. Moving beyond traditional valuation of vaccination: Needs and opportunities. Vaccine 2017;35(Suppl 1): A29–35.
- [59] Verguet S, Memirie ST, Norheim OF. Assessing the burden of medical impoverishment by cause: a systematic breakdown by disease in Ethiopia. BMC Med 2016;14:164.
- [60] United Nations. Coronavirus update: COVID-19 likely to cost economy \$1 trillion during 2020, says UN trade agency. In: News U, editor; 2020.
- [61] Fan VY, Jamison DT, Summers LH. Pandemic risk: how large are the expected losses?. Bull World Health Organ 2018;96:129–34.
- [62] . Washington (DC): National Academy of Medicine 2016.
- [63] Lazzerini M, Putoto G. COVID-19 in Italy: momentous decisions and many uncertainties. Lancet Glob Health 2020.
- [64] Remuzzi A, Remuzzi G. COVID-19 and Italy: what next?. Lancet 2020.
- [65] World Bank. Global economic prospects. Washington, DC; 2020.
- [66] In: Feng E, editor. Weekend Addition Saturday: NPR.
- [67] Smith N, Fraser M. Straining the system: novel coronavirus (COVID-19) and preparedness for concomitant disasters. Am J Public Health 2020:e1–2.
- [68] World Health Organization. Developing together the vision and strategy for immunization – 2021-2030. Immunization Agenda 2030. A global strategy to leave no one behind. 2019. Draft 1. Geneva2019.

- [69] Reichert TA. The Japanese program of vaccination of schoolchildren against influenza: implications for control of the disease. Semin Pediatr Infect Dis 2002;13:104–11.
- [70] Loeb M, Russell ML, Moss L, Fonseca K, Fox J, Earn DJ, et al. Effect of influenza vaccination of children on infection rates in Hutterite communities: a randomized trial. JAMA 2010;303:943–50.
- [71] Tsaban G, Ben-Shimol S. Indirect (herd) protection, following pneumococcal conjugated vaccines introduction: A systematic review of the literature. Vaccine 2017;35:2882–91.
- [72] Shiri T, Datta S, Madan J, Tsertsvadze A, Royle P, Keeling MJ, et al. Indirect effects of childhood pneumococcal conjugate vaccination on invasive pneumococcal disease: a systematic review and meta-analysis. Lancet Glob Health 2017;5:e51–9.
- [73] Kash JC, Taubenberger JK. The role of viral, host, and secondary bacterial factors in influenza pathogenesis. Am J Pathol 2015;185:1528–36.
- [74] Kwong JC, Maaten S, Upshur RE, Patrick DM, Marra F. The effect of universal influenza immunization on antibiotic prescriptions: an ecological study. Clin Infect Dis 2009;49:750–6.
- [75] von Gottberg A, de Gouveia L, Tempia S, Quan V, Meiring S, von Mollendorf C, et al. Effects of vaccination on invasive pneumococcal disease in South Africa. N Engl J Med 2014;371:1889–99.
- [76] Gabutti G, d'Anchera E, Sandri F, Savio M, Coronavirus SA. Update related to the current outbreak of COVID-19. Infect Dis Ther 2020:1–13.
- [77] Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the chinese center for disease control and prevention. JAMA 2020.
- [78] Kim D, Quinn J, Pinsky B, Shah NH, Brown I. Rates of co-infection between SARS-CoV-2 and other respiratory pathogens. JAMA 2020.
- [79] Privor-Dumm L, Vasudevan P, Kobayashi K, Gupta J. Archetype analysis of older adult immunization decision-making and implementation in 34 countries. Vaccine 2020;38(26):4170–82.
- [80] Ortiz JR, Perut M, Dumolard L, Wijesinghe PR, Jorgensen P, Ropero AM, et al. A global review of national influenza immunization policies: Analysis of the 2014 WHO/UNICEF Joint Reporting Form on immunization. Vaccine 2016;34:5400–5.
- [81] Poudel A, Lau ETL, Deldot M, Campbell C, Waite NM, Nissen LM. Pharmacist role in vaccination: Evidence and challenges. Vaccine 2019;37:5939–45.
- [82] Philip RK, Attwell K, Breuer T, Di Pasquale A, Lopalco PL. Life-course immunization as a gateway to health. Expert Rev Vaccines 2018;17:851–64.
- [83] MacDonald NE. Hesitancy SWGoV. Vaccine hesitancy: Definition, scope and determinants. Vaccine 2015;33:4161–4.
- [84] Hickler B, MacDonald NE, Senouci K, Schuh HB. Informal working group on vaccine D, strategic advisory group of experts on immunization working group on decade of V. Efforts to monitor global progress on individual and

community demand for immunization: development of definitions and indicators for the global vaccine action plan strategic objective 2. Vaccine 2017;35:3515–9.

- [85] Betsch C, Fiske ST, Böhm R, Chapman GB. Using behavioral insights to increase vaccination policy effectiveness. Policy Insights from the Behavioral and Brain Sciences 2015:2:61–73.
- [86] World Health Organization. Ten threats to global health in 2019; 2019.
- [87] Lahariya C, Bhardwaj P. Adult vaccination in India: status and the way forward. Hum Vaccin Immunother 2019:1–3.
- [88] Heymann DL, Shindo N, Scientific WHO. Technical Advisory Group for Infectious H. COVID- 19: what is next for public health?. Lancet 2020;395:542–5.
- [89] Commonwealth of Australia Department of Health. National Immunisation Strategy for Australia 2019 to 2024; 2018.
- [90] European centre for disease prevention and control. Designing and implementing an immunisation information system. Stockholm; 2018.
- [91] Kim E, Erdos G, Huang S, Kenniston TW, Balmert SC, Carey CD, et al. Microneedle array delivered recombinant coronavirus vaccines: Immunogenicity and rapid translational development. EBioMedicine 2020. 102743.
- [92] World Health Organization. Global strategy and action plan on ageing and health. Geneva; 2017.
- [93] The World Health Organization. The decade of healthy ageing 2020-2030; 2020.
- [94] Levine OS, Hajjeh R, Wecker J, Cherian T, O'Brien KL, Knoll MD, et al. A policy framework for accelerating adoption of new vaccines. Hum Vaccin 2010;6:1021–4.
- [95] Sauer M, Vasudevan P, Meghani A, Luthra K, Garcia C, Knoll M, et al. Situational assessment of adult vaccine preventable disease and the potential for immunization advocacy and policy in low- and middle-income countries 2020. Manuscript under review.
- [96] Esposito S, Bonanni P, Maggi S, Tan L, Ansaldi F, Lopalco PL, et al. Recommended immunization schedules for adults: Clinical practice guidelines by the Escmid Vaccine Study Group (EVASG), European Geriatric Medicine Society (EUGMS) and the World Association for Infectious Diseases and Immunological Disorders (WAidid). Hum Vaccin Immunother 2016;12:1777–94.
- [97] Gaurau J, Sinclair D, Banks I, Braun K, Bernabel R, Holt D, et al. Adult vaccination: a key component of healthy ageing. The benefits of life-course immunisation Europe 2013.
- [98] National Vaccine Program Office. National Adult Immunization Plan 2016-2020. Washington D.C.2016.
- [99] Teresa Aguado M, Barratt J, Beard JR, Blomberg BB, Chen WH, Hickling J, et al. Report on WHO meeting on immunization in older adults: Geneva, Switzerland, 22–23 March 2017. Vaccine 2018;36:921–31.