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Application of mRNA Vaccine Platforms for Emerging Infectious Diseases: Progress and Challenges

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A B S T R A C T

Emerging infectious diseases (EIDs) such as COVID-19, Zika, Ebola, and others pose a significant global health threat due to their rapid transmission and high morbidity. Traditional vaccine development methods are often too slow to respond effectively to new outbreaks. mRNA vaccine platforms have recently emerged as a transformative technology, offering rapid, scalable, and adaptable solutions for pandemic preparedness and response. This review aims to evaluate the progress of mRNA vaccine platforms in addressing emerging infectious diseases, examine their underlying mechanisms, highlight key successes, and discuss the challenges that remain for broad global implementation. A comprehensive literature review was conducted using databases including PubMed, Scopus, and Web of Science. Peer-reviewed articles, clinical trial results, and regulatory reports published between 2010 and 2025 were analyzed to assess the development, efficacy, and deployment of mRNA vaccines for EIDs. The success of mRNA vaccines against SARS-CoV-2 has validated their potential as a rapid-response platform. Preclinical and early clinical studies show promising results for other pathogens such as Zika virus, influenza, and Ebola. Advantages of mRNA platforms include rapid design, high potency, and reduced risk of insertional mutagenesis. However, challenges such as cold-chain storage requirements, limited data on long-term immunity, and manufacturing scalability remain significant barriers, especially in low- and middle-income countries. mRNA vaccines represent a critical advancement in the fight against EIDs, offering a flexible and accelerated pathway for vaccine development. Future efforts should focus on improving delivery systems, enhancing thermal stability, and building global infrastructure for equitable access. Continued research and international collaboration will be essential to fully harness the potential of mRNA vaccine technology for future public health emergencies.

Introduction

Emerging infectious diseases (EIDs) continue to pose serious threats to global public health, as demonstrated by recent outbreaks such as the COVID-19 pandemic, the Zika virus epidemic in Latin America, and recurrent Ebola virus outbreaks in West and Central Africa (1,2).

These pathogens, often zoonotic in origin, can spread rapidly across regions, overwhelm healthcare systems, and cause significant morbidity and mortality (3). The increasing frequency of EID outbreaks is driven by a complex interplay of ecological, social, and environmental factors, including globalization, climate change, urbanization, and human encroachment into wildlife habitats.

In the face of such rapidly evolving threats, the ability to respond with effective medical countermeasures—particularly vaccines—is critical. Traditional vaccine development platforms, while historically successful, often require years to progress from concept to licensure (4,5,6). This timeline is incompatible with the urgent nature of pandemic and outbreak responses. Consequently, there has been a growing emphasis on flexible, rapid-response vaccine platforms that can be adapted swiftly to novel pathogens.

Among these, messenger RNA (mRNA) vaccine technology has emerged as a transformative platform. Unlike conventional approaches that rely on live-attenuated or inactivated pathogens, mRNA vaccines utilize synthetic RNA sequences encoding viral antigens to elicit immune responses (9,10).

This approach offers several key advantages: rapid design and synthesis, scalable manufacturing, and strong immunogenicity without the need for live virus handling. The successful deployment of mRNA vaccines against SARS-CoV-2 has validated the platform's potential in real-world settings.

This article aims to review the current progress of mRNA vaccine platforms in addressing emerging infectious diseases, explore their underlying mechanisms and development pipelines, and identify the key challenges that must be addressed to enable broader and more equitable global implementation. By synthesizing recent advances and ongoing research, this review provides insights into the future role of mRNA vaccines in pandemic preparedness and infectious disease control.

mRNA Vaccine Technology: An Overview

History and Evolution

The concept of using messenger RNA (mRNA) as a therapeutic tool dates back to the early 1990s, but significant technical barriers—such as instability, inefficient delivery, and innate immune activation—initially limited its practical application. Over the following decades, scientific breakthroughs in RNA stabilization, chemical modification, and delivery systems laid the groundwork for mRNA's clinical viability (7,8).

The COVID-19 pandemic marked a pivotal moment, as mRNA vaccines developed by Pfizer-BioNTech and Moderna became the first mRNA-based products to receive emergency use authorization and widespread global deployment. Their success validated decades of research and positioned mRNA as a leading platform for rapid vaccine development.

Mechanism of Action

mRNA vaccines work by delivering a synthetic mRNA sequence encoding a viral antigen—most commonly a surface protein—into the host's cells. Once inside, host ribosomes translate the mRNA into the target protein, which is then presented on the cell surface or secreted, triggering both humoral and cellular immune responses. This mimics natural infection and trains the immune system to recognize and neutralize the pathogen upon future exposure, without the risks associated with using live or inactivated viruses.

Types of mRNA Vaccines

There are two main types of mRNA vaccines:

Non-replicating mRNA (nrRNA)

These contain the mRNA sequence for the antigen of interest and are structurally simple. They rely solely on the host's cellular machinery for translation and are used in approved vaccines like those for COVID-19.

Self-amplifying mRNA (saRNA)

Derived from alpha virus genomes, these constructs encode both the antigen and viral replication machinery,

allowing for intracellular amplification of the mRNA. This results in higher antigen expression from a smaller initial dose, potentially improving immunogenicity and reducing costs.

Delivery Systems

Effective delivery is crucial to protect the fragile mRNA molecule and ensure its uptake by target cells. Key delivery systems include:

Lipid Nanoparticles (LNPs)

Currently the most widely used method, LNPs encapsulate mRNA and facilitate its entry into cells via endocytosis. LNPs also protect the mRNA from degradation and can be engineered for targeted delivery.

Electroporation

A technique more commonly used in experimental and therapeutic settings, electroporation involves applying an electric field to transiently permeabilize cell membranes, allowing mRNA to enter cells directly (11, 12).

Polymeric Nanoparticles and Peptide-based Carriers

These are being explored as alternatives to LNPs for improved biocompatibility, targeting, and reduced toxicity.

Applications in Emerging Infectious Diseases

The flexibility and speed of mRNA vaccine platforms have made them a leading candidate in the global effort to respond to emerging infectious diseases (EIDs). Below is a summary of their application across several high-priority pathogens (13, 14).

COVID-19 (SARS-CoV-2)

The COVID-19 pandemic provided the first large-scale real-world test for mRNA vaccines. Both Pfizer-BioNTech (BNT162b2) and Moderna (mRNA-1273) rapidly developed vaccines using non-replicating mRNA technology. These vaccines encode the spike (S) protein of SARS-CoV-2 and were shown to be highly effective (~94–95%) in preventing symptomatic COVID-19 in large phase III clinical trials. Their development, testing, and emergency use approval occurred within a historic timeframe of less than one year. Booster formulations have since been adapted to target new variants such as Delta and Omicron (15, 16).

Zika Virus

Zika virus gained international attention during the 2015–2016 outbreaks in the Americas, due to its association with microcephaly and neurological complications. Multiple preclinical studies using mRNA vaccines encoding Zika envelope (E) and premembrane (prM) proteins have demonstrated strong protective immunity in mice and non-human primates. Moderna's ZIKV mRNA vaccine candidate (mRNA-1893) advanced to early-phase clinical trials (Phase I), where it showed acceptable safety and immunogenicity profiles, although further development has been deprioritized due to waning transmission rates (17, 18).

Ebola Virus

The Ebola virus, responsible for severe hemorrhagic fever outbreaks in Africa, remains a high-priority pathogen. mRNA vaccines targeting the glycoprotein (GP) of the Ebola virus have shown promising results in animal models, with effective protection observed in both rodents and non-human primates. Several candidates, including those developed by CureVac and the U.S. Army, have progressed through preclinical stages. However, no mRNA Ebola vaccine has yet reached advanced clinical trials, partly due to the success of viral vector-based vaccines like rVSV-ZEBOV (19, 20).

Influenza

Seasonal influenza viruses require annual vaccine reformulation, making mRNA platforms particularly attractive for their speed and flexibility. Moderna (mRNA-1010) and Pfizer-BioNTech are both developing multivalent mRNA-based flu vaccines, which are currently in Phase I/II trials. Early results suggest strong immunogenicity and strain coverage. Additionally, research is ongoing into universal influenza vaccines using conserved antigens to provide broader and longer-lasting protection (21, 22).

Respiratory Syncytial Virus (RSV)

RSV is a significant cause of respiratory illness in infants and older adults. Traditional vaccine development has

struggled due to safety concerns and weak immune responses. mRNA vaccines encoding stabilized prefusion forms of the RSV F protein have demonstrated robust immunogenicity in animal models. Moderna's mRNA-1345 has entered Phase III trials, showing high efficacy in older adults and receiving regulatory attention for potential licensure (23, 24).

Advantages of mRNA Vaccine Platforms

The emergence of mRNA vaccine platforms has revolutionized the field of vaccinology, offering several distinct advantages over traditional vaccine technologies. These benefits make mRNA vaccines especially suited for rapid responses to emerging infectious diseases (25).

Rapid Development Timelines

One of the most transformative features of mRNA vaccines is their speed of development. Unlike conventional vaccines that require culturing live viruses or producing recombinant proteins in cell lines, mRNA vaccines are designed using only the genetic sequence of the target pathogen. This enables the creation of a vaccine candidate within weeks of identifying a new pathogen. The rapid development of COVID-19 mRNA vaccines—progressing from genome sequencing to human trials in under two months—is a compelling demonstration of this capability (26).

Scalable and Flexible Manufacturing

mRNA vaccine production relies on a cell-free, enzymatic synthesis process that is highly scalable and adaptable. Once the manufacturing infrastructure is in place, it can be reprogrammed to produce mRNA for different pathogens by simply altering the sequence of the encoded antigen. This modular production process not only supports faster manufacturing at scale but also reduces the complexity and cost associated with traditional vaccine production methods, which often require pathogen-specific culture systems or large bioreactors (27).

Strong and Versatile Immune Responses

mRNA vaccines are capable of inducing both humoral and cellular immune responses, providing robust protection against infection. The in situ expression of antigens allows for native-like protein folding and post-translational modifications, which enhance the immune system's ability to recognize and target the pathogen. Moreover, mRNA vaccines can be engineered to express prefusion-stabilized antigens or immunogenic domains, improving the quality of the immune response (28, 29).

Modularity and Adaptability

The modular nature of mRNA technology allows for quick redesign in response to pathogen mutation or the emergence of new variants. For example, mRNA vaccines for COVID-19 have been rapidly updated to target evolving variants like Omicron (46, 46). This adaptability is especially valuable for pathogens with high mutation rates or for responding to outbreaks of previously unknown diseases. Furthermore, the same platform can be used to develop vaccines against a wide range of pathogens, including viruses, bacteria, and even cancer-associated antigens (30).

Challenges and Limitations

Despite the transformative potential of mRNA vaccine platforms, several challenges and limitations must be addressed to fully realize their global utility, particularly in the context of emerging infectious diseases. These barriers span technical, logistical, regulatory, and societal domains (45).

Cold Chain and Storage Requirements

A major limitation of current mRNA vaccines is their dependence on ultra-cold storage conditions. For instance, the Pfizer-BioNTech COVID-19 vaccine initially required storage at -70°C, posing significant logistical challenges, particularly in low-resource or remote settings with limited cold chain infrastructure. While newer formulations with improved thermal stability are being developed, cold chain dependence remains a key obstacle to equitable global distribution (31).

Manufacturing Scale-Up

Although mRNA vaccines can be rapidly designed and prototyped, scaling up manufacturing to meet global demand remains a complex and resource-intensive process. High-purity raw materials (e.g., nucleotides, enzymes, lipid nanoparticles) are required, and production facilities must meet stringent regulatory

standards. Establishing decentralized or regional manufacturing hubs is a promising solution, but it requires significant investment, technology transfer, and skilled workforce development (32, 33).

Regulatory and Safety Concerns

As a relatively new platform, mRNA vaccines face evolving regulatory scrutiny. While their safety profile has been favorable in large-scale COVID-19 deployments, long-term effects, potential autoimmunity risks, and rare adverse reactions require continued surveillance. The novelty of the platform also means that regulatory pathways are still being defined for non-COVID mRNA vaccines, which may delay approval timelines for future candidates (34, 35).

Public Trust and Misinformation

Public perception and acceptance of mRNA vaccines can significantly influence uptake. The rapid development and emergency use authorizations of COVID-19 vaccines, though scientifically justified, fueled skepticism in some populations. Misinformation and conspiracy theories, often amplified via social media, have led to vaccine hesitancy and distrust in scientific institutions. Addressing this requires sustained public education, transparent communication, and community engagement (42, 43, 44).

Long-Term Data Gaps

Because mRNA vaccines are still relatively new, there is limited long-term data on the duration of protection, potential need for frequent boosters, and the effects of repeated dosing over time. Additionally, more research is needed to evaluate their performance in special populations such as immunocompromised individuals, pregnant women, and young children across different pathogens (35, 36, 37).

Future Directions

mRNA Vaccines for Bacterial and Parasitic Infections

While mRNA technology has primarily focused on viral antigens, there is growing interest in applying it to bacterial and parasitic infections, which present unique immunological challenges. Advances in antigen selection and delivery could enable mRNA vaccines to target complex bacterial pathogens like *Mycobacterium tuberculosis* or parasitic diseases such as malaria and leishmaniasis, areas where traditional vaccines have struggled (40, 41).

Pan-Pathogen and Universal Vaccines

The adaptability of mRNA platforms makes them ideal candidates for developing universal vaccines that target conserved antigens across multiple strains or species (47, 48). For example, universal influenza vaccines aim to provide broad and long-lasting protection regardless of seasonal mutations. Similarly, pan-coronavirus vaccines could offer defense against future coronavirus outbreaks by targeting shared epitopes among variants.

Personalized mRNA Vaccines

The modular nature of mRNA technology also enables personalized vaccine approaches, particularly in oncology. Personalized mRNA vaccines encoding patient-specific tumor neoantigens are being investigated as a new frontier in cancer immunotherapy. Beyond cancer, rare genetic diseases and autoimmune conditions may benefit from mRNA-based therapies tailored to individual molecular profiles (38).

Improvements in Stability and Delivery

Current limitations related to mRNA stability and delivery are driving research into novel formulations. Innovations include lyophilized (freeze-dried) mRNA vaccines that eliminate cold chain requirements, next-generation lipid nanoparticles with enhanced targeting and reduced toxicity, and alternative delivery routes such as oral or intranasal vaccines. These improvements will broaden access, reduce costs, and enhance immunogenicity (39).

Collectively, these future directions highlight the transformative potential of mRNA vaccine technology across diverse fields of medicine. Continued investment in research, infrastructure, and global collaboration will be essential to fully harness these opportunities and prepare for emerging health challenges.

Table.1 Summary of mRNA Vaccine Progress for Emerging Infectious Diseases

Pathogen	Vaccine Candidate	Developer	Status	Antigen Target
SARS-CoV-2	BNT162b2 / mRNA-1273	Pfizer-BioNTech / Moderna	Approved (Global)	Spike (S) protein
Zika Virus	mRNA-1893	Moderna	Phase I (Completed)	prM-E proteins
Ebola Virus	Various (preclinical)	CureVac, US Army, others	Preclinical	Glycoprotein (GP)
Influenza Virus	mRNA-1010 (Quadrivalent)	Moderna	Phase I/II	HA (Hemagglutinin)
RSV	mRNA-1345	Moderna	Phase III	Prefusion F protein

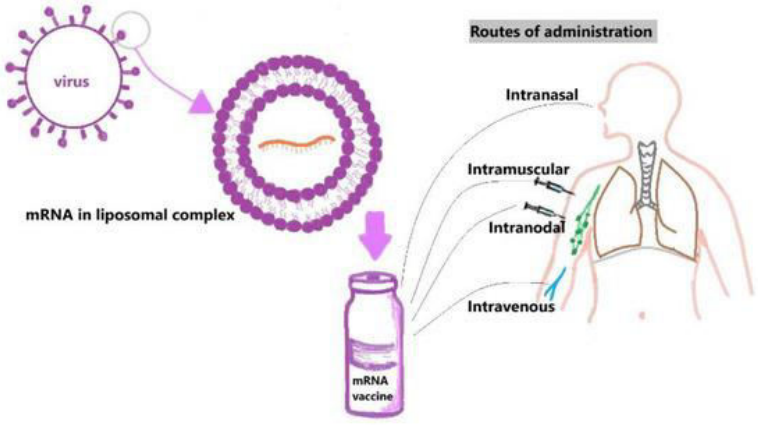
Table.2 mRNA Vaccine Development Pipeline for Emerging Infectious Diseases

Pathogen	Vaccine Candidate	Developer	Stage of Development	Antigen Target	Delivery System
SARS-CoV-2	BNT162b2	Pfizer-BioNTech	Approved (Global)	Spike (S) protein	Lipid nanoparticles (LNPs)
SARS-CoV-2	mRNA-1273	Moderna	Approved (Global)	Spike (S) protein	LNPs
Zika Virus	mRNA-1893	Moderna	Phase I Completed	prM and E proteins	LNPs
Ebola Virus	Various (e.g., CV7201)	CureVac, US Army, others	Preclinical	Glycoprotein (GP)	LNPs, others
Influenza Virus	mRNA-1010	Moderna	Phase II	Hemagglutinin (HA) proteins	LNPs
RSV	mRNA-1345	Moderna	Phase III	Prefusion F protein	LNPs

Table.3 Comparative Advantages and Challenges of mRNA Vaccine Platforms

Category	Advantages	Challenges
Development Speed	Rapid design within weeks of pathogen sequencing	Regulatory hurdles for novel targets
Manufacturing	Scalable and modular production	Need for high-purity materials and GMP facilities
Immune Response	Induces both humoral and cellular immunity	Long-term immunogenicity data still limited
Adaptability	Easily modified for variants or new pathogens	Requires validated bioinformatics pipelines
Distribution	Suitable for centralized or regional manufacturing models	Cold chain requirements limit use in low-resource settings
Public Health Impact	High efficacy demonstrated in pandemic response	Vaccine hesitancy and misinformation

Figure.1 Diagrammatic representation of liposomal-complex vaccine development and common routes of administration of mRNA vaccines.



mRNA vaccine platforms have demonstrated remarkable potential in transforming the landscape of vaccine development for emerging infectious diseases. Their rapid design, scalable manufacturing, and robust immune responses have been exemplified by the unprecedented success of COVID-19 vaccines. Beyond viral pathogens, ongoing research is expanding their application to a broader array of diseases, including bacterial, parasitic, and personalized medical conditions.

However, despite these advances, significant challenges remain—ranging from cold chain logistics and manufacturing scale-up to regulatory hurdles and public acceptance. Addressing these limitations will require continued scientific innovation, transparent communication, and equitable distribution strategies.

To fully realize the promise of mRNA vaccines, global collaboration and sustained investment in research infrastructure are essential. By fostering partnerships among governments, academia, industry, and international organizations, the scientific community can ensure that mRNA technology remains a cornerstone of pandemic preparedness and global health security for years to come.

Author Contributions

Densingh Johnrose: Investigation, formal analysis, writing—original draft. Mihir Sharma: Validation, methodology, writing—reviewing. Azaarudin Gohil:—Formal analysis, writing—review and editing. Shivam Singh: Investigation, writing—reviewing.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical Approval Not applicable.

Consent to Participate Not applicable.

Consent to Publish Not applicable.

Conflict of Interest The authors declare no competing interests.

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