Research Report

ANNETTE PRIETO, ROBERT HUANG, CHRISTOPHER A. EUSEBI, MELISSA SHOSTAK

A Brief Overview of Emerging Vaccine Technologies for Pandemic Preparedness

The past two decades provide many examples of the importance of pandemic preparedness. Outbreaks of SARS, swine flu, MERS, Ebola, and coronavirus disease 2019 (COVID-19) have caused major social, political, and economic disruptions around the world. In light of these events, pandemic preparedness has proven to be critical to health, national, and economic security. Now, countries are investing billions of dollars in various pandemic preparedness tools, such as vaccines and broad-spectrum medical countermeasures (MCM), to address the threats arising from outbreaks. These tools not only offer protection against naturally occurring and accidental biological incidents but can also help provide some protection against deliberate biological attacks.

Furthermore, pandemic preparedness has substantial economic implications for both the public and private sectors because of its connection with the biotechnology industry, an important component of the worldwide economy. The industry is critical for economic competition, but it also provides opportunities for relationship-building among allies, academia, and industry partners.

With so many aspects of pandemic preparedness tied to public health, national security, and economic competition, understanding the key technology and policy trends of the major country stakeholders in this space provides valuable insights into pandemic preparedness gaps and ways of addressing them. Therefore, in this report, we discuss both technical and policy aspects of vaccine concepts and technologies, broad-spectrum MCM, and immunization facilitation. We researched these topics to provide insights for Japan's National Graduate Institute for Policy Studies, focusing specifically on the national policies of the United States, China, and Russia. However, the results of this research should be relevant to audiences beyond Japan. While Japan's rapidly aging population makes it particularly vulnerable to pandemics, many other nations also have growing numbers of older people; Japan is a harbinger rather than an outlier. Moreover, many of the capabilities and policies that Japan could develop to counter pandemic threats could also be pursued by other countries. This research is therefore relevant to broader audiences around the globe.

Emerging Vaccine Concepts and Technologies and Broad-Spectrum Medical Countermeasures

Scope and State of Emerging Vaccine Concepts and Technologies and Broad-Spectrum Medical Countermeasures

Conventional vaccines typically use attenuated pathogens, inactivated pathogens, or subunits of pathogens to stimulate the body's immune system to fight back against and destroy the live pathogen when it is encountered. However, such vaccines have limitations. For example, they may not be able to effectively counter emerging communicable or non-communicable diseases, are sometimes unable to be rapidly developed in response to new threats, and may not be easily produced at large scales. To address these gaps, new vaccine concepts and technologies have emerged to provide further protection. Below is a brief characterization of several emerging vaccine technologies: mRNA vaccines, nanoparticle (NP) vaccines, viral-like particle (VLP) vaccines, and universal vaccines.

KEY FINDINGS

- Vaccines have multiuse applications that not only protect individual and public health but also have economic and national security considerations.
- The United States invests heavily in various emerging vaccine technologies and broad-spectrum medical countermeasures.
- China has a strong and stable vaccine industry, while Russia falls behind the United States, Japan, and China.
- There have been well-founded questions about the efficacy of both the Chinese and Russian coronavirus disease 2019 vaccines.

POLICY IMPLICATIONS

Governments that want to reduce their vulnerability to pandemics can take the following approaches:

- Invest in emerging vaccine technologies that can protect against both current diseases and novel pathogens.
- Invest in the development of vaccines that can protect against multiple variants of a single pathogen.
- Invest in the development of vaccines that provide long-term immunity.
- Invest in the development of oral, inhalational, or other less invasive methods of administering vaccines.
- Invest in research on how to reduce the side effects of vaccines.
- Further invest in regulation to ensure that laboratories handling pathogens are safe and secure and that new vaccines can be rapidly and accurately assessed.
- Invest in stockpiles of diverse medical countermeasures, including vaccines, drugs, biologics (medications derived from living sources), and devices.
- Foster and incentivize relationships between academia and industry partners, as well as between researchers in other democracies, to accelerate advances in vaccine technology.
- Facilitate immunization by making it more accessible and by further investing in public health education to overcome vaccine hesitancy and vaccine fatigue.
- Ensure that vaccine distribution channels are open to accelerate vaccination processes in future pandemics.

In mRNA vaccines, mRNA is used instead of subunits of the pathogen. In cells, mRNA in the nucleus is necessary for DNA to produce proteins, but the mRNA from mRNA vaccines does not enter the nucleus or alter DNA. These vaccines work by introducing a piece of mRNA that corresponds to a viral protein that the immune system recognizes as foreign, so it produces antibodies to fight against the infection.[1] mRNA vaccine technology is paving the way for new vaccines that are quicker and easier to modify and develop against emerging viruses. The COVID-19 pandemic confirmed how quickly mRNA vaccines can be designed and produced against a novel pathogen. Not only is this technology being used for preventive measures, but it is also being used in the development of treatments for non-infectious diseases, such as cancer.[2] Furthermore, researchers in a Moderna mRNA skin cancer vaccine trial demonstrated that mRNA vaccines can be personalized for individuals in as little as six weeks.[3] However, while the effective use of mRNA vaccines for COVID-19 revealed that this technology has great promise, the potential and setbacks of mRNA vaccine technology are not fully understood. Further research is needed on different ways this technology can be used and how it can be used more efficiently—specifically, how the vaccines can remain efficacious even against virus variants or mutations.

Both NP vaccines and VLP vaccines are alternative vaccine approaches with increased stability and immunogenicity compared to vaccines that use subunits of a pathogen. NP vaccines work by encapsulating antigens needed to elicit an immune response. Overall, NP vaccines can be simpler in design than conventional vaccines, can be safer than live-attenuated vaccines, and can improve vaccine efficacy by using targeted delivery to achieve a desired immune response.[4] NP vaccines may also eliminate the need for vaccines to be injected, enabling them to be administered intranasally or through an inhaler. Their simpler design can decrease overall production cost relative to subunit vaccines.[5] VLP vaccines, a subset of NP vaccines, do not have any viral genetic material but are made with virus-like molecules that mimic the virus. As a result, the VLPs are unable to replicate in cells but are still able to trigger an immune response. One key advantage of such a vaccine is that it can be more suitable than conventional vaccines for people with weakened immune systems, who would otherwise be at risk of contracting the disease.[6]

A universal vaccine can counter multiple variants of a specific disease. It can trigger an immune response by displaying a specific protein presented by multiple variants of that disease. For example, a coronavirus vaccine candidate from the Walter Reed Army Institute of Research uses a coronavirus spike surface protein to elicit a response.[7] Universal vaccines can incorporate some of the emerging technologies mentioned above. A research team funded by the National Institutes of Health designed an mRNA universal vaccine that included a viral protein from 20 different influenza types.[8] Before the COVID-19 pandemic, a few efforts were underway in the United States to create a universal influenza vaccine; vaccines were in the preclinical stage or the clinical development stage.[9] So far, the trials are demonstrating promising results of "high levels of cross-reactive and subtype-specific antibodies."[10] If successful, the vaccine will provide longer-lasting protection against a wide variety of seasonal influenza viruses and influenza viruses with pandemic potential. Although there are currently no universal vaccines approved for public use, they could be effective despite pathogen mutations, while requiring few or no booster shots.

While vaccines are vital for pandemic preparedness, broad-spectrum MCMs—including antiviral drugs, biologics (medicines derived from living sources), and antibiotics—are also needed to complement them. Broad-spectrum MCMs also include medical devices, such as wearable devices, ventilators, and personal protective equipment, that can be used to diagnose, prevent, or treat diseases. Because of the potential speed with which outbreaks can

Abbreviations

COVID-19	coronavirus disease 2019
MCM	medical countermeasures
NIP	National Immunization Program
NP	nanoparticle
VLP	viral-like particle

occur and the fact that the pathogens involved may have been previously unknown, broad-spectrum MCMs are vital for public health preparedness and early response efforts.

U.S. and Allied Policy Trends Regarding Emerging Vaccine Concepts and Broad-Spectrum Medical Countermeasures

In October 2022, the White House released its *National Biodefense Strategy and Implementation Plan for Countering Biological Threats, Enhancing Pandemic Preparedness, and Achieving Global Health Security*, highlighting the United States' emphasis on pandemic preparedness. The strategy outlines the national vision for addressing challenges arising from naturally occurring, accidental, or deliberate biological threats. The United States is focusing on building its technology sector, including biotechnology and biomanufacturing. The goal is to work with allies and partners to pioneer new medicines and treatments.[11] In total, the United States will be investing $88 billion in pandemic preparedness over the next five years.[12]

In recent years, many new patents have been filed for key vaccination technologies. The exponential increases in patent filings indicate widespread interest in these technologies (although the sheer number of patents does not distinguish them in terms of quality). Figure 1 shows the number of patents in 2022, by country, in two vaccine-related categories. The tremendous disparities among the various nations are apparent. The United States generates an order of magnitude more of these patents than either Japan or China does, while each of those nations generates an order of magnitude more than Russia does.

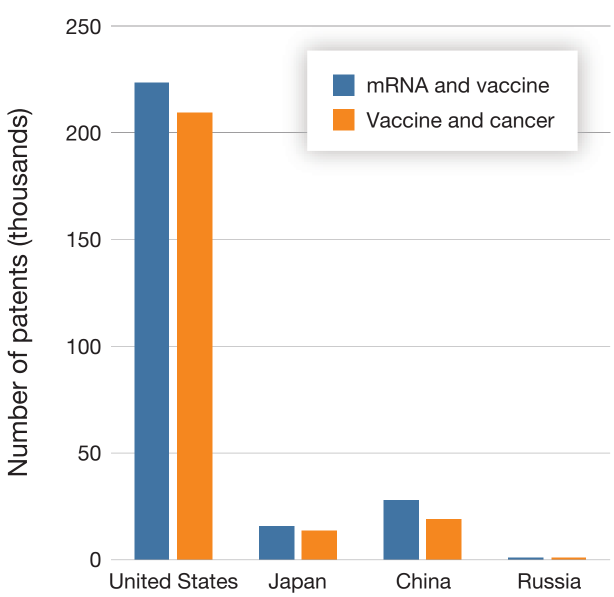
Figure 2 shows the numbers of patents in those and two additional areas of vaccination research, by year, for the United States, Japan, China, and Russia. Note that we used a different scale for each country's graph so that the graphs are legible; the topmost number on each vertical scale is underlined to emphasize this point. As shown in the figure, across all four nations, the number of patents in these areas has been rising exponentially over the past three decades.

Vaccine development requires vigilant oversight to prevent safety lapses that can lead to people being exposed to pathogens, as well as to prevent security lapses that can enable vaccine intellectual property to be stolen by malevolent actors. In an effort to address such risks, the U.S. Government Accountability Office has documented a lack of sufficient oversight of U.S. laboratories that handle pathogens and has made recommendations on how to reduce risks.[13]

The United States is also focused on developing broad-spectrum MCMs. In 2023, the U.S. Department of Defense released a report stating its intention to focus more on broad-spectrum MCMs to address both natural outbreaks and bioattacks.[14] It will be investing in the development of nonspecific MCMs and test products and capabilities to rapidly move from nonspecific to specific MCMs and test products. This shift is being made to help lessen symptoms and reduce transmission of any disease outbreak, but especially those from novel pathogens.

FIGURE 1

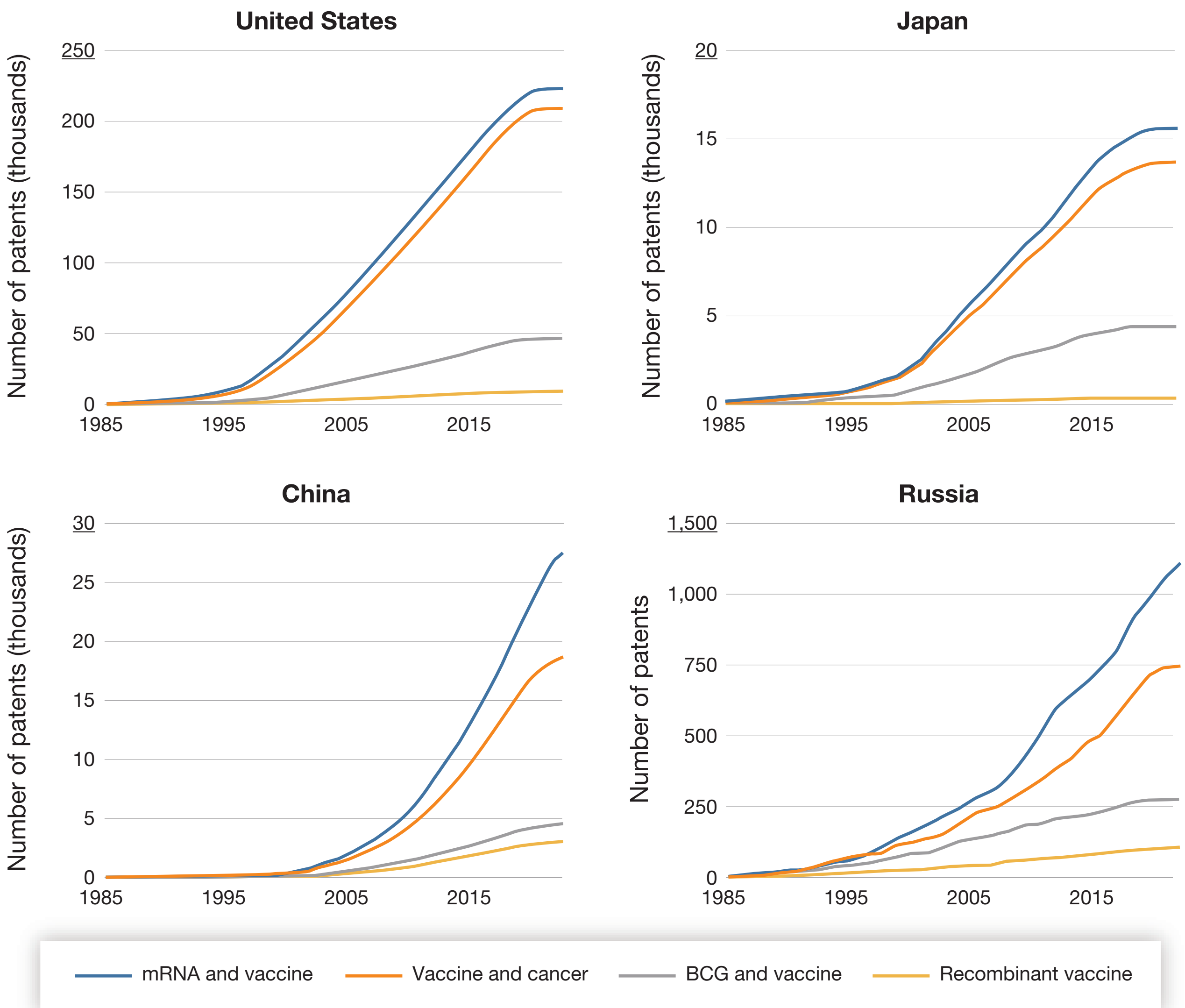
Patents Granted in 2022 in Two Areas of Vaccine Technology, by Country



SOURCE: Features global data from IFI Claims, IFI Claims Direct Platform.

FIGURE 2

Patents in Key Areas of Vaccine Technology, by Country, over Time



SOURCE: Features global data from IFI Claims, IFI Claims Direct Platform. The data points were derived from searching for word combinations or phrases appearing in patents.

NOTE: BCG = Bacillus Calmette-Guérin. The top number of patents on the left-hand scale of each of the graphs is underlined as a reminder that the graphs use different scales.

Multiuse Applications of Emerging Vaccine Concepts and Technologies and Broad-Spectrum Medical Countermeasures

Emerging vaccine concepts and technologies are being used to rapidly develop highly effective vaccines. However, they are also being used to help reduce the impact of noncommunicable diseases, such as cancer. It is anticipated that they could eventually be used to address hypertension, atherosclerosis, and diabetes.[15] Broad-spectrum MCM also play a key role in curtailing the effects of a pandemic, particularly at early stages when the threat is still not well understood and vaccines may not yet be available. In addition to protecting public health, these items can be used to protect defense personnel against biological attacks or routine infections.

Globally, the multibillion-dollar vaccine industry contributes greatly to many nations' economies. The industry boosts scientific innovation and collaboration, allowing opportunities for greater partnerships between researchers, academics, and industry partners, both internally and with allies. This innovation and collaboration on vaccines can have benefits in terms of developing a nation's wider biotechnology industry, enabling it to supply its own population and export its products. Manufacturing vaccines can also provide opportunities for vaccine diplomacy: Donating vaccines to less developed nations is a form of soft power that achieves goodwill in other countries. It also helps reduce the extent of outbreaks globally, diminishing the frequency of novel mutations and opportunities for transmission (including to the donor nation).

Chinese Development of Emerging Vaccine Concepts and Broad-Spectrum Medical Countermeasures

China has a robust vaccine industry that enables it to design and produce vaccines domestically. It has a well-developed, government-funded, and government-administered National Immunization Program (NIP), but citizens can also voluntarily choose and pay for additional vaccines (non-NIP vaccines).[16] China's NIP vaccines are much less expensive than vaccines in countries with a market-based approach, such as the United States and the United Kingdom, allowing a greater number of vaccinations for a given budget. However, China's NIP does not include several vaccines recommended by the World Health Organization, and far fewer people receive these non-NIP vaccines than receive the NIP ones.[17]

The Chinese government's "Made in China 2025" policy aims for China to achieve scientific self-reliance and to dominate in specific technology fields, including biotechnology. China has many ongoing research projects on vaccines, including some on emerging vaccine technology. Chinese researchers are currently conducting clinical trials of their own mRNA COVID-19 vaccine, which appears to be doing well.[18] However, Chinese vaccine research has sometimes been less than transparent, and there have been well-documented cases of the Chinese government or companies using espionage to acquire specific technologies.[19] There have also been some questionable scientific practices, including the collection and analysis of genetic material from foreigners for research and drug development.[20]

Russian Development of Emerging Vaccine Concepts and Broad-Spectrum Medical Countermeasures

Russian vaccine development has a long history, dating back to the Soviet Union. However, like China's vaccine industry, Russia's has been marred by a lack of transparency. Furthermore, although Russian scientists are still pursuing the development of new vaccines, Russian efforts tend to emphasize traditional vaccine technology more than innovative approaches. The Russo-Ukrainian War also inhibits vaccine innovation in Russia because of increased sanctions against state vaccine development laboratories, decreased international collaboration, decreased funding for science and technology, and the exodus of Russian scientists.

Russia's Sputnik V vaccine provides a good case study of the current state of Russian vaccine innovation and the problems it is facing. While Sputnik V was the first effective COVID-19 vaccine to be developed, Russian scientists opted to use older vaccine methodologies to create it rather than pursue mRNA vaccine technology to improve safety, efficacy, and effectiveness.[21] In addition, one of the major developers of the Sputnik V vaccine, the 48th Central Research Institute of the Ministry of Defense of the Russian Federation, has been sanctioned by the U.S. government over its involvement in biological weapon development for the Russian military.[22] As a result, some countries, such as India, have pulled out of agreements for the purchase, production, and distribution of Sputnik V.[23] Domestically, researchers have reported high levels of vaccine hesitancy for Sputnik V. Forty-three percent of Russian adults report that they are resistant to, or determined not to be vaccinated with, Sputnik V, and another 13 percent report that they are hesitant, or unsure, about the vaccine.[24] International scientists have also challenged the stated efficacy of Sputnik V, noting that datasets regarding its performance appeared to have been manipulated. Some of these scientists wrote, "Given the relative opacity of the conduct of this trial, the context of previous unexpectedly homogenous results, and the low likelihood of results such as these arising in a genuine trial, it is our opinion that it is not possible for a journal or reader to have confidence in the results."[25]

Facilitating Immunization

Scope and State of Strategies and Technologies to Facilitate Immunization

People are often reluctant or unwilling to be vaccinated for a variety of reasons, including ideological beliefs, concerns about the safety of vaccines, questions about their efficacy, dislike of injections, fear of side effects or complications, the inconvenience of getting to a provider, and cost. There are various ways to facilitate immunization by addressing these issues; some of these approaches require no advanced technology at all. For example, providing public health stakeholders with the resources to address questions about vaccines can help them reassure individuals who are concerned about the vaccines' safety or efficacy.[26] Furthermore, easily accessible vaccines and testing centers can make immunization and diagnosis more convenient for patients.[27]

Other approaches require a degree of technological innovation. For example, enabling vaccines to be delivered orally or via inhalation can make people more receptive to being vaccinated.[28] Oral and inhalational vaccines often do not require refrigerated storage, making them easier to transport, especially to remote communities, and store.[29]

Diminishing the side effects of vaccines could also increase willingness to receive them. However, there is little current investigation of ways to lessen the side effects of vaccines, although there are some efforts to thoroughly document the side effects.[30]

U.S. Policy Trends Regarding Strategies and Technologies to Facilitate Immunization

In 2021, the U.S. Department of Health and Human Services released *Vaccines: National Strategic Plan for the United States 2021–2025*, which emphasizes the objectives of fostering innovation in vaccine development and technologies, supporting the development and implementation of technologies to improve vaccine distribution and delivery mechanisms, and increasing access to recommended vaccines. The plan also focuses on increasing the public's knowledge of and confidence in recommended vaccines.[31] For example, the Centers for Disease Control and Prevention has developed resources and communication toolkits for public health stakeholders to increase community trust in vaccinations.[32]

Chinese Development of Strategies and Technologies to Facilitate Immunization

While China has a well-developed vaccine industry, vaccine hesitancy has been rising in the country after several successive vaccine safety–related incidents. Public concerns were intensified by the 2018 Changchun Changsheng vaccine incident, in which Chinese vaccine maker Changsheng Bio-Technology Co., Ltd. was accused of fabricating production and inspection data and selling inferior children's vaccines.[33] Following that incident, in 2019, China created the Vaccine Administration Law and compulsory vaccine liability insurance to address vaccine hesitancy and increase public trust in vaccines.[34] China has also been working on using different vaccine delivery methods. In late 2022, China rolled out an inhalable COVID-19 booster vaccine to help increase immunization as the country relaxed its pandemic restrictions.[35]

Russian Development of Strategies and Technologies to Facilitate Immunization

Russia does not appear to have strategized specific methods to facilitate immunization. Rather, Russia's vaccine industry is marred by data discrepancies and a lack of transparency, which have hindered vaccine trust and immunization efforts in the country.

Overall Implications for Policymakers

In accordance with the above information, policymakers could consider encouraging the expansion of academic, government, and industry research on vaccine development. They could also consider fostering partnerships among researchers in those institutions and their counterparts abroad. There are several reasons why policymakers might consider this overall approach. The vulnerability of aging populations around the world makes effective, widespread immunization particularly important, which is another reason why long-lasting vaccines that can address multiple diseases or multiple strains of a disease—and that can therefore be administered before a specific outbreak—are particularly valuable. Such vaccines can also help overcome vaccine fatigue by reducing the number of times individuals need to be vaccinated. Similarly, developing oral or inhalational vaccines can help reduce vaccine hesitancy. Documenting vaccine side effects and addressing concerns through education can also help address vaccine hesitancy.

Vaccines can also serve as multiuse technologies. Some types of vaccine development can help reduce the impact of noncommunicable diseases, such as diabetes or specific types of cancer. Others may protect against biological attacks that could be launched against either the civilian population or armed forces personnel.

Investments in vaccine technology, and the fostering of partnerships, can also benefit a country's economy. Improved health due to advanced vaccines can enable people to continue working later in their lives and minimize the days lost to illness, and a high degree of immunization can reduce the extent to which normal activities are curtailed during epidemics. Moreover, biotechnology is one of the 21st century's most important economic sectors, and building a substantial base in terms of knowledge, equipment, and facilities in this area can enable various types of exports.

As countries consider whether to invest more in emerging vaccine technologies, another consideration is how to ensure sufficient regulation. Handling the dangerous pathogens that vaccines are designed to counter requires stringent safety regulations to prevent people from being exposed, as well as security measures to prevent malevolent actors from being able to steal those pathogens. It also requires ensuring that a country's regulatory bodies can accurately assess the efficacy of vaccines against a variety of potential threats rather than singular ones.

Policymakers may also want to consider whether to make additional investments in broad-spectrum MCM to reduce vulnerability in pandemics. For example, distributed stockpiles of drugs and devices (such as ventilators) can improve responses in some cases.

To overcome vaccine hesitancy and vaccine fatigue, both of which have become more common in the face of new COVID-19 vaccines that need to be administered relatively frequently, policymakers could consider making further, sustained investments in public health education regarding the benefits of vaccines. As a country's population ages and many rural communities around the world become less populated, policymakers could also consider ways to make vaccination more accessible, particularly to populations that have limited health care capacity and to individuals with limited mobility.

Closing Thoughts

Pandemics will continue to recur, as they have for thousands of years. Their frequency may rise because of increasingly dense and interconnected human populations, increasing numbers of livestock raised in crowded conditions, and intensifying human encroachment on other species' habitats, as well as consumption of them. This report's brief overview of both scientific advances and the efficacy of policy measures for pandemic preparedness can enable governments to more effectively address these threats, protecting the lives of their people and enhancing their overall security.

Notes

[1] Pardi et al., “mRNA Vaccines—A New Era in Vaccinology.”

[2] Brisse et al., “Emerging Concepts and Technologies in Vaccine Development.”

[3] Park, “Moderna’s mRNA Skin Cancer Vaccine Shows Early Promise in a New Study.”

[4] Pati, Shevtsov, and Sonawane, “Nanoparticle Vaccines Against Infectious Diseases.”

[5] Guerrini et al., “Characterization of Nanoparticles-Based Vaccines for COVID-19”; Pati, Shevtsov, and Sonawane, “Nanoparticle Vaccines Against Infectious Diseases.”

[6] Nooraei et al., “Virus-Like Particles.”

[7] This vaccine is also known as a *pancoronavirus* vaccine; see Cohen, “Why Efforts to Make Better, More Universal Coronavirus Vaccines Are Struggling”; Ramachandran, Satapathy, and Dutta, “Delivery Strategies for mRNA Vaccines”; Vashishtha and Kumar, “Looking to the Future.”

[8] National Institutes of Health, “Using mRNA Technology for a Universal Flu Vaccine.”

[9] Wang et al., “Progress Towards the Development of a Universal Influenza Vaccine.”

[10] Arevalo et al., “A Multivalent Nucleoside-Modified mRNA Vaccine Against All Known Influenza Virus Subtypes,” p. 1.

[11] White House, *National Biodefense Strategy and Implementation Plan for Countering Biological Threats, Enhancing Pandemic Preparedness, and Achieving Global Health Security*.

[12] White House, “Biden-Harris Administration Releases Strategy to Strengthen Health Security and Prepare for Biothreats.”

[13] U.S. Government Accountability Office, *High-Containment Laboratories*.

[14] Chemical and Biological Defense Program, *Approach for Research, Development, and Acquisition of Medical Countermeasure and Test Products*.

[15] Lu, Su, and Meng, “Recent Advances in the Development of Vaccines for Diabetes, Hypertension, and Atherosclerosis.”

[16] Liu, Bai, and Zheng, “Introduction and Application Recommendations of National Immunization Program (NIP) and Non-NIP Vaccine in China.”

[17] Zheng et al., “The Landscape of Vaccines in China.”

[18] Grover and Yu, “China’s CanSino Confident Its mRNA COVID Vaccine As Good As Moderna, Pfizer Shots.”

[19] Ben-Achour, “China’s State-Sponsored Industrial Espionage Is Part of a Larger System.”

[20] Needham, “Special Report.”

[21] Logunov et al., “Safety and Immunogenicity of an rAd26 and rAd5 Vector-Based Heterologous Prime-Boost COVID-19 Vaccine in Two Formulations: Two Open, Non-Randomised Phase 1/2 Studies from Russia.”

[22] Bureau of Industry and Security, U.S. Department of Commerce, “Addition of Entities to the Entity List, and Revision of Entries on the Entity List.”

[23] Vaidya and Barry, “Russia Sanctions.”

[24] Roshchina, Roshchin, and Rozhkova, “Determinants of COVID-19 Vaccine Hesitancy and Resistance in Russia.”

[25] Sheldrick, Meyerowitz-Katz, and Tucker-Kellogg, “Plausibility of Claimed Covid-19 Vaccine Efficacies by Age,” p. e499.

[26] Bjork and Morelli, “Immunization Strategies for Healthcare Practices and Providers.”

[27] Centers for Disease Control and Prevention, “Ways Health Departments Can Help Increase COVID-19 Vaccinations.”

[28] Rakhra et al., “Exploiting Albumin as a Mucosal Vaccine Chaperone for Robust Generation of Lung-Resident Memory T Cells”; Van der Weken, Cox, and Devriendt, “Advances in Oral Subunit Vaccine Design,” p. 1.

[29] Mohamed et al., “Antivenoms, Hepatitis B Vaccine and Oral Polio Vaccine Can Be Considered for Storage and Handling Outside the Cold Chain Following the Innovative ‘Controlled Temperature Chain’ Approach.”

[30] Centers for Disease Control and Prevention, “Reporting Adverse Events Following Vaccination”; Global Vaccine Data Network, homepage.

[31] U.S. Department of Health and Human Services, *Vaccines*.

[32] Centers for Disease Control and Prevention, “Ways Health Departments Can Help Increase COVID-19 Vaccinations.”

[33] Du et al., “The Determinants of Vaccine Hesitancy in China”; Liu et al., “Vaccine Confidence in China After the Changsheng Vaccine Incident.”

[34] Han, “Research on the Development of Vaccine Liability Compulsory Insurance in China”; Ministry of Civil Affairs of the People’s Republic of China, Law of the People’s Republic of China on Vaccine Management.

[35] Moritsugu, “Afraid of Needles?”

References

Unless otherwise indicated, the authors of this report provided the translations of bibliographic details for the non-English sources included in this report. The original rendering in Chinese appears in brackets after the English translation.

Arevalo, Claudia P., Marcus J. Bolton, Valerie Le Sage, Naiqing Ye, Colleen Furey, Hiromi Muramatsu, Mohamad-Gabriel Alameh, Norbert Pardi, Elizabeth M. Drapeau, Kaela Parkhouse, Tyler Garretson, Jeffrey S. Morris, Louise H. Moncla, Ying K. Tam, Steven H. Y. Fan, Seema S. Lakdawala, Drew Weissman, and Scott E. Hensley, "A Multivalent Nucleoside-Modified mRNA Vaccine Against All Known Influenza Virus Subtypes," *Science*, Vol. 378, No. 6622, November 2022.

Ben-Achour, Sabri, "China's State-Sponsored Industrial Espionage Is Part of a Larger System," Marketplace, December 9, 2021.

Bjork, Adam, and Valerie Morelli, "Immunization Strategies for Healthcare Practices and Providers," webpage, Centers for Disease Control and Prevention, August 18, 2021. As of February 7, 2023:
https://www.cdc.gov/vaccines/pubs/pinkbook/strat.html

Brisse, Morgan, Sophia M. Vrba, Natalie Kirk, Yuying Liang, and Hinh Ly, "Emerging Concepts and Technologies in Vaccine Development," *Frontiers in Immunology*, Vol. 11, September 2020.

Bureau of Industry and Security, U.S. Department of Commerce, "Addition of Entities to the Entity List, and Revision of Entries on the Entity List," *Federal Register*, Vol. 85, No. 167, August 27, 2020.

Centers for Disease Control and Prevention, "Ways Health Departments Can Help Increase COVID-19 Vaccinations," webpage, June 17, 2022. As of February 7, 2023:
https://www.cdc.gov/vaccines/covid-19/health-departments/generate-vaccinations.html

Centers for Disease Control and Prevention, "Reporting Adverse Events Following Vaccination," webpage, updated September 15, 2022. As of February 7, 2023:
https://www.cdc.gov/vaccinesafety/hcproviders/reportingadverseevents.html

Chemical and Biological Defense Program, *Approach for Research, Development, and Acquisition of Medical Countermeasure and Test Products*, 2022.

Cohen, Jon, "Why Efforts to Make Better, More Universal Coronavirus Vaccines Are Struggling," *Science*, July 27, 2022.

Du, Fanxing, Tracey Chantler, Mark R. Francis, Fiona Yueqian Sun, Xuan Zhang, Kaiyi Han, Lance Rodewald, Hongjie Yu, Shiyi Tu, Heidi Larson, and Zhiyuan Hou, "The Determinants of Vaccine Hesitancy in China: A Cross-Sectional Study Following the Changchun Changsheng Vaccine Incident," *Vaccine*, Vol. 38, No. 47, November 3, 2020.

Global Vaccine Data Network, homepage, undated. As of February 7, 2023:
https://www.globalvaccinedatanetwork.org

Grover, Natalie, and Sophie Yu, "China's CanSino Confident Its mRNA COVID Vaccine As Good As Moderna, Pfizer Shots," Reuters, February 3, 2023.

Guerrini, Giuditta, Davide Magrì, Sabrina Gioria, Donata Medaglini, and Luigi Calzolai, "Characterization of Nanoparticles-Based Vaccines for COVID-19," *Nature Nanotechnology*, Vol. 17, No. 6, June 2022.

Han, Min, "Research on the Development of Vaccine Liability Compulsory Insurance in China" ["我国疫苗责任强制保险发展研究"], Hebei University of Economics and Business, May 2020.

IFI Claims, IFI Claims Direct Platform, database, undated.

Liu, Baohua, Ruohui Chen, Miaomiao Zhao, Xin Zhang, Jiahui Wang, Lijun Gao, Jiao Xu, Qunhong Wu, and Ning Ning, "Vaccine Confidence in China After the Changsheng Vaccine Incident: A Cross-Sectional Study," *BMC Public Health*, Vol. 19, November 27, 2019.

Liu, Zhaoqiu, Yunhua Bai, and Dongyi Zheng, "Introduction and Application Recommendations of National Immunization Program (NIP) and Non-NIP Vaccine in China" ["我国免疫规划疫苗和非免疫规划疫苗简介及应用建议"], *Chinese Journal of Pediatrics* [中华儿科杂志], Vol. 58, No. 6, June 2, 2020. As of February 2, 2023:
https://doi.org/10.3760/cma.j.cn112140-20200309-00202

Logunov, Denis Y., Inna V. Dolzhikova, Olga V. Zubkova, Amir I. Tukhvatulin, Dmitry V. Shcheblyakov, Alina S. Dzharullaeva, Daria M. Grousova, Alina S. Erokhova, Anna V. Kovyrshina, Andrei G. Botikov, et al., "Safety and Immunogenicity of an rAd26 and rAd5 Vector-Based Heterologous Prime-Boost COVID-19 Vaccine in Two Formulations: Two Open, Non-Randomised Phase 1/2 Studies from Russia," *The Lancet*, Vol. 396, No. 10255, September 26, 2020.

Lu, Kongye, Benli Su, and Xiuxiang Meng, "Recent Advances in the Development of Vaccines for Diabetes, Hypertension, and Atherosclerosis," *Journal of Diabetes Research*, Vol. 2018, 2018.

Ministry of Civil Affairs of the People's Republic of China [中华人民共和国民政部], Law of the People's Republic of China on Vaccine Management [中华人民共和国疫苗管理法], April 15, 2021. As of February 3, 2023:
https://www.mca.gov.cn/article/zt_gjaqr2021/flfg/202104/20210400033211.shtml

Mohamed, Shereen H., Osama A. Hady, Mona T. Kashef, and Hamdallah Zedan, "Antivenoms, Hepatitis B Vaccine and Oral Polio Vaccine Can Be Considered for Storage and Handling Outside the Cold Chain Following the Innovative 'Controlled Temperature Chain' Approach," *Biologicals*, Vol. 78, July 2022.

Moritsugu, Ken, "Afraid of Needles? China Using Inhalable COVID-19 Vaccine," Associated Press, October 26, 2022.

National Institutes of Health, "Using mRNA Technology for a Universal Flu Vaccine," webpage, December 6, 2022. As of February 8, 2023:
https://www.nih.gov/news-events/nih-research-matters/using-mrna-technology-universal-flu-vaccine

Needham, Kirsty, "Special Report: Covid Opens New Doors for China's Gene Giant," Reuters, August 5, 2020.

Nooraei, Saghi, Howra Bahrulolum, Zakieh Sadat Hoseini, Camellia Katalani, Abbas Hajizade, Andrew J. Easton, and Gholamreza Ahmadian, "Virus-Like Particles: Preparation, Immunogenicity and Their Roles as Nanovaccines and Drug Nanocarriers," *Journal of Nanobiotechnology*, Vol. 19, February 25, 2021.

Pardi, Norbert, Michael J. Hogan, Frederick W. Porter, and Drew Weissman, "mRNA Vaccines—A New Era in Vaccinology," *Nature Reviews Drug Discovery*, Vol. 17, No. 4, April 2018.

Park, Alice, “Moderna’s mRNA Skin Cancer Vaccine Shows Early Promise in a New Study,” *Time*, December 13, 2022.

Pati, Rashmirekha, Maxim Shevtsov, and Avinash Sonawane, “Nanoparticle Vaccines Against Infectious Diseases,” *Frontiers in Immunology*, Vol. 9, October 2018.

Rakhra, Kavya, Wuhbet Abraham, Chensu Wang, Kelly D. Moynihan, Na Li, Nathan Donahue, Alexis D. Baldeon, and Darrell J. Irvine, “Exploiting Albumin as a Mucosal Vaccine Chaperone for Robust Generation of Lung-Resident Memory T Cells,” *Science Immunology*, Vol. 6, No. 57, March 2021.

Ramachandran, Sivakumar, Soumya Ranjan Satapathy, and Tathagata Dutta, “Delivery Strategies for mRNA Vaccines,” *Pharmaceutical Medicine*, Vol. 36, No. 1, February 2022.

Roshchina, Yana, Sergey Roshchin, and Ksenia Rozhkova, “Determinants of COVID-19 Vaccine Hesitancy and Resistance in Russia,” *Vaccine*, Vol. 40, No. 39, September 16, 2022.

Sheldrick, Kyle A., Gideon Meyerowitz-Katz, and Greg Tucker-Kellogg, “Plausibility of Claimed Covid-19 Vaccine Efficacies by Age: A Simulation Study,” *American Journal of Therapeutics*, Vol. 29, No. 5, September–October 2022.

U.S. Department of Health and Human Services, *Vaccines: National Strategic Plan for the United States 2021–2025*, 2021.

U.S. Government Accountability Office, *High-Containment Laboratories: Coordinated Actions Needed to Enhance the Select Agent Program’s Oversight of Hazardous Pathogens*, GAO-18-145, October 2017.

Vaidya, Manasi, and Fiona Barry, “Russia Sanctions: What Next for Sputnik Covid-19 Vaccine Production Around the World,” *Pharmaceutical Technology*, March 8, 2022.

Van der Weken, Hans, Eric Cox, and Bert Devriendt, “Advances in Oral Subunit Vaccine Design,” *Vaccines*, Vol. 9, No. 1, January 2021.

Vashishtha, Vipin M., and Puneet Kumar, “Looking to the Future: Is a Universal Coronavirus Vaccine Feasible?” *Expert Review of Vaccines*, Vol. 21, No. 3, March 2022.

Wang, Wen-Chien, Ekramy E. Sayedahmed, Suryaprakash Sambhara, and Suresh K. Mittal, “Progress Towards the Development of a Universal Influenza Vaccine,” *Viruses*, Vol. 14, No. 8, August 2022.

White House, *National Biodefense Strategy and Implementation Plan for Countering Biological Threats, Enhancing Pandemic Preparedness, and Achieving Global Health Security*, October 2022.

White House, “Biden-Harris Administration Releases Strategy to Strengthen Health Security and Prepare for Biothreats,” fact sheet, October 18, 2022.

Zheng, Yaming, Lance Rodewald, Juan Yang, Ying Qin, Mingfan Pang, Luzhao Feng, and Hongjie Yu, “The Landscape of Vaccines in China: History, Classification, Supply, and Price,” *BMC Infectious Diseases*, Vol. 18, October 4, 2018.

About This Report

This report provides a brief characterization of the trends and strategic implications associated with specific aspects of pandemic preparedness in the United States, Russia, and China. We initially wrote it to provide considerations to Japanese policymakers after researching issues related to pandemic preparedness and sustainment of high degrees of immunity. The considerations provided—although originally written for a Japanese audience—are applicable to other countries hoping to strengthen global health security and promote pandemic preparedness development.

RAND National Security Research Division

This research was sponsored by the National Graduate Institute for Policy Studies and conducted within the Acquisition and Technology Policy Program of the RAND National Security Research Division (NSRD). NSRD conducts research and analysis for the Office of the Secretary of Defense, the U.S. Intelligence Community, the U.S. State Department, allied foreign governments, and foundations.

For more information on the RAND Acquisition and Technology Policy Program, see www.rand.org/nsrd/atp or contact the director (contact information is provided on the webpage).

Acknowledgments

We would like to thank the National Graduate Institute for Policy Studies for sponsoring this research and providing useful feedback. In addition, we would like to thank Yun Kang and Christopher Mouton for overseeing this work within the RAND Acquisition and Technology Policy Program, as well as James Powers for managing quality assurance, with assistance from Saci Haslam and Zachary Pandl. Finally, we would like to thank Taylor Frey and Christopher Whaley for providing valuable reviews that improved this report.

For more information on this publication, visit www.rand.org/t/RRA2619-1.

RR-A2619-1