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PERSPECTIVE

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The role of mRNA vaccines in infectious diseases: a new era of immunization

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Abstract

The emergence of messenger RNA (mRNA) vaccines has marked a seminal shift in the field of immunization, heralding an era characterized by unprecedented speed and efficacy in the face of infectious diseases. The global crisis caused by the COVID-19 pandemic catalyzed the rapid development and deployment of two leading mRNA vaccines, Comirnaty and SpikeVax, showcasing not only the technological promise of mRNA, but also its transformative potential in public health strategies. This study seeks to provide an in-depth exploration of the foundational elements of mRNA vaccine technology, elucidate its unique advantages over traditional vaccine platforms, analyze the existing challenges that public health officials face, and envision future applications that extend far beyond current expectations. Through this exploration, we advocate for the integration of mRNA technology into existing public health frameworks to enhance global health security and adaptability in the face of emerging infectious threats.

Keywords m-RNA vaccines, Infectious diseases, Public health, Global health security

Introduction

Infectious diseases have posed significant challenges to public health for centuries, leading to morbidity and mortality worldwide [1]. From the catastrophic impact of the Black Death in the 14th century to the more recent outbreaks of Ebola and Zika, the narrative surrounding infectious diseases has been one of resilience, adaptation, and remarkable scientific progress. Vaccination has historically played a vital role in controlling infectious diseases, significantly reducing the incidence rates, hospitalizations, and death tolls associated with diseases such as smallpox and measles [2, 3]. However, as pathogens evolve and new diseases emerge, the need for innovative immunization strategies has become increasingly apparent [1]. Traditional vaccine development relies primarily on live-attenuated, inactivated, or subunit vaccines [4]. Although effective in many contexts, these conventional approaches often encounter limitations, including lengthy development timelines, complex manufacturing processes, logistical challenges for distribution, and difficulties in adapting to rapidly changing pathogens. The onset of the COVID-19 pandemic has served as a high-stakes testbed for innovation, accelerating scientific inquiry and technological advancements in vaccine platforms [5]. During this unprecedented global challenge, mRNA vaccines have emerged as novel interventions capable of producing robust immune responses with remarkable speed and efficacy [6]. mRNA vaccine technology is an elegant solution for harnessing the cellular mechanisms of the body to produce proteins that elicit a specific immune response [7]. By introducing synthetic mRNA encoding viral antigens directly into host cells, mRNA vaccines effectively instruct the immune system to produce the components necessary

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for mounting a protective response [8]. The revolution of mRNA vaccines leverages lipid nanoparticle technology to stabilize mRNA transcripts, enhancing the efficacy of antigen translation within host cells. This advancement provides substantial advantages over traditional vaccination methods and warrants further scientific investigation. This innovative approach to mRNA vaccination represents a paradigm shift in immunization strategies and offers distinct benefits that require further exploration. As we reflect on the lessons learned and opportunities presented by mRNA vaccines, it is crucial to consider their broad implications for public health, especially regarding future strategies for infectious disease control and their applications in the treatment of malignancies.

Understanding the mechanism of mRNA vaccines

To fully understand the transformative nature of mRNA vaccines, it is essential to investigate their fundamental mechanisms. Unlike traditional vaccines that utilize inactivated or live pathogens [9], mRNA vaccines function by introducing strands of synthetic messenger RNA that encode target antigens [10]. mRNA vaccines utilize lipid nanoparticles (LPNs) to encapsulate synthetic mRNA strands, which encode viral antigens such as the spike protein from SARS-CoV-2, prompting cells to produce this protein and trigger an immune response (see Fig. 1) [11]. This mechanism is crucial for vaccine efficacy as it allows efficient delivery and translation within host cells, therefore LPNs ensure the effective functioning of mRNA vaccines [10]. These nanoparticles are composed of lipids that form a protective shell around the mRNA molecule [12]. This lipid coating serves a dual purpose: it protects unstable mRNA from degradation by nucleases present in the body and enables efficient cellular uptake [13]. Advances in lipid nanoparticle technology have contributed significantly to the stability and efficacy of mRNA vaccines [14]. This lipid coating serves a dual purpose: it protects unstable mRNA from degradation by nucleases in the body and enables efficient cellular uptake [14]. Once the mRNA is internalized by cells, cellular ribosomes initiate translation, producing encoded viral proteins, such as the spike protein in the case of SARS-CoV-2 [15]. Following this process, newly synthesized proteins are displayed on the surface of host cells, promptly signaling the immune system to recognize them as foreign entities [15]. The immune system responds rapidly by activating both humoral and cellular immune responses [10]. B cells are stimulated to produce antibodies, some of which may have neutralizing potential to effectively target the virus if encountered, whereas cytotoxic T cells are trained to recognize and destroy infected cells, contributing to a comprehensive immune response [16]. mRNA vaccines induce a robust and durable immune response through direct translation of antigen-encoding mRNA into proteins, which are subsequently presented by antigen-presenting cells. For instance, studies have shown that mRNA vaccines elicit strong immune responses, resulting in effective protection against viruses, such as SARS-CoV-2. Furthermore, the generation of immunological memory through the activation of memory T and B cells enhances long-term protection against future infections, making mRNA vaccine platforms reactive and proactive in their approach to disease prevention [16]. It is worth noting Although mRNA vaccine technology has been under investigation for decades [17], advances in lipid nanoparticle delivery systems have propelled these vaccines to success in recent years [18]. Prior to these advancements, native mRNA was less immunogenic and unstable, making it challenging to achieve desired therapeutic effects [19]. The development of LNPs has addressed these issues by stabilizing mRNA molecules and enhancing their immunogenicity through improved delivery methods [10, 20]. This combination of stabilization and effective delivery has made mRNA vaccines a powerful tool for preventive medicine [12, 20].

mRNA vaccines: more than just rapid development

Although the remarkable speed at which mRNA vaccines have been developed during the COVID-19 pandemic has attracted considerable attention, their advantages extend well beyond this impressive feat. One of the most profound benefits of the mRNA technology is its inherent adaptability. Given the clear genetic blueprint for novel pathogens, scientists can rapidly design mRNA vaccines tailored to express relevant antigens [21, 22]. This ability to pivot quickly in response to emerging variants, such as during the rise of highly transmissible variants of SARS-CoV-2, ensures that vaccination efforts remain effective even as the virus evolves [23]. mRNA also allows scalability of vaccine production, and once the initial processes and technologies are developed, large volumes can be synthesized relatively quickly [24]. The manufacturing of mRNA vaccines involves the initial process of synthesizing mRNA, which encodes target virus spike proteins such as those of SARS-CoV-2, which is then encapsulated in LPNs for stability and delivery [25]. This encapsulation not only protects fragile mRNA from degradation but also facilitates efficient cellular uptake once administered [25]. Strict quality control ensures regulatory compliance throughout the process including rigorous testing to confirm the purity and potency of the final product, with validation steps that monitor every stage of production to detect any potential contaminants or deviations from established standards, followed packaging and distribution for use [26, 27]. The establishment of regional facilities, such as BioNTech's site in Rwanda, marks a significant step towards self-sufficiency as it

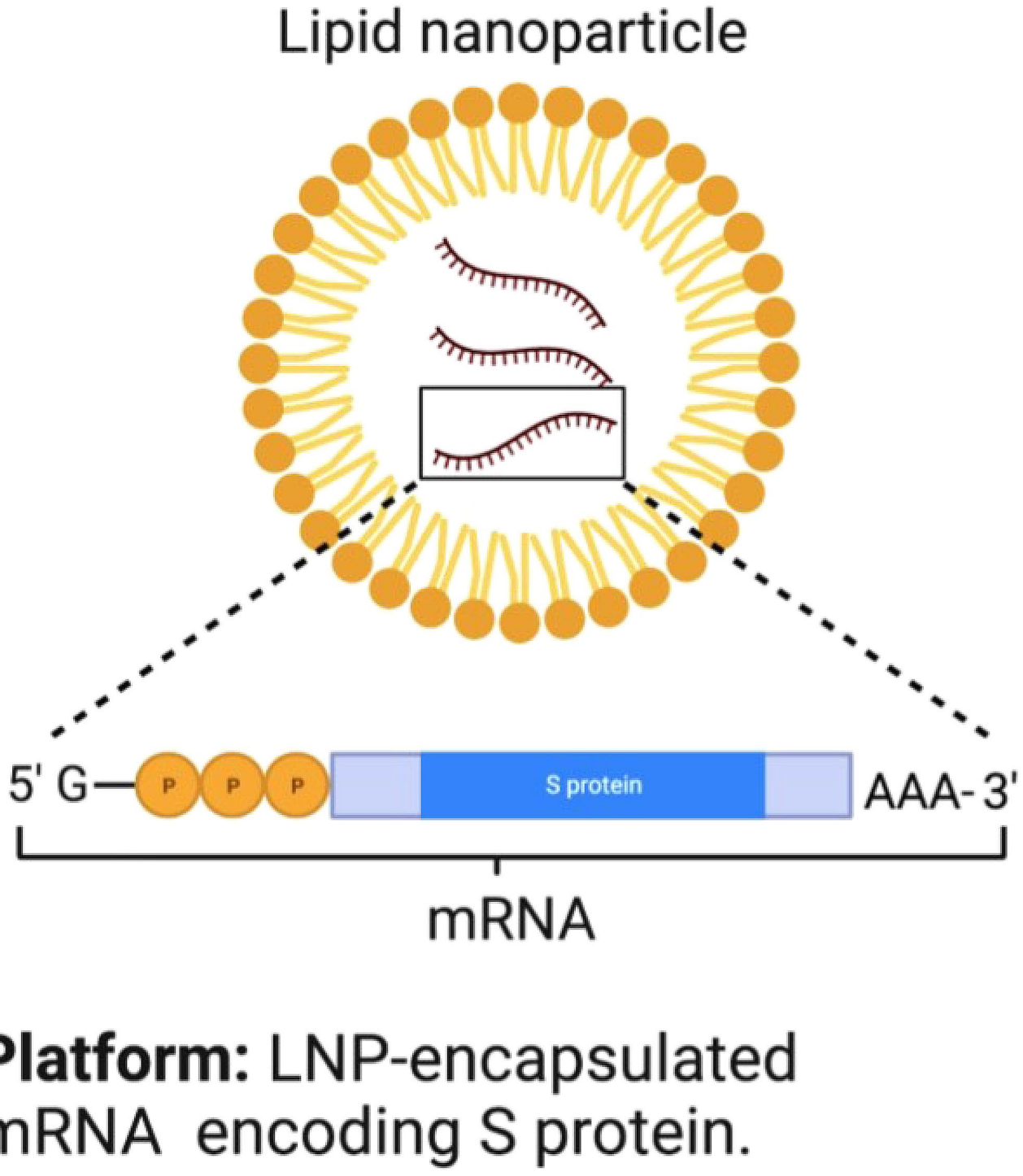

Fig. 1 Structural representation of LNP-encapsulated mRNA 1273 by Moderna encoding the S protein structure created by Biorender

enhances production capabilities and supports global vaccination efforts in response to health challenges. This unprecedented scalability not only enhances readiness for potential pandemics but also supports more routine vaccination against infectious diseases, allowing for rapid responses to outbreaks that could otherwise escalate [28].

In addition to its speed and adaptability, the safety profile of mRNA vaccines is particularly reassuring as studies for the Comirnaty and SpikeVax vaccines have demonstrated that most adverse effects tend to be mild to moderate, including local reactions at the injection site, fatigue, headache, fever, and muscle aches [29, 30]. While rare

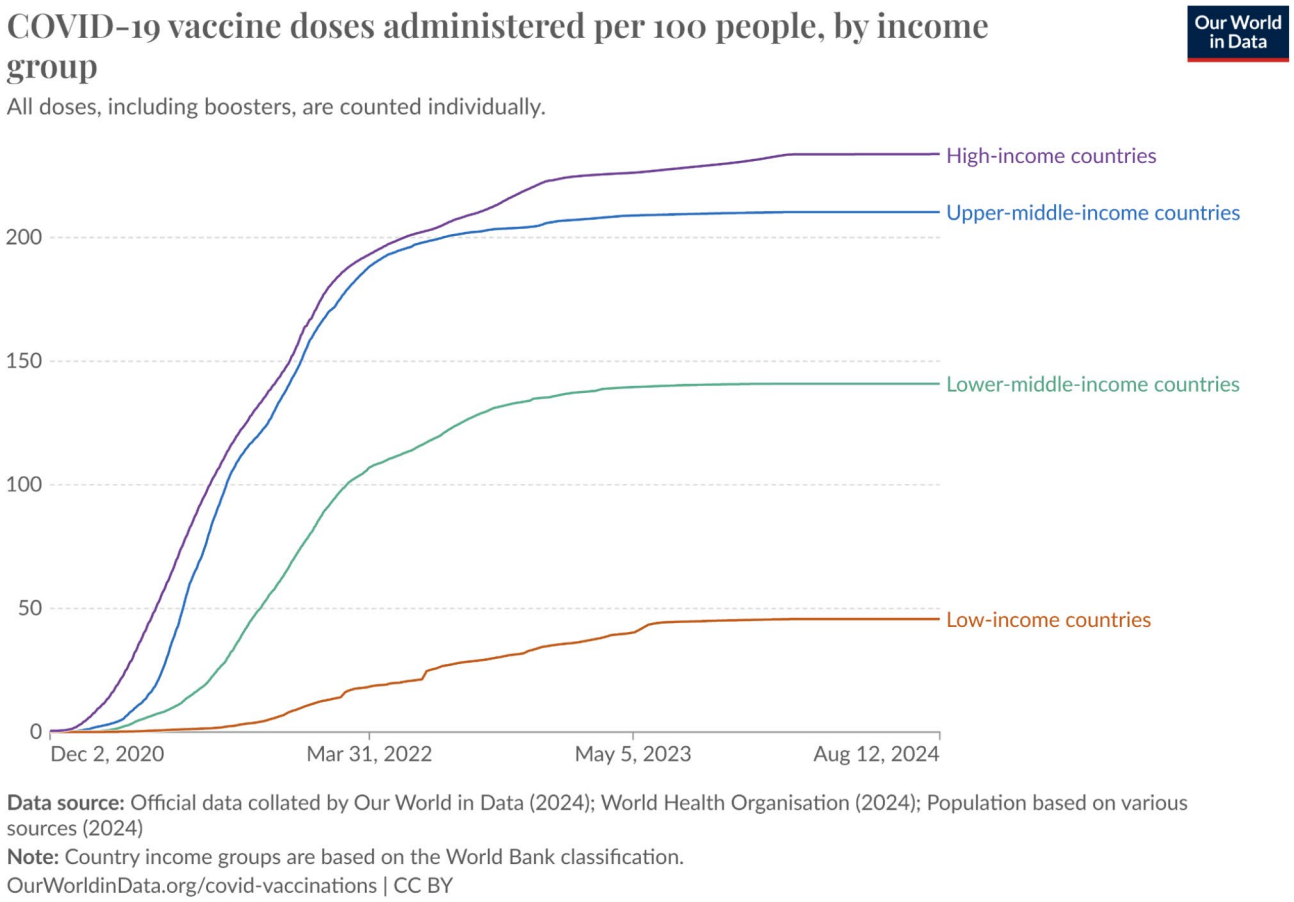

Fig. 2 A visual representation highlighting the disparities in vaccine doses administered across various countries, with a focus on the differences between low-income and high-income nations

safety signals have emerged, such as myocarditis, pericarditis, and urticaria, these occurrences remain infrequent relative to the large, vaccinated population [31]. Continuous monitoring by regulatory agencies ensures that healthcare providers and the public are informed about all reported adverse events, enhancing our understanding of the long-term safety profile of mRNA vaccines [32, 33]. This vigilant approach is critical for promoting confidence in innovative vaccines. As they contain no live viral components, mRNA vaccines carry a significantly lower risk of vaccine-induced infections [34]. Moreover, the versatility of mRNA technology allows for fine-tuning formulations that can maximize immunogenicity while mitigating any adverse effects, thus ensuring that vaccination against infectious agents remains a safe and viable public health strategy [35].

Challenges of mRNA vaccine deployment: the case of Africa

Although mRNA vaccine technology offers numerous advantages, several challenges remain, which require thoughtful consideration and innovative solutions. One primary barrier to widespread implementation is the stringent storage and transport conditions required for these vaccines, which typically require ultra-cold refrigeration [36]. This presents significant logistical hurdles, particularly in low-resource settings where healthcare infrastructure may not support the cold chain requirements essential for maintaining vaccine efficacy. Additionally, last mile delivery remains a challenge, as inadequate transport networks and a shortage of trained personnel can hinder timely vaccinations in remote areas. Equally important are the equity considerations in vaccine distribution, as disparities in access disproportionately affect low-income and middle-income countries [36]. Addressing these intertwined challenges through collaborative efforts and technological advancements is crucial for the effective deployment of mRNA vaccines across Africa's diverse landscapes.

Logistical challenges

In many regions of Africa, weak healthcare infrastructure poses substantial challenges for the distribution of vaccines. For instance, many rural healthcare facilities lack the necessary cold chain equipment to store vaccines at the required temperatures, leading to concerns regarding

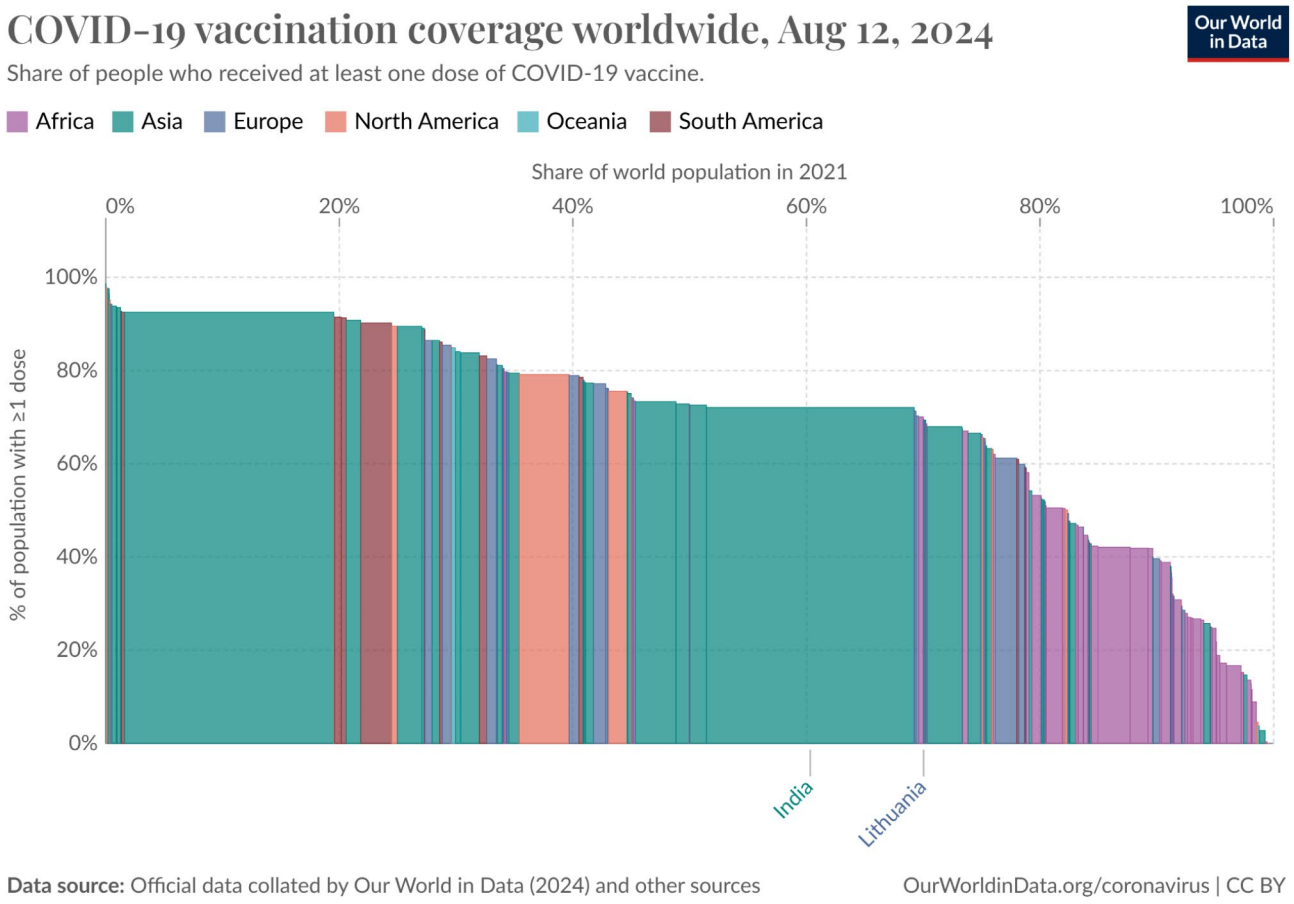

Fig. 3 A graphical illustration showcasing the distribution of COVID-19 vaccine doses across continents, emphasizing the significantly lower number of doses received by regions such as Africa compared to other continents

vaccine efficacy [37]. The difficulty in maintaining ultra-cold temperatures can result in significant vaccine wastage, exacerbating existing health crises, and reducing public trust in vaccination programs. To address the cold chain issue, it is vital to develop stable mRNA formulations that can withstand high temperatures. Recently, researchers have explored innovative approaches such as thermostable LPNs and alternative delivery systems such as microneedle patches, which can facilitate easier storage and distribution [38]. Ultimately, these technological advancements are crucial for overcoming the logistical hurdles inherent in delivering mRNA vaccines across the diverse climates and geographies in Africa.

Last mile delivery

Even when vaccines reach their regional distribution points, last-mile delivery remains challenging. Issues such as inadequate transport networks, unreliable power supplies, and a lack of trained personnel can hinder timely vaccination efforts in remote areas [38]. Ensuring efficient last-mile delivery will involve not only addressing logistical issues but also engaging communities and fostering public trust to encourage vaccination uptake. To enhance the last-mile delivery of mRNA vaccines in remote areas, a community-based distribution model could be implemented, which involves training local health workers to understand their communities' unique needs and dynamics, enabling them to administer vaccines directly where they are most needed. Utilizing mobile vaccination units such as vans and drones in hard-to-reach places can facilitate access to isolated populations and ensure timely delivery [39]. By integrating these strategies, last-mile delivery can be made more efficient and effective, ultimately improving vaccine access in underserved regions such as Africa.

Equity considerations in vaccine distribution

Equity in vaccine distribution has emerged as a crucial concern during the COVID-19 pandemic [39]. Disparities in access to healthcare, including vaccinations, disproportionately affect low- and middle-income countries [38]. It is essential that the global response to the pandemic underscores the fairness of vaccine allocation, ensuring that everyone, regardless of geographical or socioeconomic status, has access to effective preventive measures [40]. Figure 2 shows a visual representation of

COVID-19 vaccine doses administered across different countries, illustrating the significant disparities between low-income and high-income nations, Furthermore, Fig. 3 depicts the distribution of COVID-19 vaccine doses across continents, clearly showing how regions like Africa are receiving substantially fewer doses compared to other continents [41]. Collaboration through international partnerships and initiatives aimed at improving vaccine manufacturing and distribution capabilities in resource-limited settings is essential for overcoming these obstacles and closing existing health disparities [24].

Imagining future horizons: beyond infectious diseases

The potential applications of mRNA vaccine technology extend far beyond the management of infectious diseases, and researchers are actively exploring the capabilities of mRNA to address multiple infectious disease conditions [42]. By leveraging mRNA technology, these platforms present opportunities to develop combination vaccines that address multiple pathogens within a single formulation [43]. A prime example is the multivalent vaccine developed by Moderna, which was designed to effectively target both COVID-19 and seasonal influenza [44]. In contrast, Pfizer/BioNtech's attempt to create a similar multivalent COVID/Flu vaccine did not succeed in Phase III trials [45], highlighting the competitive landscape of mRNA vaccine development. Advancements in mRNA technology also offer the possibility of developing combination vaccines that address multiple pathogens within a single formulation, which is particularly significant for regions with predominant infectious diseases such as TB, HIV, and COVID-19 [46]. By uniting African researchers across borders, we can create robust platforms for developing vaccines that address region-specific pathogens, effectively reducing our vulnerability to epidemics [47]. The feasibility of mRNA vaccines as vehicles for personalized medicine is yet another exciting frontier, wherein tailored Immunotherapeutics can be developed to meet individual patient profiles based on their unique genetic and immunological characteristics [48]. For instance, in a groundbreaking study, researchers introduced individualized mutanome vaccines using an RNA-based poly neo-epitope approach, demonstrating their potential in melanoma. They created patient-specific vaccines targeting identified mutations, leading to T-cell responses against multiple neo-epitopes, with findings showing a significant reduction in metastatic events and sustained progression-free survival among participants, with two of five patients experiencing objective responses. One patient achieved a complete response when the vaccine was combined with PD-1 blockade therapy [49]. Their study emphasized the potential of exploiting individual mutations to develop personalized cancer immunotherapies, highlighting the importance of similar approaches in infectious disease research. The frontier of personalized medicine, enabled by mRNA technology, also holds promise for Africa, as the ability to create individualized Immunotherapeutics based on unique genetic and immunological profiles represents a significant leap forward in treatment efficacy [50, 51]. Similarly, by identifying and targeting specific genetic variations in pathogens prevalent in Africa and host responses, we can develop vaccines and treatments that resonate with the local population. Such initiatives could lead to improved health outcomes, particularly in the context of infectious diseases, which disproportionately affect African communities.

Conclusion

mRNA vaccines represent a groundbreaking advancement in the field of immunization, fundamentally altering our approach to combat infectious diseases. The COVID-19 pandemic has served as a catalyst, showcasing the remarkable speed, efficacy, and adaptability of mRNA technology. By harnessing the body's cellular mechanisms, mRNA vaccines create robust immune responses with the potential to respond swiftly to emerging pathogens and variants. However, despite its significant advantages, challenges such as logistic processes, cold chain requirements, and equity in vaccine distribution, particularly in low-resource settings such as Africa, must be addressed to ensure universal vaccine access. Future horizons for mRNA technology extend beyond infectious diseases, presenting opportunities for innovations in personalized medicine and combination vaccines that target multiple pathogens. The integration of mRNA vaccine technology into existing public health frameworks can enhance global health security and preparedness for pandemics, ultimately leading to improved health outcomes. Collaboration among researchers, governments, and communities is vital for overcoming obstacles and maximizing the potential of mRNA vaccines in diverse settings. As we embrace this new era of immunization, it is essential to remain committed to fostering equitable access and harnessing the full capabilities of mRNA technology for the benefit of global health.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Ethics declaration not applicable.

Transparency Statement
The lead author Kesaobaka Batisani affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Competing interests
The authors declare no competing interests.

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