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Review

Leveraging artificial intelligence in vaccine development: A narrative review

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ABSTRACT

Vaccine development stands as a cornerstone of public health efforts, pivotal in curbing infectious diseases and reducing global morbidity and mortality. However, traditional vaccine development methods are often time-consuming, costly, and inefficient. The advent of artificial intelligence (AI) has ushered in a new era in vaccine design, offering unprecedented opportunities to expedite the process. This narrative review explores the role of AI in vaccine development, focusing on antigen selection, epitope prediction, adjuvant identification, and optimization strategies. AI algorithms, including machine learning and deep learning, leverage genomic data, protein structures, and immune system interactions to predict antigenic epitopes, assess immunogenicity, and prioritize antigens for experimentation. Furthermore, AI-driven approaches facilitate the rational design of immunogens and the identification of novel adjuvant candidates with optimal safety and efficacy profiles. Challenges such as data heterogeneity, model interpretability, and regulatory considerations must be addressed to realize the full potential of AI in vaccine development. Integrating emerging technologies, such as single-cell omics and synthetic biology, promises to enhance vaccine design precision and scalability. This review underscores the transformative impact of AI on vaccine development and highlights the need for interdisciplinary collaborations and regulatory harmonization to accelerate the delivery of safe and effective vaccines against infectious diseases.

1. Introduction

Vaccines have been one of the most impactful advancements in the history of medicine, playing a pivotal role in saving millions of lives and reducing the burden of infectious diseases worldwide (Alawam and Alwethaynani, 2024; Chen et al., 2022). The concept of vaccination dates back centuries, with pioneers like Edward Jenner paving the way for modern immunization practices (Mohite et al., 2024; Zuo et al., 2024). Today, vaccines are recognized as one of the most effective and cost-efficient public health interventions, contributing substantially to the control and eradication of various infectious pathogens (Dai et al., 2023). However, traditional methods of vaccine development have long been associated with challenges that hinder efficiency and efficacy (Huang et al., 2024; Malik et al., 2022). The conventional approach involves a painstakingly slow process characterized by laborious steps, from pathogen isolation and antigen identification to immunogen formulation and clinical trials (Rawal et al., 2022). This methodical approach often spans years, if not decades, before a vaccine can be approved for widespread use (Alawam and Alwethaynani, 2024).

The first step in vaccine development typically involves the isolation and characterization of the target pathogen (Zhang et al., 2022). This process can be time-consuming and technically demanding, particularly for emerging or poorly understood pathogens (Rawal et al., 2022). Once the pathogen is identified, researchers must then identify suitable

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antigens that can stimulate an immune response without causing harm. This process often involves trial-and-error experimentation, which can be both resource-intensive and unpredictable (Sarker et al., 2023). After antigen identification, the next challenge lies in formulating an immunogen that can effectively mimic the pathogen and trigger a robust immune response. This step requires a thorough understanding of immunology and antigen presentation mechanisms to ensure the vaccine elicits the desired immune response. Additionally, the formulation must be stable, safe, and suitable for mass production (Pishesha et al., 2022).

Following immunogen formulation, preclinical testing is conducted to assess safety, immunogenicity, and efficacy in animal models. However, preclinical studies can be time-consuming and may not always accurately predict human immune responses (Chugh et al., 2024). The final and most critical phase of vaccine development involves clinical trials, which are conducted in multiple stages to evaluate safety, immunogenicity, and efficacy in human populations. These trials are highly regulated, requiring significant investment of time, resources, and expertise (Ahirwar et al., 2024). Moreover, the success of clinical trials is not guaranteed, as evidenced by the high attrition rates and failures in vaccine development pipelines, with typical attrition rates exceeding 80% from preclinical stages to market approval (Gulati et al., 2023).

Despite significant advancements in biotechnology, immunology, and vaccine manufacturing, the traditional approach to vaccine development remains fraught with challenges. The process is time-consuming, costly, and often inefficient, leading to delays in vaccine availability and deployment, particularly during outbreaks or pandemics (Bollaerts et al., 2024). In recent years, however, the landscape of vaccine development has been transformed by the emergence of artificial intelligence (AI) and computational techniques. These cutting-edge technologies offer unprecedented opportunities to accelerate vaccine design, optimize immunogen formulations, and predict immune responses with greater precision and efficiency (Aileni et al., 2022; Farzan, 2024).

While significant progress has been made in biotechnology and immunology, the lengthy and resource-intensive nature of vaccine development remains a barrier to timely responses to outbreaks and pandemics (Dodds et al., 2023). By leveraging AI algorithms for antigen selection, epitope prediction, adjuvant identification, and optimization strategies, this review aims to streamline the vaccine development landscape, accelerate vaccine design, and ultimately improve global health outcomes. The objective of this review is to provide a comprehensive review of AI approaches in vaccine development, highlighting recent advancements, challenges, and prospects for leveraging AI-driven methodologies to address current and emerging infectious diseases. Through a thorough examination of the current evidence and emerging trends, this review seeks to contribute to the growing body of knowledge in the field of computational vaccinology and pave the way for the development of next-generation vaccines with enhanced efficacy, safety, and accessibility.

Table 1 provides an overview of various AI tools employed in different aspects of vaccine development, including epitope prediction, adjuvant identification, immunogen design, and molecular dynamics simulations. These AI tools play a crucial role in accelerating vaccine discovery and design processes, ultimately contributing to the development of safe and effective vaccines against infectious diseases.

Table 1
AI tools employed in different aspects of vaccine development.

AI Tool	Description	Specific Applications in Vaccine Development
Machine Learning (ML)	ML algorithms, such as decision trees and random forests, predict antigenic epitopes, assess immunogenicity, and prioritize antigens based on diverse features.	- Predicting antigenic epitopes (Han et al., 2021; Hoze et al., 2013) - Assessing immunogenicity (Khanna and Rana, 2019) - Prioritizing antigens for experimentation (Ong et al., 2020a; Ye et al., 2021; Zhang et al., 2011, 2014)
Deep Learning (DL)	DL techniques, including convolutional neural networks (CNNs) and recurrent neural networks (RNNs), are used for sequence-based prediction, protein folding, and vaccine candidate identification.	- Sequence-based epitope prediction (Beznik et al., 2022) - Protein folding prediction (Martinez et al., 2024) - Vaccine candidate identification (Tataje-Lavanda et al., 2023)
Hidden Markov Models (HMMs)	HMMs are probabilistic models used to predict B-cell and T-cell epitopes by capturing sequence motifs and structural patterns.	- Predicting B-cell and T-cell epitopes (Jandrlić, 2016)
Neural Networks (NNs)	NNs, including feedforward neural networks and recurrent neural networks, are utilized for epitope prediction, protein-protein interaction prediction, and structure-based vaccine design.	- Epitope prediction (Abelin et al., 2017) - Protein-protein interaction prediction (Lundegaard et al., 2011) - Structure-based vaccine design (Williams and Zhan, 2022; Zhang et al., 2023)
Generative Models	Generative models, such as variational autoencoders and generative adversarial networks (GANs), are employed for de novo immunogen design and generation of novel vaccine candidates.	- De novo immunogen design (Gaurav et al., 2022) - Generation of novel vaccine candidates with desired properties (Keshavarzi Arshadi et al., 2020)
Molecular Dynamics (MD)	MD simulations are used to study the dynamic behavior and structural stability of immunogens, facilitating the rational design and optimization of vaccine constructs.	- Studying immunogen conformational changes (Alawam and Alwethaynani, 2024) - Predicting antigen-antibody interactions (Yang et al., 2021)
Virtual Screening	Virtual screening techniques, such as molecular docking and ligand-based screening, screen large compound libraries to identify potential adjuvant candidates.	- Screening compound libraries for adjuvants (Abdelmageed et al., 2020) - Predicting interactions between adjuvants and immune receptors (Taft et al., 2022; Yang et al., 2021)
Structure-Activity Relationship (SAR) Models	SAR models analyze the structure-function relationships of adjuvant molecules, guiding the rational design and optimization of adjuvant formulations.	- Designing adjuvants with enhanced efficacy and safety profiles (Kaushik et al., 2023)

2. Method

A comprehensive literature search was conducted to identify relevant studies on the role of artificial intelligence (AI) in vaccine development. PubMed, Scopus, Web of Science, and Google Scholar databases were searched using keywords such as “artificial intelligence,” “machine learning,” “vaccine design,” “antigen selection,” “epitope prediction,” “adjuvant identification,” and “immunomodulation.” The search was limited to articles published in English between January 2010 and May 2024. The titles and abstracts of retrieved articles were screened for relevance to the review topic, and full-text articles were obtained for further assessment as shown in Fig. 1. Studies were included if they focused on AI-driven approaches in vaccine development, including antigen selection, epitope prediction, adjuvant identification, and optimization strategies. Reviews, editorials, conference abstracts, and non-peer-reviewed articles were excluded from the analysis.

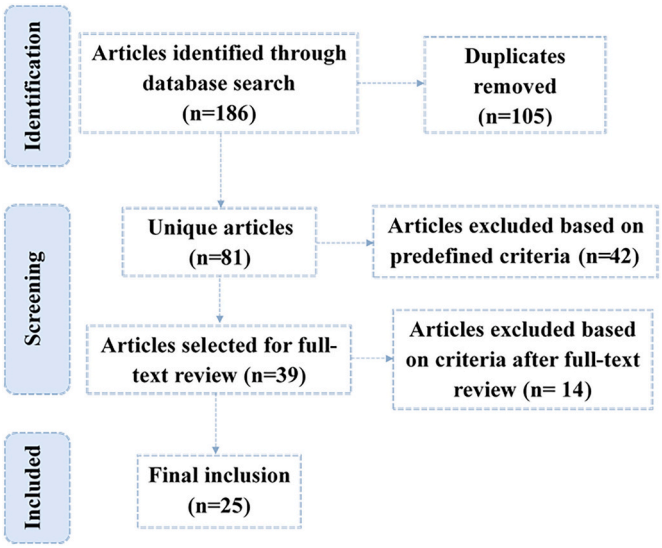

Fig. 1. Prisma flowchart of the articles selection stages.

3. Traditional methods in vaccine development

Traditional methods in vaccine development face several challenges, despite their historical success. These challenges persist in various stages of vaccine development, from antigen selection to clinical testing, and they hinder the timely and efficient deployment of vaccines to combat infectious diseases. Traditional vaccine development typically involves a series of sequential steps, including pathogen isolation, antigen identification, formulation, preclinical testing, and clinical trials. This process is inherently time-consuming and can take several years to decades to bring a vaccine from conception to market (Brisse et al., 2020).

Vaccine development is expensive, with estimates ranging from hundreds of millions to billions of dollars per vaccine (Snyder et al., 2023). The high costs are primarily attributed to research and development (R&D) expenses, preclinical and clinical testing, regulatory approvals, and manufacturing scale-up. These financial barriers limit the investment in vaccine candidates for diseases prevalent in low-resource settings or those with limited market potential. Identifying suitable antigens for vaccine development can be challenging, especially for complex pathogens with multiple antigenic targets. Traditional methods often rely on empirical approaches, such as whole-pathogen inactivation or attenuation, which may not always yield optimal immunogenicity or safety profiles (Chen et al., 2023a). Moreover, the selection of antigens may be biased toward well-characterized proteins, overlooking potentially important but less-studied antigens (Saylor et al., 2020).

Traditional vaccine development methods may struggle to address the antigenic diversity of pathogens, particularly those prone to antigenic variation or escape. Vaccines targeting highly variable pathogens, such as influenza viruses or HIV, often require frequent updates to match circulating strains. The reliance on strain-specific antigens may limit the breadth of vaccine coverage and effectiveness against emerging variants. Vaccine manufacturing processes are often complex and resource-intensive, involving multiple steps such as antigen production, formulation, purification, and quality control (Baker, 2024). Traditional manufacturing methods, such as egg-based or cell culture-based production, may lack flexibility and scalability, leading to supply shortages during pandemics or global health emergencies (da Fonseca et al., 2023; Milián and Kamen, 2015).

Regulatory approval for vaccines entails rigorous evaluation of safety, efficacy, and manufacturing processes by regulatory agencies such as the U.S. Food and Drug Administration (FDA) or the European Medicines Agency (EMA) (Souto et al., 2024). Meeting regulatory requirements involves extensive preclinical and clinical testing, which can prolong the development timeline and increase costs. Moreover, navigating the regulatory pathway may be challenging, particularly for innovative vaccine platforms or products targeting neglected diseases (Sampene and Nyirenda, 2024). Even after regulatory approval, ensuring equitable access to vaccines remains a significant challenge, particularly for low- and middle-income countries (LMICs) with limited healthcare infrastructure and resources. Market forces, intellectual property rights, and geopolitical factors may hinder the equitable distribution of vaccines, exacerbating health disparities and vaccine coverage gaps (Fox, 2024).

Addressing these challenges requires innovative approaches and collaborative efforts across academia, industry, and public health organizations. Emerging technologies, such as AI, genomics, and synthetic biology, offer promising opportunities to overcome these challenges and accelerate vaccine development timelines (Wong et al., 2023). By leveraging these technologies and fostering global partnerships, researchers can develop safer, more effective, and globally accessible vaccines to combat infectious diseases and improve public health outcomes (Gulati et al., 2023; Han and Kim, 2017; Lakkis et al., 2022; Vizcaíno et al., 2010).

Table 2 provides a structured overview of the challenges faced by traditional methods in vaccine development, along with specific examples of vaccine development efforts for various diseases. These examples illustrate how these challenges can impact vaccine development timelines, costs, coverage, manufacturing, regulatory approval, and accessibility.

4. AI in antigen selection and immunogen design

In recent years, AI has emerged as a powerful tool in antigen selection and immunogen design, revolutionizing the traditional vaccine development process (Aswathy and Sumathi, 2024; Kannan et al., 2023). For instance, AI algorithms have been pivotal in identifying novel antigens for the COVID-19 vaccines, enabling rapid response to the pandemic (Abdelmageed et al., 2020; Sharma et al., 2022). AI-driven approaches leverage advanced computational algorithms to analyze vast amounts of genomic data, protein structures, and immune system interactions, leading to the rapid identification of potential vaccine candidates as shown in Fig. 2. Machine learning algorithms, such as deep learning and random forest, have played a pivotal role in this endeavor by facilitating the prediction of antigenic epitopes and assessing immunogenicity with unprecedented accuracy and efficiency (Bravi, 2024). For example, deep learning models have been used to predict epitopes for the Zika virus, demonstrating high accuracy in identifying regions that elicit strong immune responses (Meydan et al., 2013; Bukhari et al., 2021). These algorithms analyze diverse features, including sequence motifs, physicochemical properties, and structural characteristics, to identify regions of the pathogen that are likely to elicit an immune response (Abdelmageed et al., 2020; Meydan et al., 2013; Rahman et al., 2020). Another notable example is the use of random forest algorithms in the identification of antigens for the malaria vaccine, which significantly accelerated the experimental validation process (Rahman et al., 2020; Olawade et al., 2024a; Wistuba-Hamprecht et al., 2024). By training on large datasets of known antigens and immune responses, these algorithms can effectively prioritize antigens for further experimental validation, significantly reducing the time and resources required for antigen discovery (Müller et al., 2023).

"Moreover, AI-powered generative models and molecular dynamics simulations enable the rational design of immunogens with enhanced stability, immunogenicity, and antigenic coverage (Rakitina et al., 2023). For instance, generative adversarial networks (GANs) were used to design novel immunogens for the influenza virus, leading to improved antigenicity and cross-reactivity (Kim et al., 2024). Generative models, such as variational autoencoders and GANs, can generate novel immunogen sequences with desired properties by learning from existing

Table 2
Overview of challenges faced by traditional methods in vaccine development with specific examples.

Challenge	Description	Examples of Specific Vaccine Development
Time-Consuming process	Traditional vaccine development involves sequential steps, leading to long development timelines.	- Human Papillomavirus (HPV) Vaccine: The development of HPV vaccines, such as Gardasil and Cervarix, took over 15 years from initial research to regulatory approval (O'Neill and Dwyer, 2023). - Rotavirus Vaccine: The development of Rotarix and RotaTeq, two vaccines against rotavirus, incurred significant R&D expenses and clinical testing costs, estimated at over $1 billion for each vaccine (Shuning Chen et al., 2023b; Gomez et al., 2023).
High Costs	Vaccine development is expensive, with costs ranging from hundreds of millions to billions of dollars per vaccine.	- Tuberculosis (TB) Vaccine: Developing a vaccine against TB has been hindered by the complexity of *Mycobacterium tuberculosis* and the lack of well-defined antigens, leading to challenges in antigen selection and vaccine design (Lai et al., 2023).
Complexity of Antigen Identification	Identifying suitable antigens for vaccine development can be challenging, especially for complex pathogens with multiple antigenic targets.	- Influenza Vaccine: Influenza vaccines require frequent updates to match circulating strains, but their effectiveness can be limited by antigenic drift and shift, resulting in reduced vaccine coverage against new strains (McGovern et al., 2024). - COVID-19 Vaccine: The rapid scale-up of COVID-19 vaccine production faced challenges in manufacturing capacity, supply chain disruptions, and shortages of raw materials, delaying vaccine distribution and equitable access globally (Tirkolaee et al., 2023).
Limited Vaccine Coverage	Traditional vaccines may struggle to address the antigenic diversity of pathogens, limiting their effectiveness against emerging variants.	- Ebola Vaccine: Regulatory approval for Ebola vaccines, such as Ervebo and Johnson & Johnson's vaccine, required extensive preclinical and clinical testing, as well as regulatory review processes, delaying vaccine deployment during outbreaks (Osterholm et al., 2016; Sridhar, 2015). - Meningitis Vaccine: The MenAfriVac vaccine, developed for meningitis in sub-Saharan Africa, faced challenges in distribution and access due to logistical constraints, funding shortages, and regulatory hurdles, delaying vaccine deployment in endemic regions (Mustapha and Harrison, 2018).
Inefficient Manufacturing Processes	Vaccine manufacturing processes are complex and resource-intensive, leading to supply shortages during pandemics or global health emergencies.	
Regulatory Hurdles	Regulatory approval for vaccines involves rigorous evaluation of safety, efficacy, and manufacturing processes, prolonging development timelines.	
Limited Accessibility and Equity	Ensuring equitable access to vaccines remains challenging, particularly for low- and middle-income countries with limited healthcare infrastructure.	

antigen sequences and their associated immunogenicity data. These models allow researchers to explore vast sequence space and identify optimized immunogen candidates that exhibit superior antigenicity and epitope presentation (Kim et al., 2024). Furthermore, molecular dynamics simulations provide valuable insights into the dynamic behavior and structural stability of immunogens. For example, MD simulations were critical in optimizing the stability of the SARS-CoV-2 spike protein used in COVID-19 vaccines, enhancing their efficacy and immunogenicity (Sharma et al., 2022; Alawam and Alwethaynani, 2024). By simulating the interactions between immunogens and immune receptors at the atomic level, these simulations facilitate the rational design of immunogens that elicit robust and specific immune responses, ultimately leading to the development of more effective vaccines against a wide range of pathogens.

AI-driven approaches in antigen selection and immunogen design have revolutionized vaccine development by accelerating the discovery and optimization of vaccine candidates (Martinez et al., 2024). These computational techniques leverage the power of machine learning and molecular modeling to analyze complex biological data and predict immune responses with unprecedented accuracy (Park et al., 2020). By integrating AI algorithms with experimental validation and clinical testing, researchers can expedite the vaccine development process and address pressing global health challenges, including emerging infectious diseases and antimicrobial resistance (Federico et al., 2023). As AI continues to advance and computational resources become more accessible, the potential for AI-driven vaccine design to transform public health and combat infectious diseases on a global scale is immense.

5. Epitope prediction and vaccine targeting

Epitope prediction and vaccine targeting represent critical components of vaccine design, as they allow researchers to identify specific regions of pathogens that can stimulate an immune response (Mortazavi et al., 2024). In recent years, the advent of AI has significantly accelerated epitope prediction algorithms, enabling the precise identification of antigenic determinants recognized by the immune system (Ward et al., 2021). These AI-based methods leverage sequence data, structural information, and advanced computational techniques to enhance the accuracy and efficiency of epitope prediction, paving the way for targeted vaccine design strategies (Sela-Culang et al., 2015).

One of the key strengths of AI-based epitope prediction algorithms lies in their ability to analyze large datasets and extract meaningful patterns from complex biological data (Lawrence and Ning, 2022). Machine learning algorithms, including neural networks, hidden Markov models, and support vector machines, are commonly employed to predict B-cell epitopes, T-cell epitopes, and major histocompatibility complex (MHC) binding motifs. These algorithms learn from training datasets comprising known epitopes and non-epitope sequences, allowing them to identify sequence motifs, physicochemical properties, and structural features associated with antigenicity (Abelin et al., 2017; Giguère et al., 2013; Meydan et al., 2013; Nawaz et al., 2021; Qin et al., 2024).

By accurately delineating immunodominant regions within pathogen proteins, epitope prediction algorithms enable the targeted design of vaccines tailored to specific pathogen strains and host populations. For example, in the context of viral infections such as influenza or HIV, AI-based epitope prediction algorithms can identify conserved epitopes that are shared among different viral strains or subtypes, facilitating the development of broad-spectrum vaccines with cross-protective efficacy (Shanthappa et al., 2024). Moreover, these algorithms can prioritize epitopes that are highly immunogenic and capable of eliciting robust and long-lasting immune responses, thereby enhancing the efficacy of vaccine candidates (Anwar et al., 2023).

Furthermore, AI-driven epitope prediction algorithms play a crucial role in personalized vaccine design, particularly in the context of cancer immunotherapy and autoimmune diseases (Akinsulie et al., 2024). By

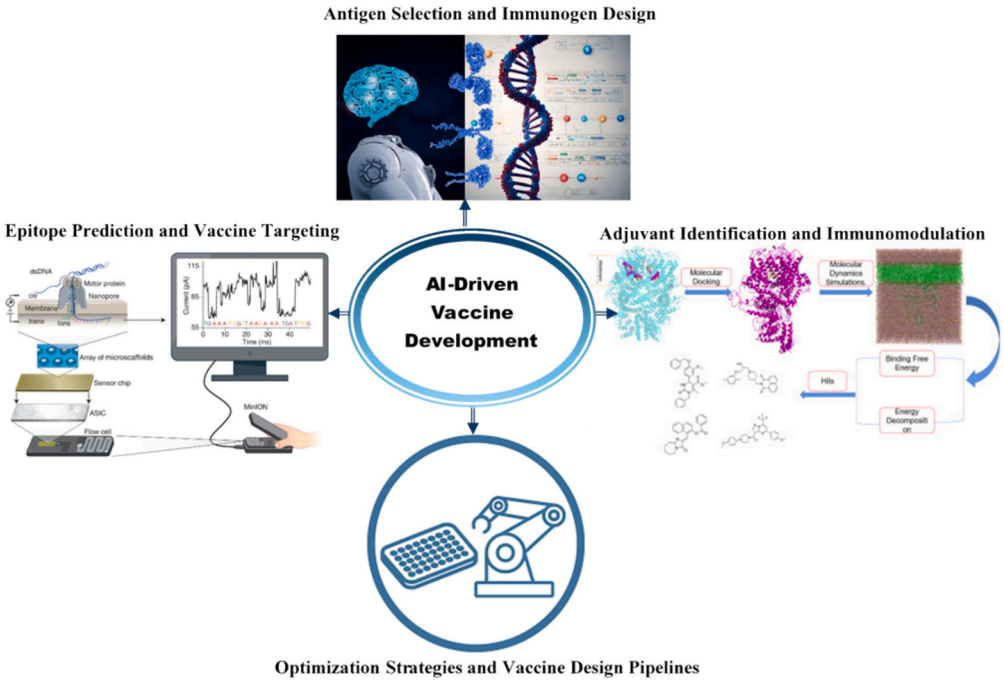

Fig. 2. AI-Driven innovations in antigen selection and vaccine design: revolutionizing the immunogen development process.

analyzing patient-specific genomic and proteomic data, these algorithms can identify neoantigens and autoantigens that are unique to individual patients, enabling the development of personalized vaccines tailored to their specific immune profiles (Ott et al., 2017). This personalized approach holds immense promise for improving the efficacy and safety of vaccines by minimizing off-target effects and maximizing therapeutic outcomes.

Epitope prediction algorithms powered by AI represent a groundbreaking advancement in vaccine targeting and design (Shey et al., 2019). These AI-based methods leverage the predictive power of machine learning and computational biology to accurately identify antigenic determinants recognized by the immune system, enabling the development of targeted and personalized vaccines against infectious diseases, cancer, and autoimmune disorders. As AI continues to evolve and computational resources become more accessible, the potential for AI-driven epitope prediction to revolutionize vaccine development and personalized medicine is boundless (Ghosh et al., 2023).

6. Adjuvant identification and immunomodulation

Adjuvants serve as indispensable components in vaccine formulations, augmenting the immune response to antigens and enhancing the efficacy of vaccines. Their ability to promote antigen presentation, immune activation, and memory formation is crucial for eliciting robust and long-lasting protective immune responses (Hemmati et al., 2024). In recent years, the integration of AI algorithms has revolutionized the process of adjuvant identification and immunomodulation, offering unprecedented opportunities to discover novel adjuvant candidates with optimal safety and efficacy profiles (Alawam and Alwethaynani, 2024).

AI algorithms leverage advanced computational techniques to analyze molecular interactions and immune response profiles, facilitating the identification of promising adjuvant candidates from vast libraries of chemical compounds and biological molecules. By analyzing structural features, physicochemical properties, and biological activity data, these algorithms can predict the immunomodulatory effects of potential adjuvants with high accuracy and efficiency (Rawal et al., 2022). Moreover, machine learning algorithms, such as neural networks and random forests, enable the identification of adjuvant candidates that possess desirable properties, including low toxicity, high stability, and immunogenicity.

Virtual screening, docking simulations, and structure-activity relationship models are integral components of AI-driven adjuvant discovery pipelines, allowing researchers to expedite the identification and optimization of adjuvant formulations (Hemmati et al., 2024). Virtual screening techniques screen large compound libraries against target receptors or immune signaling pathways, identifying potential adjuvant candidates with specific binding affinities or biological activities. Docking simulations utilize molecular docking algorithms to predict the binding modes and interactions between adjuvants and immune receptors, providing insights into their mechanisms of action and potential immunomodulatory effects (Alawam and Alwethaynani, 2024). Furthermore, structure-activity relationship models analyze the structure-function relationships of adjuvant molecules, guiding the rational design and optimization of adjuvant formulations with enhanced efficacy and safety profiles (Goetz et al., 2024).

The integration of AI algorithms in adjuvant identification and immunomodulation has paved the way for the development of next-generation vaccine adjuvants with improved immunogenicity, safety, and stability. By harnessing the predictive power of AI, researchers can expedite the discovery and optimization of adjuvant formulations, accelerating the development of vaccines against a wide range of infectious diseases, cancer, and autoimmune disorders (Singh et al., 2020). Moreover, AI-driven approaches enable the rational design of adjuvants tailored to specific vaccine antigens and target populations, enhancing vaccine efficacy and enabling precision medicine applications. As AI continues to advance and computational resources become more accessible, the potential for AI-driven adjuvant discovery to revolutionize vaccine development and public health interventions is immense (Kaushik et al., 2023).

7. Optimization strategies and vaccine design pipelines

Optimization strategies and vaccine design pipelines represent a critical aspect of modern vaccine development, aiming to streamline the process from antigen discovery to clinical deployment (Cai et al., 2023). In recent years, the integration of computational techniques,

particularly AI, has revolutionized vaccine design pipelines by enabling the development of integrated computational frameworks that combine multiple AI algorithms and experimental data streams (Blazewicz et al., 2012; Goodswen et al., 2013; Haas et al., 2021; Liarski et al., 2019). These pipelines facilitate iterative optimization, parameter tuning, and decision-making across various stages of vaccine development, ultimately accelerating the translation of vaccine candidates from the bench to the bedside.

Integrated computational pipelines leverage a variety of AI algorithms, including machine learning, deep learning, and molecular modeling, to analyze diverse datasets and generate insights into vaccine design. These algorithms process genomic data, protein structures, immune response profiles, and clinical data to inform decision-making at each stage of the vaccine development process. By integrating feedback mechanisms and adaptive learning strategies, these pipelines enable real-time adjustments to vaccine formulations, dosages, and delivery systems, thereby maximizing efficacy and safety (Liu et al., 2022).

One of the key strengths of integrated computational pipelines lies in their ability to optimize vaccine formulations and design parameters through iterative cycles of experimentation and computational modeling (Liu et al., 2020). For example, machine learning algorithms can analyze high-throughput screening data to identify optimal antigen-adjuvant combinations with enhanced immunogenicity and safety profiles (Baldwin et al., 2021). Similarly, molecular modeling techniques can simulate the interactions between vaccine components and immune receptors, guiding the rational design of immunogens and adjuvants for improved efficacy (Ismail et al., 2022). Moreover, integrated computational pipelines facilitate the systematic evaluation of vaccine candidates across preclinical and clinical stages, enabling researchers to prioritize promising candidates for further development. These pipelines integrate data from animal studies, in vitro assays, and clinical trials, allowing researchers to assess vaccine safety, immunogenicity, and efficacy in a holistic manner. By integrating diverse data streams and computational models, these pipelines enable evidence-based decision-making and accelerate the identification of lead vaccine candidates (Islam, 2024).

Furthermore, integrated computational pipelines enable researchers to explore alternative vaccine formulations, dosages, and delivery systems to optimize vaccine efficacy, stability, and scalability. For example, machine learning algorithms can analyze vaccine manufacturing data to identify process parameters that influence product quality and yield (Khuat et al., 2023). Similarly, computational models can simulate the kinetics of vaccine release and immune response kinetics, guiding the design of controlled-release formulations and novel delivery platforms (Puri et al., 2023). Integrated computational pipelines represent a powerful approach to vaccine design and optimization, leveraging the predictive power of AI algorithms to accelerate the development of safe, effective, and globally accessible vaccines. By integrating experimental data streams, computational models, and iterative optimization strategies, these pipelines enable researchers to overcome key challenges in vaccine development and accelerate the translation of vaccine candidates from the laboratory to clinical practice. As AI continues to advance and computational resources become more accessible, the potential for integrated computational pipelines to revolutionize vaccine development and public health interventions is immense (Russo et al., 2020).

7.1. AI in preclinical and clinical trials of vaccine candidates

AI technologies hold significant potential in complementing traditional "wet" lab experimentation, cell line-based studies, animal preclinical trials, and human clinical trials (Chen, 2021). By leveraging AI, researchers can streamline and enhance various aspects of the trial process, including patient recruitment, trial design, monitoring, and data analysis. For instance, AI-driven predictive analytics can identify suitable patient populations for clinical trials by analyzing electronic health records and genomic data, thereby improving trial recruitment efficiency and ensuring diverse and representative study cohorts (Olawade et al., 2023; Wang et al., 2023; Olawade et al., 2024b). Furthermore, AI algorithms can optimize trial protocols by simulating different trial scenarios, predicting potential outcomes, and identifying optimal endpoints, which can significantly reduce the time and cost associated with vaccine development (Esmaeilzadeh, 2024).

However, it is crucial to emphasize that AI technologies are not intended to completely replace traditional preclinical and clinical testing methods. The integration of AI into these stages is meant to complement and enhance the existing processes, ensuring that vaccines meet stringent safety, efficacy, and regulatory requirements. Preclinical and clinical trials remain essential for validating the biological relevance and real-world effectiveness of AI-driven predictions and models (Kuenzi et al., 2020). AI can assist in monitoring trial progress, detecting adverse events early, and providing real-time data analysis, which can lead to more informed decision-making and adaptive trial designs. Despite these advancements, the ultimate validation of vaccine candidates through rigorous "wet" lab experimentation, animal studies, and human trials is indispensable. This comprehensive approach ensures that vaccines not only demonstrate promising computational results but also meet the high standards required for public health interventions (Kannan et al., 2023). By harmonizing AI technologies with traditional trial methodologies, the vaccine development pipeline can become more efficient, robust, and capable of addressing emerging infectious disease threats.

8. Challenges and future directions

Despite the remarkable progress made in AI-driven vaccine design, several challenges must be addressed to realize its full potential and translate research findings into tangible public health impacts. One of the primary challenges is the heterogeneity and availability of data, which often limits the performance and generalizability of AI models (Liang et al., 2022). Vaccine development relies on diverse datasets encompassing genomic sequences, protein structures, immune response profiles, and clinical outcomes. However, these datasets are often fragmented, incomplete, or biased, posing challenges for training robust and reliable AI models (Esmaeilzadeh, 2024). Addressing data heterogeneity requires concerted efforts to harmonize data collection methods, share data across research communities, and develop standardized data formats and ontologies. Furthermore, interdisciplinary collaborations between computational biologists, immunologists, clinicians, and data scientists are essential to leverage diverse expertise and address complex challenges in vaccine design. Additionally, the hardware requirements for running AI models pose a significant challenge, as advanced AI algorithms often demand substantial computational power and memory resources (Wang et al., 2023). Access to high-performance computing infrastructure is crucial for training and deploying complex models, which may not be readily available in all research settings. This limitation can hinder the widespread application of AI in vaccine development and necessitates investment in computational resources and infrastructure.

Another significant challenge in AI-driven vaccine design is the interpretability of AI models, which is crucial for understanding model predictions, identifying potential biases, and gaining insights into underlying biological mechanisms (Arevalillo et al., 2017). Many AI algorithms, particularly deep learning models, are often regarded as "black boxes" due to their complex architectures and opaque decision-making processes. As a result, interpreting model predictions and explaining the rationale behind vaccine design recommendations can be challenging (Wang et al., 2023). To address this challenge, researchers are exploring interpretability techniques, such as feature attribution methods, model visualization tools, and surrogate models, to elucidate the factors driving model predictions and enhance model transparency. Moreover, researchers are increasingly focused on ensuring the biological relevance and interpretability of AI results. For instance, integrating

domain knowledge into AI models helps to align computational findings with known biological mechanisms and validate predictions within a biological context (Arevalillo et al., 2017). This approach not only improves trust and acceptance but also facilitates collaboration between AI researchers and domain experts in vaccine development, ensuring that the AI-driven insights are both scientifically meaningful and practically applicable.

Regulatory considerations also pose significant challenges for AI-driven vaccine design, particularly concerning the approval and licensure of AI-based vaccine candidates. Regulatory agencies, such as the U. S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), have well-established frameworks for evaluating traditional vaccines based on clinical trial data and manufacturing processes. However, these frameworks may not fully accommodate the unique characteristics of AI-driven vaccines, such as algorithmic biases, model uncertainty, and dynamic learning capabilities. Addressing regulatory considerations requires close collaboration between regulatory agencies, researchers, and industry stakeholders to develop robust guidelines and standards for evaluating AI-based vaccine candidates. Moreover, transparent reporting practices, rigorous validation studies, and real-world evidence generation are essential to demonstrate the safety, efficacy, and reliability of AI-driven vaccines and gain regulatory approval (Ekpan et al., 2024).

Looking ahead, the integration of AI with emerging technologies holds promise for overcoming existing challenges and advancing vaccine design precision, scalability, and personalized medicine applications. Single-cell omics technologies, such as single-cell RNA sequencing and mass cytometry, enable researchers to dissect immune cell heterogeneity and dynamics at unprecedented resolution, providing valuable insights into vaccine-induced immune responses and host-pathogen interactions (Tian et al., 2022). By integrating single-cell omics data with AI-driven computational models, researchers can develop personalized vaccines tailored to individual immune profiles, genetic backgrounds, and disease susceptibilities. Furthermore, synthetic biology approaches, such as DNA synthesis and genome editing, offer opportunities to engineer novel vaccine platforms with enhanced immunogenicity, stability, and manufacturability. By combining AI with synthetic biology, researchers can design and optimize vaccine constructs with precise control over antigen presentation, adjuvant delivery, and immune modulation, paving the way for next-generation vaccines with improved efficacy and safety profiles (Chen et al., 2019).

In conclusion, while AI-driven vaccine design faces several challenges, including data heterogeneity, model interpretability, and regulatory considerations, addressing these challenges requires interdisciplinary collaborations, standardized benchmarking protocols, and transparent reporting practices as shown in Fig. 3 below. Moreover, the integration of AI with emerging technologies, such as single-cell omics and synthetic biology, holds promise for enhancing vaccine design precision, scalability, and personalized medicine applications. By overcoming these challenges and embracing innovative approaches, researchers can accelerate the development of safe, effective, and globally accessible vaccines against infectious diseases and other public health threats.

9. Future of AI in vaccine development

The future of AI in vaccine development holds tremendous potential to transform the landscape of global health by enabling precision, rapid, personalized, and universal vaccines. By harnessing the power of AI technologies and fostering interdisciplinary collaborations, researchers can overcome longstanding challenges in vaccine development, address emerging infectious threats, and improve public health outcomes worldwide. However, realizing this vision requires continued investment in AI research, infrastructure, and workforce development, as well as a commitment to ethical principles, transparency, and equity in AI-driven vaccine development efforts.

AI algorithms enable the design of precision vaccines tailored to specific pathogens, host populations, and immune profiles. By analyzing genomic data, protein structures, and immune system interactions, AI can identify antigenic targets, predict immunogenic epitopes, and optimize vaccine formulations for enhanced efficacy (Garcia-del Rio et al., 2022). For example, AI-driven epitope prediction models have

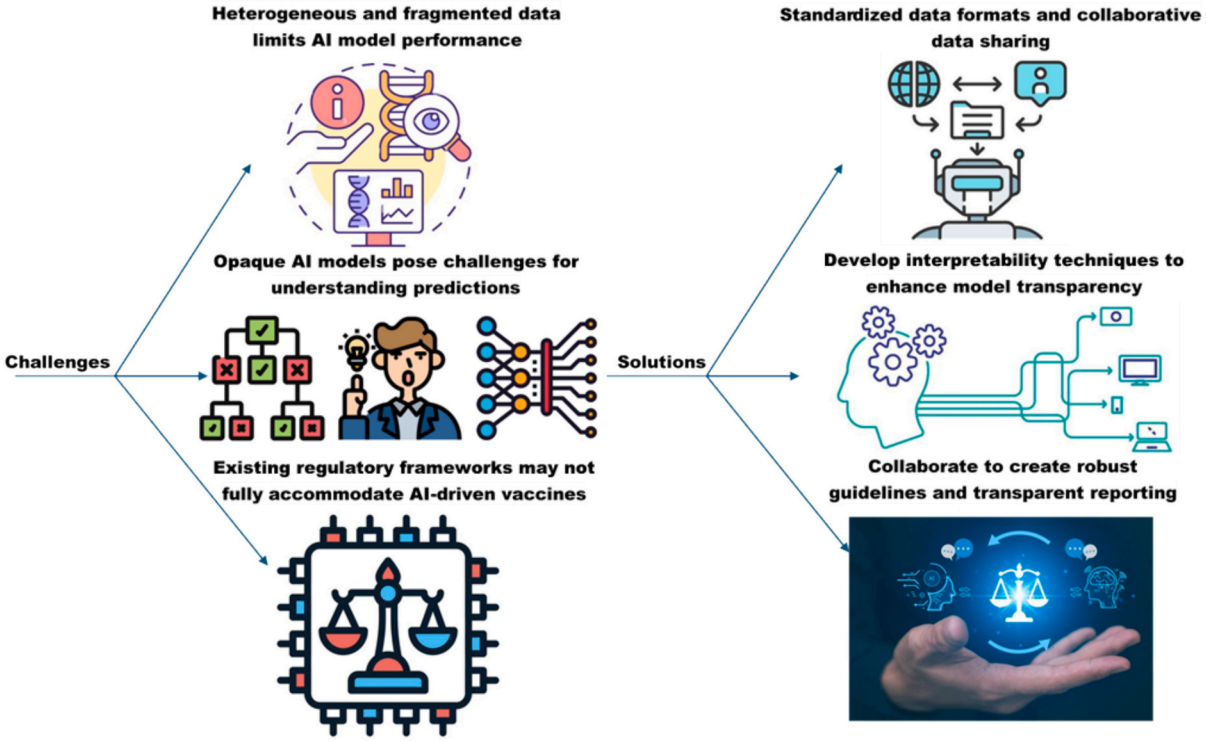

Fig. 3. Navigating challenges and innovative solutions in AI-driven vaccine design.

been successful in identifying potential vaccine candidates for infectious diseases such as HIV, malaria, and tuberculosis (Rahate and Mondal, 2024; Ren et al., 2014; Singh et al., 2024). AI-driven approaches have the potential to expedite vaccine development timelines from years to months or even weeks. Machine learning algorithms can analyze large datasets of viral sequences, clinical data, and immune responses to identify vaccine candidates and prioritize those with the highest likelihood of success. During the COVID-19 pandemic, AI played a pivotal role in accelerating the development of mRNA vaccines, such as Pfizer-BioNTech and Moderna vaccines, which were developed in record time using AI-driven antigen design and clinical trial optimization (Abubaker Bagabir et al., 2022; Saravanan et al., 2024).

AI technologies enable the development of personalized vaccines tailored to individual immune profiles and disease susceptibilities. By integrating omics data (e.g., genomics, transcriptomics, proteomics) with machine learning algorithms, researchers can identify genetic markers, immune signatures, and biomarkers associated with vaccine response variability (Abelin et al., 2017; Li et al., 2024). Personalized vaccines hold promise for improving vaccine efficacy, reducing adverse reactions, and optimizing vaccination strategies for vulnerable populations, such as the elderly or immunocompromised individuals. AI-driven approaches facilitate the discovery of universal vaccines capable of providing broad protection against multiple strains or variants of a pathogen. Machine learning algorithms can analyze viral evolution patterns, structural features, and immune responses to identify conserved epitopes and design vaccines with cross-reactive immunity. Universal vaccines have the potential to mitigate the need for frequent updates and boosters, enhance pandemic preparedness, and address challenges posed by emerging infectious diseases and antimicrobial resistance (Mazzocco et al., 2021a; Ong et al., 2020b).

AI technologies streamline clinical trial design, recruitment, and monitoring, leading to more efficient and cost-effective vaccine development (Mazzocco et al., 2021b). Predictive analytics and data-driven modeling optimize trial protocols, patient selection criteria, and endpoint assessments, improving the likelihood of trial success. AI-powered virtual clinical trials, which simulate trial scenarios using computational models and real-world data, offer opportunities to accelerate vaccine testing, reduce resource burdens, and enhance patient safety.

AI facilitates the integration of diverse data sources, including genomics, epidemiological data, electronic health records, and real-world evidence, to drive insights and discoveries in vaccine development. AI-driven knowledge graphs, natural language processing (NLP), and machine learning algorithms enable researchers to extract actionable insights from large-scale datasets, identify novel vaccine targets, and elucidate biological mechanisms underlying vaccine responses and adverse events. AI promotes collaboration and knowledge sharing among researchers, institutions, and countries, fostering a global ecosystem for vaccine research and development. Open-access AI platforms, data repositories, and collaborative networks facilitate the sharing of data, algorithms, and best practices, accelerating progress toward common vaccine goals. Capacity-building initiatives, training programs, and technology transfer partnerships empower LMICs to harness AI for vaccine development, promoting equitable access to AI-driven innovations and public health benefits.

Table 3 provides specific examples of AI tools and software platforms commonly used in vaccine development, along with their applications in various aspects of the vaccine design process, from epitope prediction to immunogen design and adjuvant identification.

Table 3
AI tools used in vaccine development.

AI Tool/Software	Description	Applications in Vaccine Development
IEDB (Immune Epitope Database and Analysis Resource)	A comprehensive database and analysis resource for epitope prediction and immune epitope characterization.	- Predicting B-cell and T-cell epitopes - Analyzing antigenic epitopes for vaccine design - Understanding immune responses to pathogens and vaccines (Abdelmageed et al., 2020) - Predicting peptide-MHC binding affinities (Aranha et al., 2020; El-Manzalawy et al., 2011; Prachar et al., 2020)
NetMHC (Net MHC Server)	A web server for predicting peptide binding to major histocompatibility complex (MHC) molecules, essential for T-cell epitope prediction.	- Identifying T-cell epitopes for vaccine design - Assessing immunogenicity of vaccine candidates (Abelin et al., 2017).
Docking Software (e.g., AutoDock, RosettaDock)	Molecular docking software used for simulating the interactions between small molecules and target proteins is crucial for virtual screening and adjuvant identification.	- Screening compound libraries for potential adjuvants (Mohammadi et al., 2022). - Predicting binding modes and interactions between adjuvants and immune receptors (Abdelmageed et al., 2020)
PyRosetta	A Python-based toolkit for protein structure prediction and design, built upon the Rosetta molecular modeling suite.	- Predicting protein structures for immunogen design (Chowdhury et al., 2022) - Designing immunogens with enhanced stability and immunogenicity - Rational design of vaccine constructs (Ford et al., 2020)
Biopython	A Python library for bioinformatics, offering tools for sequence analysis, structure prediction, and molecular biology.	- Analyzing genomic data for antigen identification - Parsing sequence data for epitope prediction (Friedman, 2024) - Scripting pipelines for vaccine design (Ros-Lucas et al., 2023)
TensorFlow / Keras	Deep learning frameworks for building and training neural networks are widely used for sequence-based epitope prediction and vaccine candidate identification.	- Training convolutional neural networks (CNNs) for epitope prediction (Chen et al., 2019). - Building recurrent neural networks (RNNs) for sequence analysis (Spencer et al., 2021). - Predicting protein-protein interactions for vaccine design (Sekaran et al., 2023). - Building machine learning models for antigenic epitope prediction (Li et al., 2023)
Scikit-learn	A machine learning library in Python, providing tools for classification, regression, clustering, and dimensionality reduction.	- Assessing immunogenicity and antigenicity of vaccine candidates - Prioritizing antigens based on diverse features (Gartner et al., 2021).
Molecular Dynamics Simulation Software (e.g.,	Software packages for simulating the dynamics of molecular systems are crucial for studying	- Simulating vaccine stability and efficacy - Predicting antigen-antibody binding kinetics (

(*continued on next page*)

10. Ethical considerations on the application of AI in vaccine development

The integration of AI into vaccine development introduces various ethical considerations that require scrutiny. While AI holds tremendous promise for accelerating vaccine discovery, design, and distribution, its

Table 3 (*continued*)

AI Tool/Software	Description	Applications in Vaccine Development
GROMACS, AMBER)	immunogen conformational changes and antigen-antibody interactions.	Alawam and Alwethaynani, 2024) - Evaluating vaccine constructs for structural integrity (Suleman et al., 2023).
Rosalind	An online platform offering bioinformatics problem-solving challenges and educational resources, helpful for training in sequence analysis and epitope prediction.	- Practicing sequence analysis techniques for epitope prediction - Learning about bioinformatics tools and algorithms used in vaccine development (Moin et al., 2023).
IEDB-AR (Immune Epitope Database and Analysis Resource - Analysis Resource)	A suite of analysis tools within the IEDB platform for predicting and analyzing B-cell and T-cell epitopes, as well as MHC binding peptides.	- Predicting B-cell epitopes and T-cell epitopes for vaccine design - Analyzing immunogenicity and antigenicity of vaccine candidates (Jalal et al., 2023). - Assessing the likelihood of peptide-MHC binding (Fleri et al., 2017).

application raises complex moral issues related to equity, transparency, safety, privacy, and autonomy. One of the foremost ethical concerns is ensuring equitable access to AI-driven vaccines. AI technologies can potentially exacerbate existing health disparities if they are not deployed equitably (Chen et al., 2023c). Low- and middle-income countries (LMICs) may lack access to AI tools and expertise, leading to disparities in vaccine development and distribution. For example, the unequal distribution of resources for AI research and development may limit LMICs' ability to benefit from AI-driven vaccine development efforts, perpetuating global health inequities.

The opacity of AI algorithms and decision-making processes raises concerns about transparency and accountability (Raja Kumar et al., 2024; Smith, 2021). AI-driven vaccine development relies on complex algorithms that may be difficult to interpret or audit, leading to questions about how decisions are made and who is responsible for them. Transparent reporting practices and open access to AI models and data are essential for ensuring accountability and fostering trust in AI-driven vaccine development. The safety and efficacy of AI-designed vaccines must be rigorously evaluated to ensure public trust and confidence. AI algorithms may identify novel vaccine candidates with enhanced immunogenicity and antigenic coverage, but their safety profiles may not be fully understood. Regulatory agencies play a crucial role in evaluating AI-driven vaccines and ensuring that they meet established safety and efficacy standards before approval for widespread use.

AI-driven vaccine development relies on vast amounts of data, including genomic information, clinical data, and personal health records. Protecting the privacy and security of sensitive data is paramount to maintaining public trust and complying with ethical principles. Data anonymization, encryption, and adherence to data protection regulations (e.g., GDPR, HIPAA) are essential safeguards to prevent unauthorized access or misuse of personal health information. Informed consent is fundamental to ethical vaccine research and development. AI algorithms may generate insights and recommendations that influence vaccine development decisions, but individuals must have the autonomy to consent to participation in clinical trials or vaccination programs. Ensuring informed consent requires transparent communication about the risks, benefits, and uncertainties associated with AI-driven vaccines, as well as the right to refuse participation without coercion or undue influence (Sharma et al., 2022).

AI algorithms are susceptible to bias, which can perpetuate or exacerbate existing disparities in healthcare. Bias in training data, algorithm design, or decision-making processes may lead to inequitable outcomes in vaccine development and distribution. Mitigating bias in AI-driven vaccine development requires careful consideration of data sources, algorithmic design, and validation methods to ensure fairness and equity in vaccine delivery. International collaboration and governance mechanisms are essential for addressing ethical challenges in AI-driven vaccine development. Global initiatives, such as the WHO's Access to COVID-19 Tools (ACT) Accelerator, aim to promote equitable access to vaccines and ensure that AI-driven technologies benefit all populations, regardless of geographical location or socioeconomic status. Multilateral agreements and standards for AI ethics and governance can help guide responsible AI deployment in vaccine development and public health (Meleouni and Efthymiou, 2023).

11. Conclusion

The integration of AI into vaccine development represents a transformative paradigm shift with profound implications for global public health. AI-driven approaches offer unprecedented opportunities to accelerate vaccine discovery, design, and deployment, addressing longstanding challenges and unlocking new avenues for innovation. From precision vaccine design and rapid development to personalized and universal vaccine strategies, AI holds promise for revolutionizing the way vaccines are conceptualized, developed, and delivered. However, the widespread adoption of AI in vaccine development also raises complex ethical considerations related to equity, transparency, safety, privacy, and autonomy. Ensuring equitable access to AI-driven vaccines, promoting transparency and accountability in algorithmic decision-making, safeguarding data privacy and security, and respecting individual autonomy and consent are paramount to realizing the potential benefits of AI while mitigating potential risks and harms.

Moreover, effective implementation of AI in vaccine development requires global collaboration, capacity building, and adherence to ethical principles. Open-access AI platforms, collaborative networks, and knowledge-sharing initiatives can facilitate the exchange of data, algorithms, and best practices, fostering a culture of collaboration and innovation in vaccine research and development. As we navigate the evolving landscape of AI-driven vaccine development, it is essential to maintain a balance between innovation and responsibility, harnessing the power of AI to address global health challenges while upholding ethical values, ensuring equitable access, and promoting the well-being of individuals and communities worldwide. By embracing a collaborative and ethical approach to AI in vaccine development, we can harness the full potential of technology to advance public health and improve lives on a global scale.

CRediT authorship contribution statement

David B. Olawade: Writing – review & editing, Writing – original draft, Resources, Project administration, Methodology, Investigation, Conceptualization. **Jennifer Teke:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Investigation. **Oluwaseun Fapohunda:** Writing – review & editing, Writing – original draft, Data curation. **Kusal Weerasinghe:** Writing – review & editing, Writing – original draft. **Sunday O. Usman:** Writing – review & editing, Writing – original draft. **Abimbola O. Ige:** Writing – review & editing, Software. **Aanuoluwapo Clement David-Olawade:** Writing – review & editing, Writing – original draft, Resources.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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