Chapter

Introductory Chapter: Global Research Efforts toward the Development of COVID-19 Vaccines

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1. Introduction

The sudden global spread of a novel coronavirus strain, infecting humans late in 2019, has created a deadly coronavirus disease 2019 (COVID-19), which has become a global threat to humanity [1, 2]. It started a new era of the COVID-19 pandemic with unprecedented socioeconomic challenges and societal crises due to long-term and periodic multiple lockdowns globally. The situation has been even more dangerous in the background of limited knowledge in understanding of the virus, its infection, and variability capacity as well as the lack of drugs and protocols of treatment. One of the most effective solutions against the COVID-19 virus in the pandemic has been a hope for rapid development of COVID-19 vaccines to overcome the global spread of virus infection via forming herd immunity. Thanks to the scientific efforts of world research communities, within a short time and with a fast-track project approach, several novel COVID-19 vaccines have been developed and made available for massive vaccination worldwide.

However, humanity still is in midst of this pandemic, and there is a need for better knowledge, understanding, technology, and innovative solutions to battle against this virus and its novel variants [e.g. see 1]. There were many challenges to rapidly developing COVID-19 vaccines against SARS-CoV-2, including designing immunogenic but nonallergic antigen molecules within a short time, proving experimentally in the appropriate *in vitro/in vivo* models, developing suitable protocols of vaccine administration, assessing the immune-response properties of candidate vaccine(s), conducting controlled and/or randomized the first to third phase safety and efficacy clinical trials involving regional and multicentral designs [1, 2].

Despite these challenges, scientific efforts have resulted in the development of several types of COVID-19 vaccines such as live-attenuated, mRNA-based, DNA-based, inactivated virus-based, and viral-vector-based vaccines. Some of the candidate vaccines have passed a rapid experimental validation in model animals with subsequent clinical studies for safety and suitability, leading to fast-track emergency use approvals (EUA) in many countries granted by World Health Organization (WHO). In particular, as of October 14, 2022, 11 candidate vaccines have been granted for emergency

#	Vaccine name	Company developed	No. trials/ countries	No. countries approved
1.	COVOVAX (Novavax formulation)	Serum Institute of India	7/3	6
2.	Nuvaxovid	Novavax	22/14	40
3.	Spikevax	Moderna	70/24	88
4.	Comirnaty	Pfizer/BioNTech	97/31	149
5.	Convidecia	CanSino	14/6	10
6.	Jcovden	Janssen (Johnson & Johnson)	26/25	113
7.	Vaxzevria	Oxford/AstraZeneca	71/33	149
8.	Covishield (Oxford/ AstraZeneca formulation)	Serum Institute of India	6/1	49
9.	Covaxin	Bharat Biotech	16/2	14
10.	Covilo	Sinopharm (Beijing)	38/17	93
11.	CoronaVac	Sinovac	40/10	56

Approval Source: extranet.who.int [3].

Table 1.
WHO-granted COVID-19 vaccines.

use by WHO [3]. Huge efforts were made toward assessment and making available of these vaccines for the massive population vaccination process, where one can see that 6–97 clinical trials in 1–33 countries have been conducted, leading to approval of emergency use of the particular vaccine(s) in 6–149 countries worldwide (**Table 1**).

The emergency use approvals of these WHO-granted vaccine candidates in each country have been specific, and vaccines have been administered in various combinations per availability and public perception. For instance, in Uzbekistan, we have had a specific experience with the COVID-19 vaccine development, clinical trial(s), acquiring/production, and massive vaccination process [4].

In Uzbekistan, we put concentrated efforts into the genetic characterization of SARS-CoV-2 genotypes in different periods of infection waves [5, 6] and have developed Uzbekistan's own PCR-based diagnostics tools, co-developed and jointly conducted third phase clinical trial for the new recombinant protein vaccine under China-Uzbekistan partnership program [4, 7]. We succeeded in co-localizing the production of recombinant vaccine jabs in the country. Further, we developed two new national vaccines based on pure recombinant protein injection and tomato-based edible COVID-19 vaccines, which are in the preclinical/clinical testing stages. Additionally, we studied and experimentally validated the new approach of obtaining immune cow and goat milk against SARS-CoV-2 [7].

Because of specific efforts from the Uzbekistan government, as of September 26, 2022, 71.9 million doses of seven types of COVID-19 vaccines have been used in the country. These are ZF-UZ-VAC2001 (as known Zifivax; China-Uzbekistan, pending WHO approval) – 48.2 million doses, Moderna (USA) – 10.7 million doses, Pfizer-BioNTech (USA) – 6.8 million doses, AstraZeneca (Great Britain) – 2.6 million doses, Sinovac (China) – 2.0 million doses, Sputnik V (Russia) – 1.3 million doses, and Sputnik light (Russia) – 345,000 doses.

According to the recommendation of the World Health Organization, the population over the age of 18 has mainly been vaccinated. The population of this age group in Uzbekistan was 21.5 million people, of which 98.5% are fully vaccinated and 76.6% (16.4 million people) received a booster dose. The distribution of administered vaccines was as follows: ZF-UZ-VAC2001 – 66.6%, Moderna – 15.5%, Pfizer-BioNTec – 8.9%, AstraZeneca – 3.8%, Sinovac – 2.7%, Sputnik V – 2.0%, and Sputnik light – 0.5%.

Today, "*68.3% of the world population has received at least one dose of a COVID-19 vaccine. A total of 12.83 billion doses have been administered globally, and 3.58 million are now administered each day. 23.3% of people in low-income countries have received at least one dose*" [8]. All these demonstrated the power and feasibility of scientific efforts and multinational collaborations in the timely development of effective vaccines against this most deadly infection of the past 100 years if concentrated attention is given and needed resources are provided [2]. There were common, fast-passing side effects with rare risky allergic reactions from the COVID-19 vaccination, but the benefits of COVID-19 vaccine administrations outweigh those risks.

However, there are more challenges ahead to address, including but not limited to the need for rapid development of novel vaccine types against emerging variants of concerns (VOCs), and the development of safe vaccination protocols for children and people with accompanying diseases. There is a need for addressing post-vaccination health issues, vaccine inequity, vaccine hesitancy, and vaccination ethics [9, 10] as well as for the establishment of large-scale production of high-quality and stable vaccines to make available needed jab volumes for all countries.

2. COVID-19 vaccine research focus during the pandemic

The scientific research articles devoted to the development and application of COVID-19 vaccines, retrieved from the *PubMed* database [11] using the keyword search of "*COVID-19 vaccine*," revealed a total of 9468 scientific publications as of October 2022 (**Figure 1**). Using Pubmed graphics and filtration tools, we observed that scientific results started to be published in 2020 (415 publications) and the

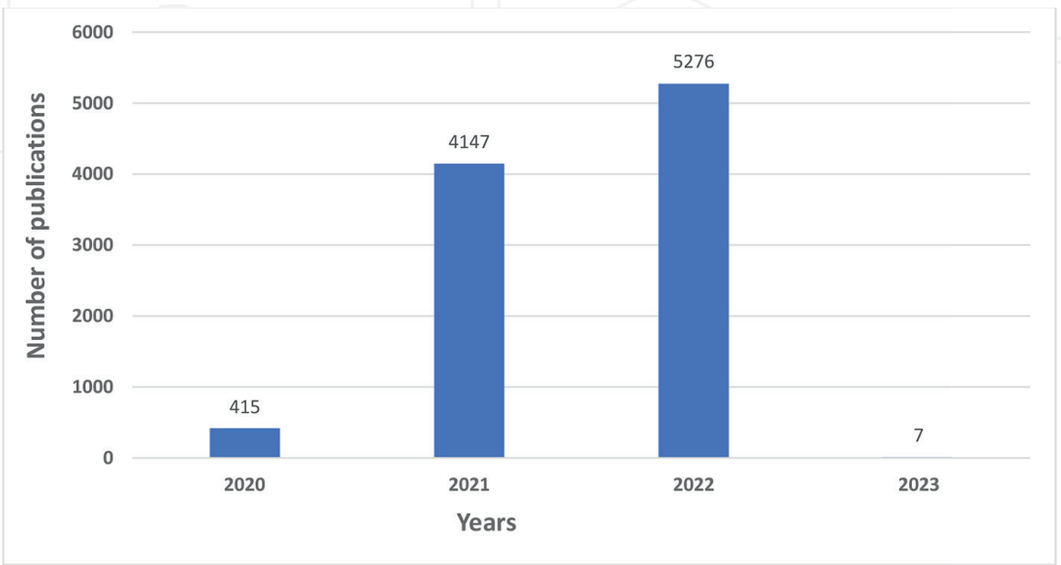

Figure 1.
PubMed [6] indexed scientific publications, retrieved using the "COVID-19 vaccine" keyword on October 12, 2022.

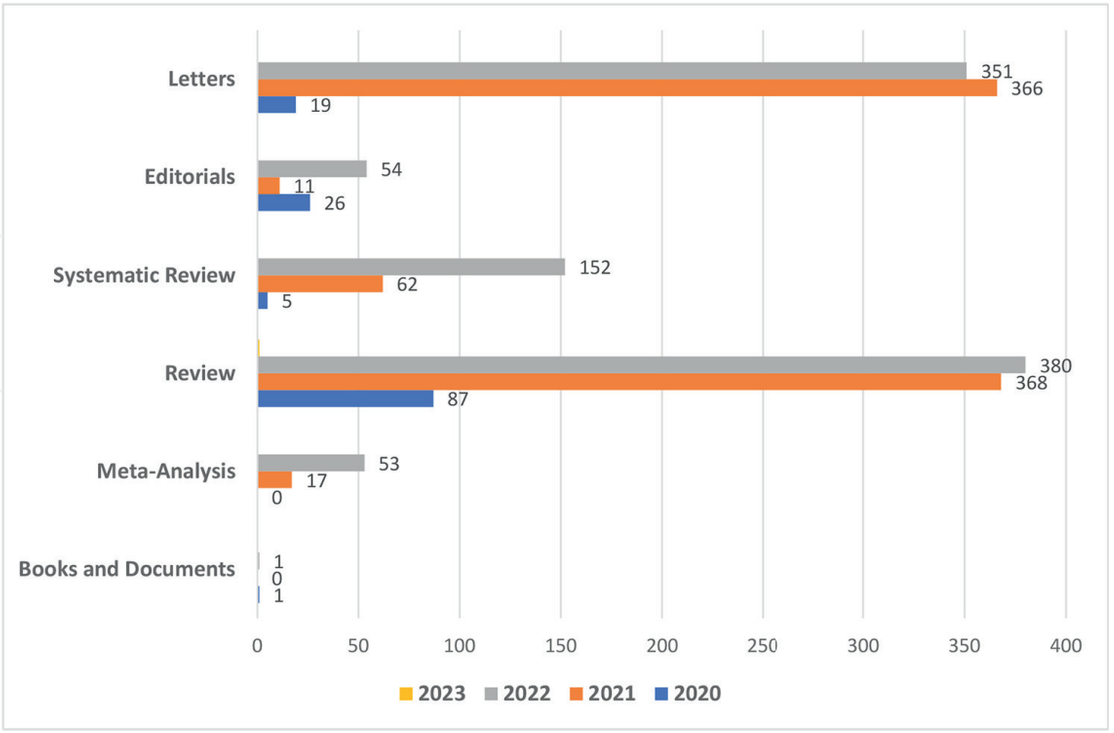

Figure 2.
Research article types on the COVID-19 vaccine development.

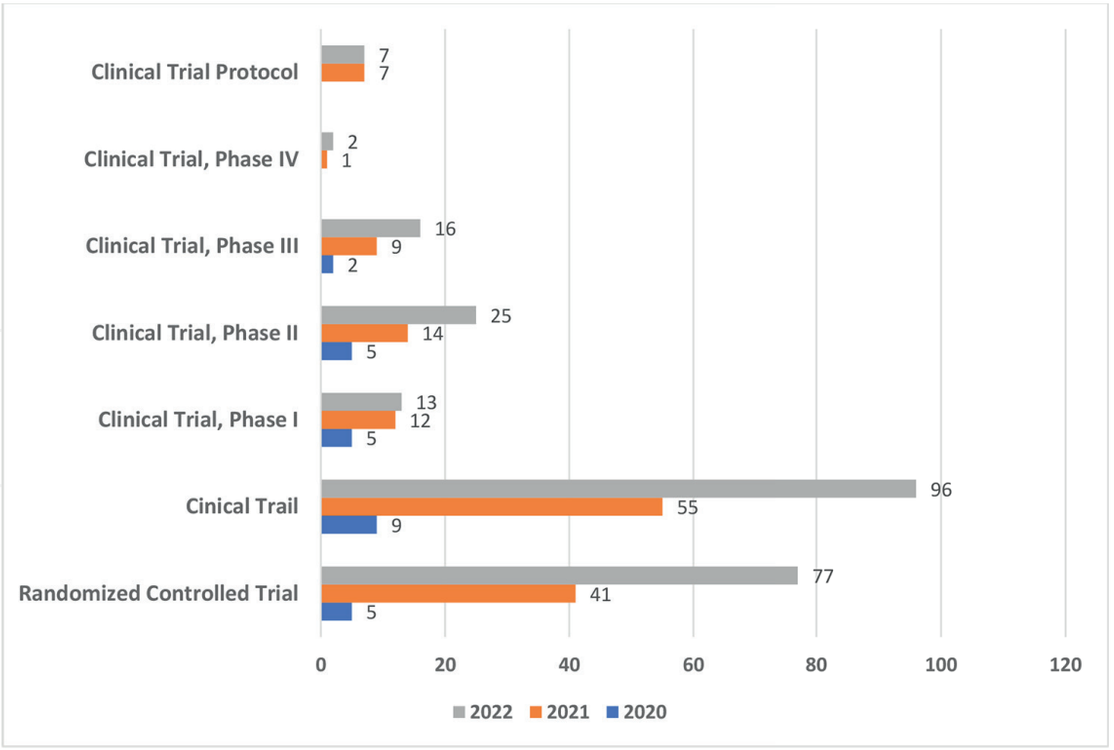

Figure 3.
Research articles on the clinical trials of the COVID-19 vaccine.

number of publications has increased by over 10-fold in 2021 and 2022. This showed the international community's very extensive and focused research efforts toward developing vaccines against this deadly pandemic SARS-CoV-2 virus.

The literature analysis and research publications on PubMed-indexed journals from 2019 to 2022 (**Figure 2**) toward the development of COVID-19 vaccines for the past 3 years of the SARS-CoV-2 pandemic revealed that the majority of publications were Reviews (835 publications) [e.g., see 1, 2, 9, 10], Letters (736 publications) [e.g., see 12–16], Clinical trial-related (401 publications) [e.g., see 4, 17–25], following Systematic reviews (219 publications) [e.g., see 26–30], Editorials (91 publications) [e.g., see 31–35], and Meta-analyses (70 publications) [e.g., see 36–38]. Almost 1200 articles published have associated data. Two books covering COVID-19 vaccines have been published in 2020 [39] and 2022 [40].

Based on the filtration for the clinical trial article category (**Figure 3**), one can see that there are more articles on clinical trials in 2021 than in 2020 and increased by almost 11 times in 2022 compared with 2020. We observed research result publication of clinical trials of phases 1–3 from 2020 to 2022 [4, 17–25] while phase 4 trial results were available in 2021 [41] and 2022 [42, 43].

3. Conclusion

Thus, global research efforts toward the development of COVID-19 vaccines provided state-of-the-art vaccines against the infectious SARS-CoV-2 virus saving millions of lives to date, demonstrating the importance of "deep science" for securing the economy, human health, and life. The current and future development trends dedicated to the development of novel vaccines will require more concentration and multi-institutional collaborative efforts.

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