

Original Article



Which Group Should be Vaccinated First?: A Systematic Review

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OPEN ACCESS

Received: May 12, 2021

Accepted: May 31, 2021

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Funding

This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (NRF-2021R1C1C2005464)

Conflict of Interest

No conflicts of interest.

ABSTRACT

Background: Since the supply of coronavirus disease 2019 (COVID-19) vaccines will be limited worldwide, it is essential to prioritize vaccination based on scientific evidence. Although several frameworks and studies on vaccine distribution have been published, no published systematic review has evaluated the prioritization of the COVID-19 vaccine.

Materials and Methods: We searched 4 different databases, PubMed, SCOPUS, Web of Science, and EMBASE for articles published between January 2019 and December 31, 2020. Studies were included if they contained the primary search terms “vaccine”, “COVID-19”, and “prioritization”. In addition, we manually included reports from national and international websites.

Results: Thirteen studies met the inclusion criteria. In these studies, older adults were the most frequently mentioned group, and healthcare workers (HCWs) were mentioned as the 1st priority group. HCWs and patients with comorbidities were the 2nd and 3rd most frequently mentioned groups in the reviewed papers. Reducing severe COVID-19 was the most frequently mentioned goal.

Conclusion: Since vaccination programs have been initiated in several countries, scientific evidence on vaccination prioritization is needed to increase our knowledge of general vaccine prioritization and improve vaccine acceptance. Our results showed that HCWs and older adults were the most frequently valued in studies.

Keywords: Coronavirus; Vaccine; Prioritization

INTRODUCTION

Coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a huge catastrophe worldwide. The World Health Organization (WHO) declared the disease a “pandemic” on March 11, 2020 [1], and 103,201,340 cases and 2,237,636 deaths have been reported till February 2021 [2]. Several strategies, including pharmaceutical and non-pharmaceutical interventions, have been formed and implemented to combat this crisis. Currently, vaccination is likely after the COVID-19 Vaccines Global Access Facility (COVAX) agreed to assess and allocate promising COVID-19 vaccines [3]. The supply of COVID-19 vaccines will be limited worldwide [4], and vaccines will become scarce before an appropriate number of citizens is immunized, especially in countries that



Author Contributions

Conceptualization: EBN, HCL. Data curation: EBN, HWN, HCL. Investigation: EBN. Methodology: EBN, HWN. Visualization: EBN. Writing - original draft: EBN. Writing - review & editing: EBN, HWN, HCL.

do not produce the COVID-19 vaccine. Which groups should be prioritized for vaccination within countries? This is a very complex situation because vaccination with scarce supply is combined with various issues, such as ethics, economics, and politics [5]. Thus, to achieve the goal of vaccination, that is, getting people immunized, and finally achieving herd immunity, it is essential to prioritize vaccination based on scientific evidence [6].

Several frameworks from the WHO, the United States of America (USA) National Academies of Science, Engineering and Medicine (NASEM), and the Centers for Disease Control and Prevention (CDC), and few studies have discussed vaccine distribution. However, reviews focusing on vaccine prioritization are limited. Given that some countries including the United Kingdom (UK) and USA have started to implement their own vaccination programs [7, 8], such review is timely.

Through a systematic review, we aim to organize the priorities that are being emphasized at this time.

MATERIALS AND METHODS

1. Definitions

We defined COVID-19 vaccine prioritization as identifying priority groups within countries in the context of a limited supply of the vaccine. We limited the vaccine to COVID-19 and did not differentiate between the different types of vaccine, due to the limited product-specific data available till February 2021 [9].

2. Search Strategies and Selection Criteria

We selected 4 databases - PubMed, SCOPUS, Web of Science, and EMBASE - for searching articles published until December 31, 2020. The databases were searched using the following 3 keywords: “COVID-19,” “vaccine,” and “prioritization” (see Supplementary Material 1 for full search strings by database). We also manually included several national and international reports that suggest frameworks for COVID-19 vaccine prioritization with regards to vaccinee groups within countries, but are not uploaded in databases. We limited the selection to articles published between January 1, 2019 and December 31, 2020.

We did not exclude any study method if the report included the author's own public health perspective of vaccine prioritization. We excluded publications with only abstracts or those that did not contain original ideas or opinions of the respective authors. We also excluded studies that were not related to vaccine prioritization (*e.g.*, those concerning the development or safety of the vaccine) or related to the distribution of vaccines between countries, not within countries. Finally, study that were not written in Korean or English were excluded.

3. Data Extraction and Quality Assessment

Three reviewers independently assessed the relevance and originality of each study in-depth. Any disagreements were resolved through discussion and articles were selected by consensus. The reviewers are specialized in epidemiology, global health, and preventive medicine.

4. Data Analysis

The details of the review process and the results at each stage are shown in the PRISMA flow diagram in **Figure 1** [10]. General characteristics of eligible research articles were

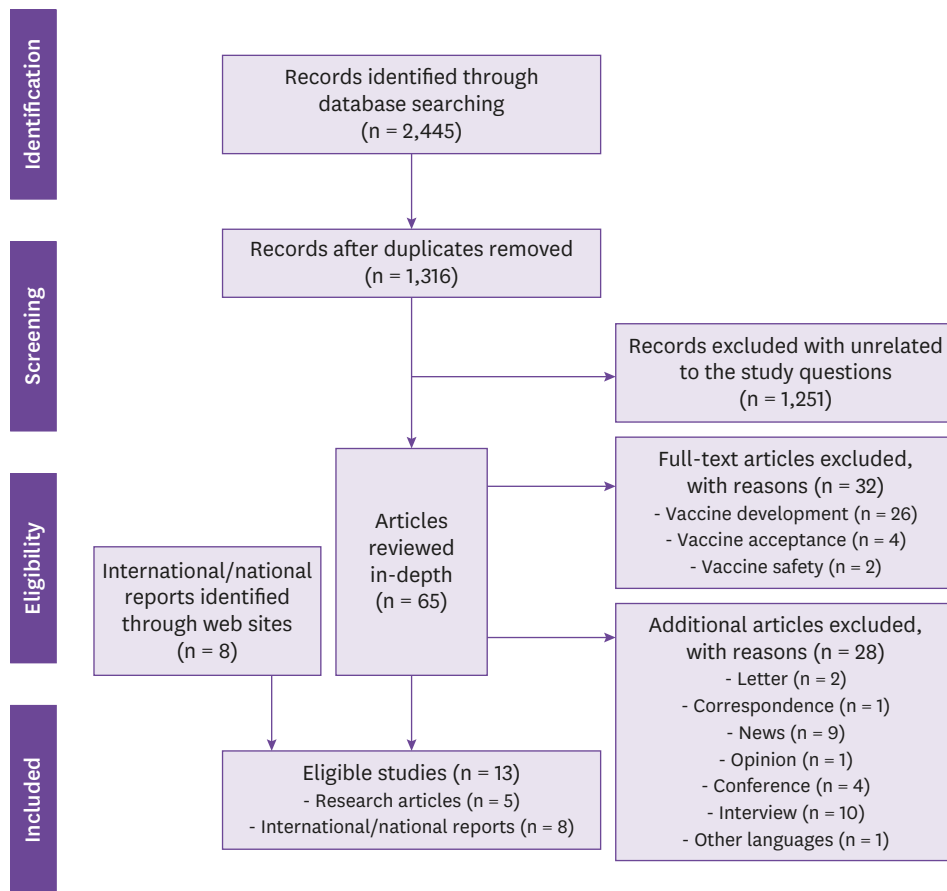


Figure 1. Study search and selection.

summarized in **Table 1**. We categorized the selected studies by occupational and socio-demographic groups suggested for vaccine prioritization (**Table 2**). Further, we divided each group according to the goals of vaccination set by the Korea Disease Control and Prevention Agency as: maintaining essential social core services, reducing severe COVID-19 disease, and reducing virus transmission [11]. The classification into groups was based on the study by Wang et al. [12] and assessed by all 3 reviewers. Priority was numbered

Table 1. Research articles on vaccine prioritization

Citation (Authors; Year; Reference)	Countries	Type of study	Main findings
Bubar et al (2020) [19]	United States, Belgium, Brazil, China, India, Poland, South Africa, and Spain	An age-stratified mathematical model	A highly effective transmission-blocking vaccine prioritized to adults ages 20 - 49 years minimized cumulative incidence, but mortality and years of life lost minimized in most scenarios when the vaccine was prioritized to adults over 60 years old.
Buckner et al (2020) [18]	United States	An mathematical model differentiated by age and essential worker status	To control spread, younger essential workers are prioritized. To directly control mortality, older essential workers are prioritized.
Giubilini et al (2020) [20]	-	REVIEW	There are strong ethical reasons to vaccinate the young to protect the old.
Matrajt L et al (2020) [16]	United States	An age-stratified mathematical model paired with optimization algorithms	To minimize deaths, for low vaccine effectiveness and a low supply of vaccine, it is optimal to allocate vaccine to high-risk (older) age-groups first. In contrast, for high vaccine effectiveness and high vaccine coverage, the optimal allocation strategy switched to allocate vaccine to high-transmission (young adults and children) age-groups first.
Moore et al (2020) [17]	United Kingdom	A compartmental age-structure model	Targeting older age groups first can both minimize future deaths and quality adjusted life year losses

Prioritizing groups for COVID-19 vaccination

Table 2. General Characteristics of Priority Groups

Authors/Countries	Occupational/Socio-demographic Groups											
	Goal 1 Maintain core essential social services				Goal 2 Reduce severe COVID-19 disease				Goal 3 Reduce virus transmission			
	Healthcare workers	Police & military	Staff working energy & food & transportation	Vaccine delivery & diagnosis	Old	Patients with co-morbidities	Pregnant woman	Long-term care home residents	Younger adults	School children and young 5 - 19 yr	Young children 0 - 4 yr	Teachers school staff
Research article												
Bubar et al (2020) [19]					1				1			
Buckner et al (2020) [18]					2				1	2		
Giubilini et al (2020) [20]	1				3					2	2	
Matrajt L et al (2020) [16]					1				1	1	1	
Moore et al (2020) [17]					1				2			
Guidelines by countries												
Australian Technical Advisory Group on Immunisation (Australia) (2020) [35]	2	3	3		1	1						
CDC (USA) (2020) [21]	1			3	2	2	2					3
JCVI (UK) (2020) [8]	1				2	3		1				
Korea Disease Control and Prevention Agency (Korea) (2021) [11]	1	3	3		2	3		1	3	3	3	3
Ministry of Health, Labour and Welfare (Japan) (2020) [36]	1				1	1						
NASEM (2020) [37]	1				2	2						
National Advisory Committee on Immunization (Canada) (2020) [38]	1				1			1				
WHO (2020) [22]	1			3	2	3	4					3

COVID-19, coronavirus disease of 2019; CDC, Centers for Disease Control and Prevention; JCVI, Joint Committee on Vaccination and Immunisation; NASEM, National Academies of Sciences, Engineering, and Medicine; WHO, World Health Organization.

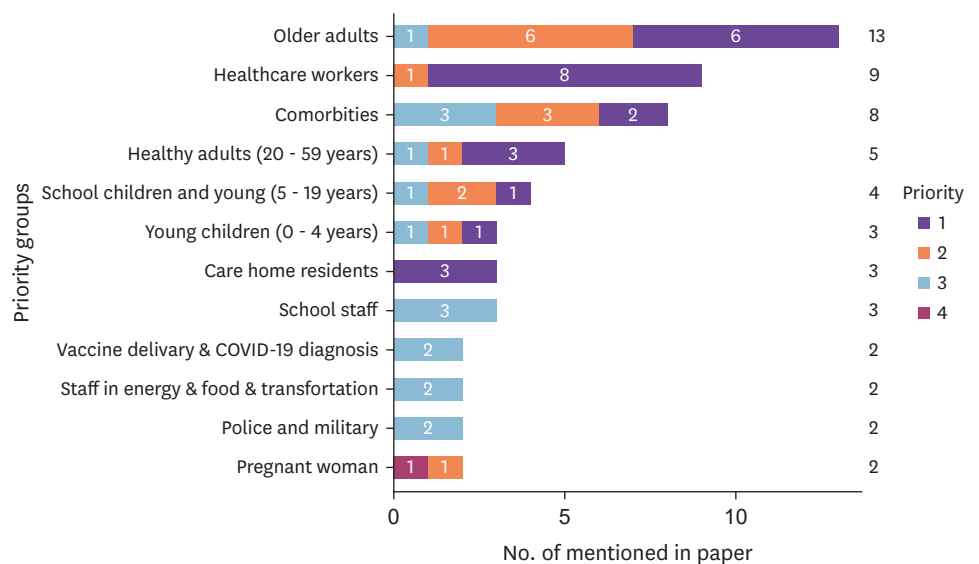


Figure 2. Frequency of prioritizing according to groups. COVID-19, Coronavirus disease 2019.

based on the outcomes and opinions of the authors of the studies. The priority groups were graphically represented by frequency (Fig. 2), which was subdivided according to the goals of vaccination (Fig. 3).

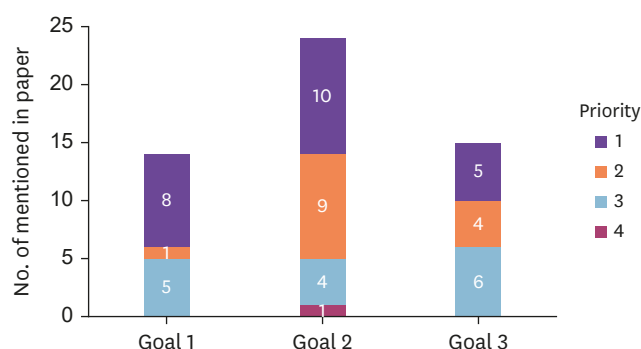


Figure 3. Frequency of prioritizing groups in papers according to goals.
 Goal 1: Maintain core essential social services.
 Goal 2: Reduce severe COVID-19 disease.
 Goal 3: Reduce virus transmission.

RESULTS

1. Study Selection

The initial search up to December 20, 2020, retrieved 2,445 articles (Fig. 1). A total of 1,316 articles remained after removing duplicates. Of these, 81 articles were selected for full-text review, along with 8 national and international reports from websites, that were not included in the databases, and were manually added. Finally, 5 were considered eligible. The reasons for exclusion are shown in Figure 1.

Among 81 articles we reviewed in depth, we found that only 28 papers discussed vaccine prioritizations (38.3%). While most of other excluded articles focused on vaccine development and safety (43.8%). Articles on vaccine prioritization but finally excluded mostly consisted of authors' opinions, including letters or correspondence, without quantitative/qualitative analysis [13-15].

2. General Characteristics of research articles

Table 1 summarized the countries, type of study, and main findings of 5 selected articles. 4 papers [16-19] discussed the direct effect of vaccination with mathematical modeling, and Giubilini et al. [20] reviewed the ethical issues of prioritizing the young to protect the old (Table 1).

3. Frequency in prioritizing by groups and goals

The selected 5 studies and 9 guidelines across countries were categorized according to the occupational/socio-demographic groups prioritized and grouped according to the 3 vaccination goals (Table 2). Each occupational/socio-demographic group was included in each goal-related group.

The frequency of prioritization according to group is shown in Figure 2. Older adults were the most frequently mentioned group in the reviewed papers. 61.5% of papers mentioned Healthcare workers (HCWs) as the 1st priority group. Patients with comorbidities and healthy adults from 20 to 59 years were the 3rd and 4th most frequently mentioned groups in the reviewed papers.

For prioritizing healthy adults from 20 to 59 years, we observed significant disagreement in the reviewed papers regarding which groups should be prioritized between older adults

and young adults (Fig. 2). The effects of minimizing transmission by prioritizing young and healthy adults are suggested in three mathematical modeling papers [16, 18, 19]. Furthermore, Buckner discussed the possibility of decreasing mortality, not only stopping transmission [18]. Giubilini discussed whether valuing young to ultimately protect the old is ethically problematic [20].

Related to pregnant women, some disagreement is seen among studies regarding the quality and quantities of evidence. The CDC suggested pregnant women should be a high priority (2nd) [21]; on the other hand, the WHO set the 4th priority, which is under the situation of moderate vaccine availability [22]. Similarly, the UK Joint Committee on Vaccination and Immunisation (JCVI) did not place much importance on vaccinating pregnant women and did not place them into priority groups [8].

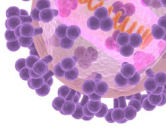
Frequent mention of older adults, comorbidities, and care home residents affects the overall frequency of Goal 2, which is the most frequently mentioned among the three vaccination goals. Goal 3 was second frequently mentioned among 3 goals. Finally, Goal 1 was the least mentioned (Fig. 3).

DISCUSSION

Several studies and international frameworks have discussed COVID-19 vaccines. However, scoping reviews investigating vaccine prioritization are limited. This systematic review aimed to organize various socio/demographic groups by their vaccine priority.

We found that only a few papers discussed vaccine prioritizations, while most of other articles focused on vaccine development and safety. Related to data analysis methods, only 4 papers [16-19] discussed the direct effect of vaccination with mathematical modeling. Other articles in the database did not contain any quantitative/qualitative analysis. There are several reasons for this result. Since only a few months had passed after COVAX agreed to assess and allocate promising COVID-19 vaccine [3], there was limited time to discuss which group should be vaccinated first. In addition, because vaccine prioritization is highly related to ethical, epidemiological, and economical aspects [23], it might not be easy for researchers to address this issue. However, vaccination has already begun in several countries and groups [24], and prioritization should be discussed more actively to maximize the effect of vaccination.

The WHO recommends that HCWs at high risk should be vaccinated first [22]. Our results show all national reports (100%) emphasize that HCWs should be prioritized, which is consistent with the WHO guidelines. The reasons for emphasizing HCWs are based on the logic that their working environment makes them vulnerable to be infected, they can easily transmit the virus to others, and ultimately, they play an important role in sustaining society (*e.g.*, healthcare systems) [25]. For example, the UK decided to vaccinate HCWs in long-term care facilities first, considering the high proportion of elderly and HCWs in long-term care facilities [26]. However, none of selected articles discussed with prioritizing HCWs. Considered that Emanuel pointed out that the effect of prioritizing HCWs is still empirical [27], further evidence is needed regarding HCWs from which areas or levels of the healthcare system should be vaccinated first. The definition of HCWs should be expanded to include not only health care professionals, such as medical doctors or nurses, but also cleaners or those who transfer patients, and medical technicians who directly contact patients with COVID-19,



as emphasized in the guidelines of the American Geriatrics Society [28]. Moreover, prior to vaccination of HCWs, investigation of transparency, accessibility, and proportions of healthcare systems in each country is essential. Moodley pointed out that in some countries in Africa, the healthcare system is not working well, and most patients with COVID-19 do not have proper access healthcare centers [29]. Similarly, Wang et al. estimated the size of the vaccinated population and showed that compared to Europe or America, where over 6 million HCWs must be vaccinated to achieve 60% of vaccine coverage, there are only 0.8 million HCWs in Africa [30].

The WHO ranked older adults immediately after HCWs in high-risk groups under the vaccine limitation [22]. Our results show compliance with the WHO guidelines, as older adults are ranked as the 2nd tier group in most studies. However, older adults are the most frequently mentioned group in the studies. This result shows the growing concern for elderly COVID-19 patients among all demographic groups. Reviewed papers suggested the possibility of reducing mortality or quality-adjusted life year losses by vaccinating them [17], based on the evidence that old age is the biggest risk factor for hospitalization and deaths in patients with COVID-19 [31].

Patients with comorbidities were the 3rd most frequently mentioned groups. Considered that Goal 2 is the most frequently mentioned among the three vaccination goals, we found that the reviewed papers emphasized the importance of reducing COVID-19 severity and mortality.

The few papers discussing prioritizing young people are based on the evidence that there is a low incidence risk for young people but a very high risk of mortality in seniors [32]. In addition, there was a disagreement on prioritizing pregnant women, which shows conflicting evidence regarding the harmful effects of COVID-19 on pregnant women compared to non-pregnant women [33, 34]. Further studies are needed to evaluate the effects of vaccinating healthy adults, children and pregnant women.

We adopted a quantitative approach to review the priorities of COVID-19 vaccines rather than current approaches, such as ethical or mathematical approaches. This method allowed us to establish objectivity in our review. Classifying each socio/demographic group by its priority give us clear insights to find out groups of the worldwide concerns (older adults and HCWs) and groups which do not have clear consensus yet and still need more research (healthy adults, children, and pregnant woman).

Our review has several limitations. Although we systematically searched articles, studies that were not included in the selected database could have been missed. We included articles in English and Korean, thus studies written in other languages were excluded, even if they were related to the topic. Although we manually included several major papers, we could not include all papers, which may have caused a selection bias. Finally, we could not evaluate the type of vaccine due to the limited product-specific data [9].

In conclusion, COVID-19 is a serious public health issue worldwide, and COVID-19 vaccination programs have been launched in several countries. Most of papers emphasize the importance of prioritizing older adults and HCWs. However, at present, the current evidence on vaccine prioritization is insufficient, especially for young adults, children, and pregnant women. There is an urgent need for methodologically adequately powered research evaluating vaccine prioritization.

SUPPLEMENTARY MATERIAL

Supplementary Material 1

List of databases and search strings used for systematic review.

[Click here to view](#)

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