



Metaheuristic Optimization in Monkeypox Detection: A Comprehensive Literature Review

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ABSTRACT

Monkeypox (mpox) has emerged as a significant re-emerging zoonotic threat, with the 2022–2023 global outbreak underscoring the need for rapid detection, genomic monitoring, and predictive intervention strategies. This work presents a structured synthesis of three major research domains: (1) detection and classification, encompassing convolutional neural networks (CNNs), transformer-based architectures, capsule networks, transfer learning, feature selection, ensemble methods, and explainability tools applied to lesion images for accurate diagnosis; (2) genomics, prediction, and reviews, covering time series modeling of viral genome mutations using long short-term memory (LSTM) networks, phylogenetic analysis, mutation hotspot identification, and critical reviews of AI-based diagnostic methods and metaheuristic optimization strategies; and (3) intervention support, focusing on outbreak forecasting, gradient boosting risk models, and non-stationary LSTM frameworks for scenario planning and resource allocation. Across categories, recurring challenges include limited and imbalanced datasets, inconsistent reporting, and the gap between algorithmic accuracy and clinical or operational integration. This synthesis highlights methodological trends, identifies limitations, and outlines research priorities: developing multicenter datasets, leveraging multimodal integration of phenotype and genotype, adopting federated and semi-supervised learning to address data scarcity, and coupling predictive models with operational feasibility assessments. By linking technical innovation with practical outbreak management needs, this work bridges the gap between computational research and public health application, offering a roadmap for mpox preparedness and control in both endemic and non-endemic regions.

Keywords: Convolutional Neural Networks ▪ Long Short-Term Memory ▪ Monkeypox ▪ Genomic Analysis ▪ Outbreak Forecasting

1. INTRODUCTION

The global landscape of infectious disease threats has undergone profound changes in the past two decades, marked by the emergence and re-emergence of zoonotic pathogens capable of sustained human-to-human transmission. Monkeypox (mpox), caused by the monkeypox virus, an Orthopoxvirus closely related to the variola virus, has transitioned from a largely neglected tropical disease to a condition of international public health concern. Historically confined to regions

of Central and West Africa, mpox has demonstrated its capacity to spread globally, with the 2022–2023 outbreak involving sustained transmission across multiple continents. This epidemiological shift has challenged existing surveillance, diagnostic, and response frameworks, underscoring the necessity for robust, rapid, and accurate diagnostic capabilities, as well as predictive modeling systems capable of anticipating outbreak trajectories in heterogeneous settings. Conventional diagnostic workflows for mpox, dominated by polymerase chain reaction (PCR) assays of lesion swabs or biopsies, re-

main the gold standard due to their high sensitivity and specificity. However, these methods are resource-intensive, reliant on laboratory infrastructure, and constrained by delays in sample transportation and processing. In outbreak situations where rapid case identification is essential, such limitations can impede timely intervention, allowing further community spread. In this context, artificial intelligence (AI) and machine learning (ML) methods have emerged as promising complements to laboratory diagnostics, capable of delivering near-real-time classification of suspected cases based on clinical imagery and metadata. These computational tools have shown particular potential in dermatological applications, where high-resolution images of cutaneous lesions can be analyzed for distinctive morphological patterns indicative of specific conditions, including mpox. A key advantage of AI-driven diagnostic systems lies in their scalability and adaptability. Once trained, deep learning models—particularly convolutional neural networks (CNNs)—can process thousands of images per hour on modest hardware, enabling deployment in field clinics and low-resource environments. Furthermore, optimization algorithms can enhance these models' performance by fine-tuning hyperparameters and network architectures, thereby improving accuracy while reducing computational overhead [1]. The integration of such models into mobile health platforms offers the possibility of broadening access to diagnostic capabilities, especially in regions where specialist dermatological expertise is limited. Beyond purely computational improvements, understanding the epidemiological and clinical spectrum of mpox is essential for building accurate detection systems. Recent studies have emphasized the heterogeneity of mpox presentations, which may vary depending on viral clade, host immunity, and coinfections. These insights are critical for the creation of robust AI models that can generalize across diverse patient populations and settings [2]. Such models must not only perform under ideal imaging conditions but also handle variability in image quality, lesion stage, and environmental factors, which are common in real-world outbreak contexts. Recent advances in hybrid optimization–deep learning pipelines have demonstrated that metaheuristic algorithms can play a pivotal role in enhancing classification performance for mpox detection. By coupling population-based search strategies with deep feature extraction, researchers have been able to achieve high-accuracy results while avoiding the pitfalls of overfitting on limited datasets [3]. These approaches are particularly valuable in the early stages of an outbreak, when available image datasets may be small but timely diagnostic capacity is nonetheless critical. Another promising development is the use of lightweight, efficiency-optimized architectures for lesion classification. These models aim to strike a balance between diagnostic accuracy and computational resource demands, making them ideal for deployment in mobile or embedded systems [4]. Such efficiency-focused designs are not only advantageous for low-resource settings but also for large-scale screening programs where throughput is a key consideration. The integration of multimodal data—combining lesion images with structured patient information and epidemiological context—has the potential to significantly improve diagnostic accuracy and resilience to noise in individual data streams. Models leveraging such multimodal fusion approaches have demonstrated robust per-

formance in varied clinical scenarios, illustrating the importance of designing AI systems that can synthesize heterogeneous data sources [5]. Hybrid architectures that combine convolutional neural networks with transformer-based attention mechanisms have emerged as particularly powerful for image-based mpox detection. While CNNs excel at capturing local texture and edge information, transformers are capable of modeling long-range dependencies and global context within images. This synergy has been shown to improve lesion classification accuracy, particularly in cases where lesions exhibit high spatial variability or are partially occluded. Furthermore, attention maps generated by such models can provide interpretable visualizations of the features most influential in the decision-making process, a factor critical to fostering clinician trust. Complementary to architectural advances, optimization-based feature selection has been applied to distill the most informative features from high-dimensional image embeddings, thereby improving generalization and reducing model complexity. By systematically eliminating redundant or irrelevant attributes, these methods can enhance both inference speed and accuracy in mpox classification systems [6]. The adoption of such techniques also facilitates deployment on hardware with limited processing capacity, broadening the potential reach of AI-assisted diagnostics. In addition to individual studies, comprehensive surveys synthesizing the rapidly expanding body of research on AI-based mpox detection provide valuable meta-level insights. These surveys categorize methodologies, highlight common challenges, and identify promising directions for future work [7]. By situating novel contributions within the broader research landscape, such syntheses help streamline development efforts and avoid redundant work, while promoting best practices for dataset curation, model evaluation, and clinical validation. Hybrid pipelines that integrate deep learning feature extraction with classical machine learning classifiers offer yet another approach to mpox detection. In these systems, convolutional or transformer-based backbones are used to extract robust visual representations, which are then classified using algorithms such as support vector machines (SVMs). When optimized using swarm-based metaheuristics, these hybrid systems have demonstrated competitive performance with the added benefit of interpretability [8]. This is particularly relevant in clinical settings where explainability is necessary for regulatory approval and clinician acceptance. Beyond detection, research has increasingly focused on end-to-end deep learning pipelines specifically designed for mpox lesion classification, incorporating specialized preprocessing stages to enhance image quality and lesion segmentation. Such integrated systems are capable of handling the full diagnostic process—from raw image acquisition to final classification—in a seamless manner [9]. These designs reduce the need for manual intervention and minimize error propagation between processing stages. Interpretability remains a central challenge in the deployment of AI-based medical diagnostics. Recent work has explored the incorporation of explainable AI frameworks into mpox detection pipelines, providing both visual and textual justifications for classification decisions [10]. These approaches aim to bridge the gap between algorithmic predictions and clinician reasoning, increasing the likelihood of adoption in real-world practice. Optimization extends beyond feature selection and hyperparameter tuning to include

the broader design of the learning architecture itself. Models incorporating multi-objective optimization strategies have been shown to balance trade-offs between accuracy, computational cost, and robustness to noisy inputs [11]. Such approaches are essential when designing diagnostic systems intended for heterogeneous deployment environments, from tertiary care hospitals to rural clinics. The role of predictive modeling in outbreak preparedness has also grown in prominence. Time series forecasting methods integrating statistical and machine learning components have been applied to predict mpox case counts across diverse geographical regions. By accounting for both linear trends and nonlinear dynamics, these hybrid models can provide more accurate short-term forecasts, informing targeted interventions and resource allocation. Transformer architectures, originally developed for natural language processing, have shown remarkable potential in medical image analysis, including mpox lesion classification. By leveraging patch-based embeddings and multi-head self-attention, these models can capture complex spatial relationships that may be overlooked by purely convolutional approaches [12]. This capability is particularly valuable for diseases like mpox, where lesion patterns can vary widely in morphology and distribution. Taken together, these advancements illustrate the diverse range of computational strategies being applied to the challenge of mpox detection and forecasting. Each methodological innovation—whether in network architecture, optimization strategy, multimodal integration, or interpretability—addresses a specific set of limitations in existing approaches. Yet the full realization of AI's potential in mpox control depends on addressing several persistent challenges. Foremost among these is the issue of data scarcity. Despite the global spread of mpox, publicly available, high-quality, and well-annotated image datasets remain limited in size and diversity. This scarcity increases the risk of overfitting, reduces generalizability, and can inadvertently encode biases that limit performance across different demographic groups and clinical contexts. Data augmentation, synthetic data generation using generative adversarial networks, and federated learning are among the strategies proposed to mitigate these constraints, but each comes with trade-offs in terms of realism, privacy, and computational demand. Another critical factor is the variability in clinical presentation. Mpox lesions can mimic those of other dermatological conditions, including chickenpox, measles, and syphilis, leading to diagnostic ambiguity even for trained clinicians. AI models trained exclusively on prototypical cases may underperform when confronted with atypical presentations. To address this, future research must prioritize dataset inclusivity, encompassing diverse lesion morphologies, stages of progression, and image acquisition conditions. Integration with public health infrastructure is equally important. AI-based diagnostic outputs must be effectively linked to surveillance systems, contact tracing efforts, and outbreak management protocols. This requires interoperability between diagnostic platforms and health information systems, as well as secure data handling practices that comply with privacy regulations. The value of AI in outbreak settings is maximized when it informs rapid decision-making, such as triggering targeted vaccination campaigns or reallocating healthcare resources to emerging hotspots. Interpretability and transparency are also essential for clinical adoption. While techniques such as Grad-

CAM, attention visualization, and feature attribution can provide insight into model decisions, these tools must be rigorously validated to ensure that highlighted features correspond to medically relevant cues rather than spurious correlations. In parallel, inherently interpretable model architectures merit further exploration, as they can provide built-in transparency without the need for post hoc explanations. The broader sociotechnical landscape must also be considered. Stigma, misinformation, and unequal access to digital infrastructure can all influence the effectiveness of AI-based interventions. Designing systems that are culturally sensitive, linguistically accessible, and affordable is crucial to ensuring equitable benefit distribution. Furthermore, close collaboration with clinicians, epidemiologists, and community stakeholders from the early stages of system design can enhance both usability and trust. Looking ahead, the convergence of advanced deep learning architectures, sophisticated optimization algorithms, and integrated epidemiological modeling offers a path toward comprehensive mpox control strategies. Future systems could couple real-time lesion classification with predictive models that forecast outbreak spread, integrate genomic data to track viral evolution, and provide tailored intervention recommendations based on local transmission dynamics. Such a holistic approach would embody the principles of precision public health, aligning technological capabilities with context-specific needs. In summary, the integration of AI and optimization methods into mpox detection, diagnosis, and forecasting represents a rapidly maturing field with significant potential to enhance global health security. The body of work reviewed here—encompassing CNN-based image analysis, optimization-enhanced neural networks, epidemiological characterization, hybrid optimization–deep learning pipelines, efficiency-focused architectures, multimodal integration, CNN–transformer hybrids, optimization-based feature selection, comprehensive surveys, deep feature–SVM hybrids, end-to-end lesion classification pipelines, explainable AI frameworks, multi-objective optimization, hybrid statistical–ML forecasting, and transformer-based lesion analysis—demonstrates both the breadth and depth of current research efforts. Together, these contributions provide a foundation upon which future innovations can build, with the ultimate goal of delivering accurate, efficient, interpretable, and widely accessible diagnostic and predictive tools for mpox control.

2. LITERATURE REVIEW

The recent proliferation of research addressing automated monkeypox (mpox) detection, epidemiological modeling, and public health integration reflects both the urgency of the disease and the breadth of computational strategies being deployed to address it. Deep learning has been central to these efforts, with convolutional neural networks (CNNs) consistently forming the backbone of image-based diagnostic pipelines. CNNs leverage hierarchical feature extraction, enabling them to capture fine-grained texture variations alongside broader morphological patterns in skin lesions. This makes them particularly effective for differentiating mpox from visually similar dermatological conditions such as varicella, measles, and bacterial skin infections. Early studies demonstrated that transfer learning from large-scale image

datasets could bootstrap mpox classifiers even when domain-specific image availability was limited, offering a practical path forward given the scarcity of publicly available mpox datasets. Feature extraction layers pre-trained on general image corpora can be fine-tuned using small collections of annotated mpox images, achieving strong performance metrics while reducing the computational cost of training from scratch. While CNNs remain a mainstay, architectural innovation has expanded into hybrid configurations that combine convolutional feature extraction with the global dependency modeling capacity of transformers. Vision transformers (ViTs), adapted from natural language processing, segment input images into patches and model the relationships among these patches via multi-head self-attention. This approach captures contextual patterns that extend beyond local neighborhoods, enabling more accurate classification in cases where lesion boundaries are irregular or where relevant visual cues are dispersed across the image. Empirical evaluations have shown that CNN–transformer hybrids outperform standalone CNNs in precision–recall balance for ambiguous lesion cases, particularly when integrated with explainability mechanisms such as Grad-CAM to highlight salient regions influencing predictions. Parallel to architectural advances, optimization techniques have emerged as critical enablers of robust mpox detection models. Hyperparameter optimization using metaheuristic algorithms—such as particle swarm optimization, genetic algorithms, and ant colony optimization—has been widely adopted to tune network parameters including learning rates, convolutional kernel sizes, activation functions, and regularization strengths. These strategies often outperform manual tuning and grid search by more efficiently exploring the high-dimensional hyperparameter space, avoiding local minima, and converging on configurations that yield better generalization. In addition, optimization has been applied at the feature selection stage, with algorithms like minimum redundancy maximum relevance (mRMR) pruning feature sets to retain only the most discriminative attributes. Such pruning not only improves model accuracy but also reduces inference time, an important factor in field-deployable diagnostic systems. Lightweight CNN architectures optimized for mobile and embedded deployment have also gained traction, reflecting the need for diagnostic capabilities in low-resource settings. Models such as MobileNet, ShuffleNet, and EfficientNet have been adapted to mpox detection, often with customized preprocessing pipelines that enhance lesion visibility while suppressing irrelevant background noise. These efficiency-focused designs can run on portable devices without sacrificing diagnostic accuracy, enabling on-site triage in rural health clinics or during mass-screening campaigns. In some cases, pruning and quantization techniques have been employed to further reduce model size and latency, facilitating integration into telemedicine applications where real-time feedback is essential. A significant line of work has investigated the integration of multimodal data into mpox diagnostic pipelines. By combining dermoscopic or clinical photographs with structured patient information—such as age, sex, recent travel history, and symptom onset dates—multimodal models can capture correlations between demographic or epidemiological factors and lesion appearance. This integration is particularly valuable when image quality is suboptimal or when early-stage lesions lack distinctive visual

characteristics. Fusion strategies range from early fusion, where modalities are combined at the input stage, to late fusion, where separate modality-specific models produce outputs that are subsequently merged. Attention-based fusion mechanisms have demonstrated superior performance by dynamically weighting each modality according to its relevance for a given prediction. Interpretability remains a persistent concern in the deployment of AI-based diagnostic systems. Black-box models, while accurate, can hinder clinician trust and complicate regulatory approval. In response, researchers have incorporated explainable AI (XAI) techniques directly into mpox detection frameworks. Gradient-weighted class activation mapping (Grad-CAM) is frequently used to produce heatmaps that visually indicate the regions of an image most responsible for a model’s decision. Complementary methods such as Local Interpretable Model-agnostic Explanations (LIME) provide feature-level explanations across tabular and image data. Beyond post hoc explanations, inherently interpretable architectures have been explored, wherein intermediate network representations correspond directly to medically meaningful features such as lesion shape, color distribution, or edge sharpness. These designs can improve both transparency and diagnostic reliability, especially in clinical training and decision-support contexts. A parallel area of development has focused on preprocessing pipelines that enhance lesion visibility and suppress noise before classification. Techniques such as contrast-limited adaptive histogram equalization (CLAHE) have been applied to improve local contrast, making subtle textural details more prominent. Morphological operations—including dilation, erosion, and opening/closing—are often employed to isolate lesion regions from surrounding skin and eliminate background clutter. Some pipelines incorporate automated segmentation using U-Net or Mask R-CNN architectures, ensuring that subsequent classification models focus solely on the lesion itself. These preprocessing stages are especially important when dealing with heterogeneous image sources, as they help normalize variations in lighting, resolution, and skin tone across datasets. In addition to purely visual analysis, several studies have examined the potential of combining image-based models with symptom-based predictive systems. These models leverage structured data on patient-reported symptoms, such as fever, lymphadenopathy, and rash progression, in conjunction with image classifiers. Hybrid systems of this nature can be particularly valuable in low-resource environments where access to high-resolution imaging devices is limited, allowing for preliminary triage based on symptom patterns before confirming diagnosis through imaging. Moreover, such systems can be integrated with telehealth platforms, enabling remote consultations and rapid triage during outbreak situations. Epidemiological modeling and outbreak forecasting form another critical pillar of the literature. Here, machine learning and statistical approaches are used to predict the spread of mpox based on historical case data, mobility patterns, and environmental variables. Hybrid models that combine autoregressive integrated moving average (ARIMA) methods with recurrent neural networks (RNNs), such as long short-term memory (LSTM) networks, have demonstrated the ability to capture both linear trends and complex temporal dependencies in outbreak data. These forecasting models can provide public health authorities with advanced warning

of potential hotspots, informing targeted interventions like vaccination drives, travel advisories, and healthcare resource allocation. Transformer-based architectures have also begun to influence time series forecasting in mpox epidemiology. By leveraging self-attention mechanisms, these models can weigh the relative importance of different time points in historical data, capturing long-range dependencies that might be overlooked by traditional RNNs. When combined with external data sources, such as climate indicators or social media trends, transformer-based forecasting models can offer a more holistic view of outbreak dynamics, potentially improving the timeliness and accuracy of public health responses. Genomic analysis represents another rapidly growing area of mpox research. The use of machine learning in genomic surveillance enables the identification of mutation patterns, clade differentiation, and potential links between genetic variation and clinical severity. Deep learning models trained on viral sequence data can classify strains, predict mutation impacts, and assist in tracking transmission pathways. By integrating genomic insights with epidemiological and clinical data, researchers can develop more targeted containment strategies and anticipate shifts in viral behavior that may impact diagnostic accuracy or vaccine efficacy. Optimization methods play a role here as well, particularly in selecting the most informative genomic features for downstream analysis. Feature selection algorithms can reduce the dimensionality of genomic datasets, improving the interpretability and computational efficiency of classification or clustering models. This is especially important given the high dimensionality of genetic sequence data and the computational expense of processing it in real time during outbreak surveillance. Several review articles within the mpox literature provide valuable syntheses of these diverse research threads. They not only summarize the state of the art in diagnostic and forecasting models but also highlight methodological limitations, such as small sample sizes, lack of standardized evaluation protocols, and limited external validation. These reviews frequently emphasize the need for multicenter collaborations to assemble larger, more diverse datasets, as well as the importance of incorporating fairness and bias assessments into model evaluation to ensure equitable performance across different population subgroups. Despite these advances, the literature also reflects several persistent challenges. Data imbalance, where positive mpox cases are vastly outnumbered by negative or unrelated cases in training datasets, can skew model performance and lead to high false-negative rates. Techniques such as synthetic minority oversampling (SMOTE), adaptive resampling, and cost-sensitive learning have been applied to mitigate this issue, with varying degrees of success. Another challenge is the rapid evolution of both the virus and its epidemiological context, which can render models trained on historical data less effective when applied to new outbreaks or emerging clades. Continual learning frameworks, capable of updating model parameters as new data become available without catastrophic forgetting, are being explored as a potential solution. An additional thread in the mpox literature emphasizes the role of ensemble learning in improving classification robustness. By aggregating the predictions of multiple base learners—whether deep CNNs with different architectures, transformer-based models, or traditional machine learning classifiers—ensembles can reduce variance

and improve generalization. Techniques such as majority voting, weighted averaging, and stacking have been employed to combine diverse model outputs. The diversity within ensembles is often achieved through varying network architectures, training datasets, or input preprocessing methods. This diversity increases the likelihood that errors from one model will be compensated for by correct predictions from another, thereby improving overall system accuracy. Some researchers have extended ensemble concepts to multimodal fusion, integrating image, genomic, and epidemiological data within a unified framework. In such systems, modality-specific models first process their respective inputs to produce embeddings or probability scores. These intermediate outputs are then combined—either through simple concatenation or via learned attention-based fusion layers—to produce a final prediction. The advantage of this approach lies in its capacity to leverage complementary information sources, increasing diagnostic reliability when individual data streams are noisy, incomplete, or inconsistent. The use of synthetic data generation has gained attention as a strategy for addressing data scarcity. Generative adversarial networks (GANs) and variational autoencoders (VAEs) have been employed to produce realistic mpox lesion images that augment existing datasets. When used appropriately, synthetic data can improve model robustness by exposing classifiers to a wider variety of lesion presentations, lighting conditions, and backgrounds. However, ensuring the clinical realism of generated images is critical, as poorly generated data can introduce artifacts that mislead the learning process. Validation of synthetic images by dermatology experts is therefore a recommended best practice. In the domain of deployment, several works have focused on translating high-performing laboratory models into practical diagnostic tools. This often involves adapting architectures for execution on constrained hardware, implementing model compression techniques such as pruning and quantization, and optimizing inference pipelines for minimal latency. Edge-computing implementations, where models run directly on diagnostic devices without requiring internet connectivity, have been proposed to facilitate use in remote or under-resourced environments. Such designs can be integrated into smartphone applications, allowing healthcare workers to perform lesion classification in the field and receive instant feedback. From a public health perspective, AI-assisted mpox detection and forecasting systems have the potential to feed directly into surveillance dashboards, enabling near real-time monitoring of outbreak dynamics. Automated alerts can be triggered when case probabilities exceed certain thresholds, prompting further investigation or immediate intervention. Integrating AI outputs into existing public health infrastructure requires standardized data formats, secure communication protocols, and interoperability with electronic health records (EHR) systems. Pilot projects in other infectious disease domains suggest that such integration is feasible, but rigorous evaluation in the context of mpox remains limited. The literature also underscores the importance of model interpretability and clinician engagement during system design. Several studies have involved end-users in the development process, soliciting feedback on interface design, explanation formats, and integration with clinical workflows. This participatory approach can help ensure that AI systems address real-world needs, reduce the

risk of workflow disruption, and increase the likelihood of sustained adoption. Moreover, explainability features such as saliency maps, textual justifications, and confidence scores can enhance clinician trust by providing transparency into model reasoning. Finally, ethical considerations permeate the discussion around AI in mpox detection and management. Issues such as algorithmic bias, equitable access to technology, data privacy, and informed consent are repeatedly raised in the literature. Bias can arise from imbalanced datasets, underrepresentation of certain demographic groups, or implicit correlations between irrelevant features and disease labels. Addressing these concerns requires proactive bias detection, algorithmic fairness interventions, and the inclusion of diverse populations in training and evaluation datasets. Data privacy safeguards, including anonymization, secure storage, and compliance with relevant legal frameworks, are essential for maintaining public trust. In sum, the mpox literature presents a rapidly evolving field where deep learning, optimization, multimodal integration, and forecasting techniques converge to address the pressing challenge of timely, accurate, and scalable diagnosis and outbreak prediction. While substantial progress has been made, the path to widespread clinical adoption and integration into public health systems will depend on continued methodological refinement, interdisciplinary collaboration, and a commitment to transparency and equity. Another emerging theme in the mpox literature involves the adaptation of continual and federated learning paradigms to address the challenges of evolving data distributions and privacy constraints. Continual learning approaches enable models to update their parameters incrementally as new data become available, without catastrophic forgetting of previously learned information. This is particularly relevant for mpox, where shifts in viral clade prevalence, geographic spread, and clinical presentation may occur over time, potentially degrading the performance of static models. By continuously integrating new examples from ongoing outbreaks, continual learning systems can maintain diagnostic accuracy while adapting to changing epidemiological contexts. Federated learning, on the other hand, allows multiple institutions to collaboratively train a shared model without directly exchanging patient data. This approach addresses the legal and ethical challenges associated with cross-border data sharing, especially in sensitive domains like infectious disease diagnosis. Participating sites train local copies of a global model on their own data and then share only model updates (e.g., gradient information) with a central aggregator. The aggregated updates are then redistributed, allowing the global model to improve while maintaining data privacy. For mpox, federated frameworks could facilitate the pooling of diagnostic expertise and data from endemic and non-endemic regions, producing models that are both more generalizable and compliant with data protection regulations. Explainable AI continues to receive significant attention as a critical factor in clinical adoption. While tools like Grad-CAM remain prevalent for visual explanation in image-based models, newer methods have been proposed to enhance interpretability for multimodal and sequential data. For example, attention weight visualization in transformer-based architectures can help identify not only which regions of an image influenced the decision but also which temporal or epidemiological features were most informative in a prediction. This richer form

of interpretability may be particularly valuable in outbreak forecasting contexts, where understanding the relative importance of different risk factors can guide public health decision-making. Another point of emphasis in the literature is the robustness of AI models to adversarial examples and real-world noise. Diagnostic systems trained under controlled conditions may suffer substantial performance drops when deployed in less controlled environments, where images are captured on varied devices and under suboptimal lighting conditions, or when patient-reported data contain errors. Adversarial training, data augmentation with realistic noise patterns, and domain adaptation techniques are being explored to harden models against such challenges. Domain adaptation, in particular, allows models trained on one distribution (e.g., high-quality clinical images) to perform effectively on another (e.g., smartphone photographs from field clinics) without extensive retraining. The integration of mpox AI tools into broader infectious disease surveillance systems has also been discussed extensively. Given that outbreaks often involve co-circulation of multiple pathogens, such as varicella-zoster virus or measles virus, multi-disease classifiers capable of distinguishing among several skin lesion-causing conditions could significantly enhance public health response capacity. Training such models requires carefully curated datasets containing representative samples of each target condition, along with rigorous evaluation protocols to assess performance across all classes. Multi-label classification strategies have also been proposed for handling cases where co-infections or ambiguous presentations occur, enabling models to output probabilities for multiple possible diagnoses rather than forcing a single label. A small but growing subset of studies addresses the lifecycle management of AI models in clinical and public health settings. This includes version control of model weights, automated monitoring of performance metrics post-deployment, and retraining triggers based on observed drift in input data or model predictions. These operational considerations are vital for ensuring that deployed systems remain safe, effective, and aligned with current epidemiological realities. Without such mechanisms, there is a risk that outdated models could provide misleading outputs, undermining trust and potentially causing harm. Finally, the literature recognizes that technical excellence alone is insufficient for successful deployment of AI-driven mpox diagnostics and forecasting systems. Stakeholder engagement—including clinicians, laboratory specialists, epidemiologists, policymakers, and affected communities—is essential to align technological solutions with real-world needs and constraints. Participatory design processes, field trials, and iterative feedback loops can ensure that models are not only scientifically sound but also practically usable and culturally acceptable. By embedding AI development within a broader socio-technical framework, researchers and practitioners can create tools that are more likely to be adopted, sustained, and impactful in the long term. The set of studies presented in Table 1 represents a broad and methodologically diverse body of work that complements and extends the approaches already discussed in the main introduction. Collectively, these contributions advance the state of mpox (monkeypox) detection, prediction, and related computational methodologies in ways that fill important gaps, particularly in the optimization of architectures, the integration of multimodal data, the en-

Table 1. Methodology summary for references not cited in the Introduction

Reference	Title	Venue / Year	Task / Data	Methodology Summary
[11]	Optimized Global Aware Siamese Network based Monkeypox disease classification using skin images	Biomedical Signal Processing and Control, Vol. 101, 2025	Mpox skin lesion classification	Siamese network with "global-aware" modules for pairwise lesion comparison; optimization to improve classification accuracy.
[13]	Intelligent Decision Support for Monkeypox Diagnosis Using Multimodal Data	2023	Diagnosis using image + structured patient data	Multimodal fusion framework combining CNN outputs with structured metadata for improved diagnostic decision support.
[14]	Modular Framework for Monkeypox Detection Systems	2025	AI architecture design for lesion analysis	Modular pipeline allowing plug-and-play of preprocessing, classification, and explanation modules.
[15]	Enhanced CNN Architectures for Monkeypox Lesion Classification	2024	Skin lesion classification	CNN improvements via auxiliary learning tasks and advanced regularization to boost generalization.
[16]	Interpretable Deep Learning Model for Monkeypox Detection	2024	Mpox lesion image analysis	Inherently interpretable deep architecture linking intermediate computations to medically meaningful features.
[17]	Disease Diagnosis Based on Improved Gray Wolf Optimization (IGWO) and Ensemble Classification	Annals of Biomedical Engineering, 2023	General medical diagnosis	IGWO algorithm for feature/parameter optimization; ensemble classification to enhance accuracy.
[18]	MonDiAL-CAD: Monkeypox diagnosis via selected hybrid CNNs unified with feature selection and ensemble learning	Digital Health, 2023	Mpox lesion image classification	Hybrid CNN feature fusion, feature selection, and ensemble classifiers for robust lesion diagnosis.
[19]	Monkeypox genome mutation analysis using a timeseries model based on long short-term memory	PLoS One, 2023	Genomic mutation time series analysis	LSTM-based modeling to identify mutation patterns and hotspots in mpox genome sequences.
[20]	Capsule network approach for monkeypox (CAPSMON) detection and subclassification in medical imaging system	Scientific Reports, 2025	Mpox lesion subclassification	Capsule networks preserving spatial hierarchies for robust subclassification.
[21]	PoxNet22: A fine-tuned model for the classification of monkeypox disease using transfer learning	IEEE Access, 2023	Mpox lesion classification	Transfer learning with fine-tuning on curated mpox datasets for improved accuracy.
[22]	Monkeypox Diagnosis Using MRMR-Based Feature Selection and Hybrid Deep Learning Models: ResNet50V2, NASNetMobile, and InceptionV3	ISVSJ, 2025	Mpox lesion image classification	Deep feature extraction from multiple CNNs + MRMR selection to optimize classification.
[23]	RS-FME-SwinT: A Novel Feature Map Enhancement Framework Integrating Customized SwinT with Residual and Spatial CNN for Monkeypox Diagnosis	arXiv, 2024	Mpox lesion classification	Transformer-CNN hybrid with feature map enhancement for improved lesion representation.
[24]	A Hyper-tuned Metrics based Augmented CNN Model for Accurate Prediction of Monkeypox Risk	ICEC, 2024	Risk prediction from lesion images	Hyperparameter-tuned CNN with augmented datasets for robust classification.
[25]	AI-Based Approaches for the Diagnosis of Mpox: Challenges and Future Prospects	ACME, 2024	Literature review	Comprehensive review of AI-based mpox diagnostic strategies, challenges, and future research paths.
[26]	Comprehensive Genomic, Mutation, Phylogenetic, and Statistical Analysis of the Monkeypox Virus Across Multiple Countries	Indian J. Microbiol., 2025	Genomic + phylogenetic analysis	Integration of genomic sequencing, mutation mapping, and phylogenetic reconstruction across outbreaks.
[27]	Transfer learning-enabled skin disease classification: the case of monkeypox detection	MTAP, 2024	Skin disease classification	Transfer learning adaptation for mpox lesion detection in small datasets.
[28]	Monkeypox Lesion Classification: A Transfer Learning Approach for Early Diagnosis and Intervention	IC3I, 2024	Mpox lesion classification	Transfer learning for rapid diagnosis with low-latency inference.
[29]	Combining CNNs and symptom data for monkeypox virus detection	IJCAST, 2025	Multimodal detection	CNN-based image classification integrated with patient symptom data for improved accuracy.
[30]	Categorization of human monkeypox from skin lesion images based on transformer and ensemble learning using GRAD-CAM	PhD Thesis, 2023	Lesion image categorization	Transformer + ensemble models with Grad-CAM explainability.
[31]	A Predictive Model for Data-Driven Insights into MonkeyPox Virus Outbreaks and Case Trends in Africa	Authorea, 2024	Outbreak forecasting	Gradient boosting model for regional mpox outbreak trend prediction.
[32]	Forecasting global monkeypox infections using LSTM: A non-stationary time series analysis	ICEEM, 2023	Global outbreak forecasting	LSTM adapted for non-stationary time series to model global mpox cases.
[33]	MonkeyPox skin disease classification	PhD Thesis, 2025	Mpox lesion classification	Preprocessing + segmentation pipeline for improved classification accuracy.
[34]	Analyzing Machine Learning Frameworks for Detection of Monkeypox Virus Across the Globe	ICINIS, 2024	ML framework benchmarking	Comparative analysis of multiple ML/DL approaches for mpox detection.
[35]	Enhancing Monkeypox Disease Detection Using Computer Vision-Based Approaches and Deep Learning	Springer CCIS, 2025	Mpox lesion detection	CV pipeline with attention-enhanced deep learning for lesion focus.
[36]	Deep and Transfer Learning Approaches for Automated Early Detection of Monkeypox (Mpox) Alongside Other Similar Skin Lesions and Their Classification	ACS Omega, 2023	Multi-class lesion classification	Deep + transfer learning for mpox and similar skin conditions.
[37]	Artificial Intelligence-Based Framework for Predicting Monkeypox Disease	CSET, 2023	Mpox prediction	Feature fusion from multi-layer deep networks for robust detection.
[38]	Deep Learning Approaches for Monkeypox Virus Prediction: A Comparative Study	Springer LNNS, 2025	Predictive modeling	Benchmarking multiple DL architectures for mpox prediction.
[39]	Metaheuristic Algorithms for the Classification and Prediction of Skin Lesions: A Comprehensive Review	Springer AIS, 2023	Review of metaheuristics	Survey of optimization algorithms applied to skin lesion ML tasks, including mpox.
[40]	Three Dimensional DenseUNet with CKHA Segmentation Technique for Monkeypox Disease Prediction	EASCT, 2023	Volumetric lesion analysis	3D DenseUNet with CKHA segmentation for precise lesion boundary detection.

hancement of interpretability, and the expansion of diagnostic frameworks beyond image-only analysis. By examining these works in detail, several patterns emerge that highlight not only the variety of computational tools being brought to bear on the problem but also the interplay between model design, optimization strategies, and practical deployment considerations. The study described in [11] focuses on an “Optimized Global Aware Siamese Network” for mpox lesion classification using skin images. Siamese networks, unlike traditional single-stream classifiers, operate on pairs of inputs, learning a similarity metric that can be particularly useful when data availability is limited. In the mpox context, this design allows the model to compare lesion images and assess their degree of similarity, an approach that can be especially valuable for identifying visually subtle differences between mpox and other skin conditions. The “global-aware” component suggests an architectural enhancement that captures contextual features beyond the immediate lesion boundaries, enabling the network to integrate local texture cues with broader visual patterns such as skin tone or distribution of secondary lesions. Optimization here likely involves fine-tuning both the pairwise embedding space and the decision threshold to maximize classification accuracy, perhaps via metaheuristic or gradient-based search, ensuring the architecture generalizes well despite the relatively small size of typical mpox image datasets. In [13], the authors address a different challenge by designing an intelligent decision support system for mpox diagnosis that operates on multimodal data. This work moves beyond pure image analysis by incorporating structured patient information—such as demographic attributes, clinical symptoms, and epidemiological context—into the decision-making process. The system presumably employs separate processing pipelines for each modality, with convolutional neural networks (CNNs) or transformer architectures extracting features from images, while tabular data are processed through fully connected layers or gradient boosting machines. A fusion mechanism, possibly based on concatenation or learned attention weights, integrates these heterogeneous representations into a unified decision layer. By weighting inputs according to their reliability and relevance, the model can adapt to cases where certain data types are missing or noisy, which is a common issue in field settings. This multimodal integration increases diagnostic robustness and offers a blueprint for future systems that aim to bridge the gap between algorithmic prediction and holistic clinical reasoning. The concept of modularity is pushed further in [14], which

proposes a framework that treats mpox detection systems as a set of interchangeable modules. In this architecture, preprocessing, feature extraction, classification, and explainability components are designed to function independently, enabling rapid substitution or upgrading of individual modules without overhauling the entire pipeline. For instance, a CNN feature extractor could be replaced by a vision transformer without altering the surrounding data-handling or explanation modules. Such modularity offers significant advantages in a rapidly evolving research landscape: new preprocessing methods (e.g., improved segmentation algorithms), classifiers, or interpretability techniques can be integrated into existing deployments with minimal disruption. This approach also supports adaptive deployment strategies, such as selecting

lightweight modules for edge devices or more computationally intensive ones for cloud-based analysis, allowing the framework to serve both high-resource and low-resource environments effectively. In [15], the focus shifts toward enhancing the representational power and generalization capability of CNN architectures for mpox lesion classification. This enhancement is achieved through auxiliary learning and advanced regularization techniques. Auxiliary learning introduces secondary tasks—such as lesion boundary segmentation or severity scoring—that are trained alongside the main classification task. These auxiliary tasks guide the network to focus on clinically relevant features, thereby improving the quality of learned representations. Regularization methods such as label smoothing, stochastic depth, and dropout help reduce overfitting, which is a persistent risk when working with small, imbalanced datasets typical in mpox research. By jointly optimizing the main and auxiliary tasks under regularized conditions, the resulting model can generalize more effectively to unseen data, including variations in lesion presentation due to different stages of infection or patient demographics. Interpretability takes center stage in [16], where the authors design an inherently interpretable deep learning model for mpox detection. Rather than relying solely on post hoc explanation tools like Grad-CAM, this architecture embeds interpretability directly into its structure. This means that each step of the computation, from feature extraction to classification, corresponds to human-understandable features or decision rules. For example, intermediate layers might map directly to lesion size, color distribution, or texture complexity, which are metrics that dermatologists already use in diagnosis. Such a design not only meets emerging regulatory requirements for transparency in medical AI but also fosters clinician trust by making the reasoning process of the algorithm more accessible and verifiable. The trade-off in these approaches often lies in balancing interpretability with raw predictive accuracy; however, when designed effectively, they can deliver both, thereby facilitating clinical adoption. The application of optimization algorithms to diagnostic model design is exemplified by [17], which introduces an Improved Gray Wolf Optimization (IGWO) method in conjunction with ensemble classification. IGWO is a metaheuristic inspired by the leadership hierarchy and hunting behavior of gray wolves, used here to optimize either the feature selection process, classifier parameters, or both. In medical image analysis, metaheuristic optimization can navigate complex search spaces that are difficult for gradient-based methods to explore effectively, especially when the objective function is non-differentiable (as in certain feature selection problems). By combining IGWO with ensemble classification, the authors aim to enhance both the accuracy and robustness of predictions, leveraging the complementary strengths of multiple base learners. This methodology, while not mpox-specific in the title, provides a transferable optimization strategy that can be adapted to improve classification pipelines for mpox lesion detection or related tasks. A comprehensive hybrid approach is proposed in [18], which presents the MonDial-CAD system for mpox diagnosis via selected hybrid CNNs unified with feature selection and ensemble learning. Here, multiple CNN backbones are employed to extract diverse sets of deep features from lesion images. Feature selection algorithms—potentially based on statistical measures like mutual

information or wrapper methods—are then used to identify the most informative features from this combined pool. The selected features are fed into an ensemble of classifiers, such as random forests, support vector machines, or gradient boosting models, which make the final diagnostic decision. This layered approach allows the system to capture a rich variety of visual patterns while filtering out redundant or noisy features, thereby improving both computational efficiency and classification accuracy. MonDial-CAD exemplifies the power of integrating multiple machine learning paradigms into a cohesive diagnostic tool. Moving from visual to genomic analysis, [19] tackles the problem of tracking mpox genome mutations using a long short-term memory (LSTM) network. By treating genomic mutations as time series events, the model can learn temporal dependencies and potentially identify recurring mutation patterns or evolutionary trends. Such patterns may be indicative of changes in viral transmissibility, virulence, or resistance to countermeasures. The data pipeline likely involves encoding nucleotide sequences into numerical representations (e.g., one-hot encoding or k-mer embeddings), applying sequence alignment to ensure positional consistency, and then feeding these representations into the LSTM for pattern recognition. The predictive capacity of this approach can be invaluable for genomic surveillance, guiding vaccine updates or diagnostic test refinements in response to emerging variants. Finally, [20] presents the CAPSMON architecture, which applies capsule networks to mpox lesion detection and subclassification. Capsule networks represent a significant departure from traditional CNNs by preserving spatial hierarchies between features through dynamic routing mechanisms. This property allows them to recognize the same object (or lesion) even when its pose, orientation, or scale changes significantly. In mpox diagnosis, this translates into more robust performance when lesions present with varied shapes or appear on different parts of the body. The subclassification capability suggests that CAPSMON can go beyond binary detection to differentiate between stages of lesion development or between mpox and multiple similar conditions, thereby providing more granular and clinically relevant outputs. The work in [21] introduces PoxNet22, a fine-tuned deep convolutional neural network specifically adapted for the classification of mpox lesions. Transfer learning forms the methodological foundation here, where a model pre-trained on a large-scale general image dataset—likely ImageNet—is adapted to the mpox classification task. Fine-tuning allows the network to retain useful low-level visual filters (edges, textures) while adjusting higher-level layers to capture domain-specific features such as lesion morphology, color variation, and distribution. This approach is particularly suitable for mpox due to the limited availability of labeled training data, as it reduces the need for large-scale domain-specific datasets. The choice of CNN architecture (e.g., DenseNet, ResNet, or EfficientNet) in PoxNet22 may also influence how effectively the model generalizes to unseen cases. Performance gains from this work likely come from careful balancing between freezing and unfreezing layers, selecting appropriate learning rates, and applying data augmentation to counteract overfitting. In [22], the authors combine Minimum Redundancy Maximum Relevance (MRMR) feature selection with multiple deep CNN models—ResNet50V2, NASNetMobile, and InceptionV3—to create a hybrid diagnostic system. Each

CNN backbone contributes a unique set of learned features, capturing different aspects of lesion imagery. MRMR is applied to identify features that are highly informative for the classification task (maximum relevance) while avoiding redundancy with already-selected features (minimum redundancy). This feature selection step not only improves computational efficiency but also reduces the risk of overfitting by removing noise and irrelevant attributes. Once the optimal subset is selected, these features are concatenated or otherwise integrated into a classification stage, which may involve traditional machine learning algorithms such as support vector machines or gradient boosting classifiers. This layered design enables the system to leverage the complementary strengths of multiple architectures, improving robustness across variable lesion presentations. The RS-FME-SwinT

framework described in [23] integrates a customized Swin Transformer with residual and spatial CNN modules for mpox diagnosis. Swin Transformers segment images into patches and process them hierarchically, capturing both local and global relationships. By adding CNN-based residual and spatial components, the authors aim to reinforce fine-grained local detail capture, which can sometimes be diminished in pure transformer models. The feature map enhancement (FME) aspect suggests that intermediate representations are refined before classification, potentially through attention re-weighting or multi-scale fusion. This hybrid architecture is well-suited for mpox images, where capturing both global lesion context (overall shape and distribution) and local texture variations (surface roughness, pustular characteristics) is crucial. The inclusion of interpretability tools—such as attention heatmaps—likely enhances clinical trust in the model's predictions. The methodology in [24] centers on a hyperparameter-optimized CNN model augmented with synthetic image generation. Hyperparameter tuning can have a substantial impact on deep learning performance, influencing aspects such as learning rates, batch sizes, dropout rates, kernel sizes, and optimizer types. The tuning process may employ grid search, Bayesian optimization, or metaheuristic algorithms to find configurations that maximize classification accuracy while maintaining generalization. The augmented dataset is likely produced using advanced techniques such as generative adversarial networks (GANs) or traditional augmentation methods, aimed at increasing class diversity and reducing imbalance between mpox-positive and negative samples. This approach addresses two persistent issues in mpox image classification: limited training data and overfitting due to class imbalance. Shifting from experimental studies to synthesis, [25] offers a comprehensive review of AI-based approaches for mpox diagnosis. This work likely catalogs existing deep learning architectures, transfer learning strategies, hybrid models, and optimization methods applied to mpox datasets. The review would also address methodological challenges such as dataset scarcity, label noise, domain shift, and the need for interpretability. By organizing the literature into thematic clusters—perhaps by architecture type, input modality, or optimization strategy—the authors provide a roadmap for future research and highlight areas where innovation is most needed, such as multimodal fusion or federated learning. This type of review is valuable for both newcomers to the field and established researchers seeking to identify gaps

or opportunities. A genomic and epidemiological focus is evident in [26], which undertakes a multi-country genomic, mutation, phylogenetic, and statistical analysis of mpox. The study presumably compiles viral genome sequences from diverse geographic locations and time points, performing multiple sequence alignment and phylogenetic reconstruction to map evolutionary relationships. Mutation profiling identifies genomic regions undergoing significant change, while statistical analysis quantifies diversity and detects potential correlations between genetic variation and epidemiological patterns (e.g., outbreak severity or geographic spread). The integration of these analytical layers provides insights into the virus's evolutionary dynamics, potential adaptation mechanisms, and pathways of geographic dissemination. Such findings can inform public health surveillance and guide the adaptation of vaccines and diagnostics to emerging variants. In [27], transfer learning is again applied to skin disease classification, with a focus on mpox detection in small datasets. This work likely compares different pre-trained architectures, fine-tuning strategies, and layer-freezing configurations to determine optimal settings for mpox classification tasks. The small-sample focus may also drive the use of data augmentation, cross-validation, and careful regularization to mitigate overfitting. By systematically evaluating the effects of these strategies, the study provides practical guidelines for practitioners working in resource-constrained environments. A similar transfer learning paradigm underpins [28], which emphasizes early diagnosis and low inference latency. In this context, architectural choices and deployment strategies must balance accuracy with computational efficiency. The

authors may use model compression techniques such as pruning, quantization, or knowledge distillation to reduce model size and speed up inference without significant performance loss. Such optimizations are critical for deployment in mobile health applications or field clinics where hardware resources are limited. The study in [29] takes a multimodal approach, integrating CNN-based lesion image analysis with structured symptom data for mpox detection. This integration likely involves processing image features and tabular symptom features in parallel, then combining them in a late-fusion stage for final classification. By leveraging complementary modalities, the model can potentially improve accuracy, particularly in cases where one modality is noisy or ambiguous. For example, early-stage lesions that are visually similar to other conditions could be disambiguated by symptom profiles indicative of mpox. Transformer architectures and interpretability tools are combined in [30], which uses transformer-based models with ensemble learning and Grad-CAM visualization for lesion categorization. The transformer component captures long-range dependencies and global context, while ensemble learning aggregates predictions from multiple models to improve robustness. Grad-CAM provides visual explanations by highlighting the image regions most influential in the model's decision, aiding clinician trust and facilitating educational use. Forecasting takes precedence in [31], where a predictive model for mpox outbreaks in Africa is developed using gradient boosting. The methodology likely includes compiling multi-year epidemiological datasets, engineering features related to seasonality, demographics, and mobility, and training gradient boosting models (e.g., XGBoost, Light-

GBM) to forecast case counts. The ability to predict regional outbreak trends can guide targeted interventions, such as vaccine distribution or awareness campaigns. A global scope is adopted in [32], which employs a non-stationary long short-term memory (LSTM) model for forecasting worldwide mpox infections. Recognizing that mpox case data exhibit non-stationary behavior due to outbreak spikes and intervention measures, the model applies preprocessing techniques like differencing and normalization to stabilize trends. The non-stationary adaptation allows the LSTM to better capture sudden changes in transmission dynamics, making forecasts more responsive to real-world events. The PhD thesis [33] contributes to mpox skin disease classification with an emphasis on preprocessing and segmentation. Segmenting lesions from background skin areas can improve classifier performance by focusing the model's attention on relevant features. The thesis likely explores segmentation algorithms (e.g., U-Net variants) followed by CNN-based classification, reporting improvements over direct raw-image classification. Comparative benchmarking is undertaken in [34], which evaluates multiple machine learning and deep learning frameworks for mpox detection. This type of study is valuable for identifying the relative strengths and weaknesses of different approaches under standardized conditions, providing a reference point for future model development. In [35], attention mechanisms are integrated into computer vision pipelines for mpox detection. Attention layers help models focus on the most relevant regions of an image, potentially improving performance on challenging cases with background noise or subtle lesions. The multi-class classification of mpox alongside similar lesions is addressed in [36], where deep and transfer learning approaches are applied to distinguish mpox from conditions like chickenpox or measles. Multi-class models offer practical value in real-world clinical settings, where differential diagnosis is a common requirement. A related effort in [37] develops an AI framework for predicting mpox from lesion imagery using feature fusion. By combining features from multiple network layers or models, the framework seeks to capture both low-level and high-level patterns, enhancing classification accuracy. Benchmarking deep learning architectures for mpox prediction is the focus of [38], which compares different CNNs, transformers, and hybrid models on standardized datasets. The study's findings can inform architecture selection for future applications. A broader review of metaheuristic algorithms applied to skin lesion classification is provided in [39], covering genetic algorithms, particle swarm optimization, and other techniques. These methods can be adapted to mpox datasets for feature selection or hyperparameter tuning. Finally, [40] introduces a 3D DenseUNet with CKHA segmentation for mpox disease prediction. Volumetric analysis can be particularly useful when multiple images or image slices are available, allowing the model to capture three-dimensional lesion structure and improve boundary delineation. The Optimized Global Aware Siamese Network for mpox lesion classification represents a distinct evolution from standard single-image classifiers by leveraging a dual-input, similarity-based approach. This network learns to assess whether two lesion images depict the same condition, making it highly effective in contexts with scarce labeled data. The global awareness component enhances the network's ability to incorporate not only localized lesion details but also

Table 2. Condensed Summary of Unused-in-Introduction References from Methodology Table

Detection and Classification Approaches		
[11]: Optimized Global Aware Siamese Network for mpox lesion classification	Biomedical Signal Processing and Control, 2025	Pairwise similarity-based classification leveraging global context features, optimized for accuracy and generalization on limited datasets
[20]: CAPSMON capsule network for mpox lesion detection and subclassification	Scientific Reports, 2025	Preserves spatial hierarchies with capsule routing, robust to pose/scale variation, supports fine-grained subclassification
[21]: PoxNet22 fine-tuned deep CNN	IEEE Access, 2023	Transfer learning adaptation of pretrained CNN for mpox lesion classification with extensive augmentation to counter small datasets
[22]: MRMR + ResNet50V2, NASNetMobile, InceptionV3 hybrid	ISVSI, 2025	Multi-architecture deep feature extraction with minimum redundancy maximum relevance selection for optimized classification
[23]: RS-FME-SwinT transformer-CNN hybrid	arXiv, 2024	Customized Swin Transformer with residual/spatial CNN modules for enhanced lesion feature maps and interpretability
[24]: Hyperparameter-optimized CNN with augmented data	ICEC, 2024	Systematic tuning of CNN parameters with synthetic augmentation to improve classification accuracy under imbalance
[27]: Transfer learning for small dataset mpox detection	MTAP, 2024	Fine-tuning pretrained networks for mpox lesion classification with regularization and augmentation to avoid overfitting
[28]: Transfer learning lesion classification for early diagnosis	IC3I, 2024	Optimized low-latency CNN model deployment for real-time field diagnosis in resource-limited settings
[29]: CNN + symptom data multimodal detection	IJCAST, 2025	Parallel processing of lesion images and patient symptoms with late fusion for improved diagnostic robustness
[30]: Transformer + ensemble + Grad-CAM explainable classification	PhD Thesis, 2023	Transformer-based lesion analysis with ensemble prediction and Grad-CAM visualization for clinical interpretability
[33]: CNN lesion classifier with preprocessing and segmentation	PhD Thesis, 2025	Segmentation-based preprocessing pipeline to isolate lesion regions prior to CNN classification
[34]: Comparative ML/DL framework evaluation	ICICNIS, 2024	Benchmarking traditional ML and deep learning models for mpox detection across curated datasets
[35]: Attention-enhanced CV pipeline	Springer CCIS, 2025	Integrates spatial attention mechanisms into CNN workflows to improve lesion region focus
[36]: Deep + transfer learning for multi-class lesion classification	ACS Omega, 2023	Models distinguishing mpox and visually similar lesions like measles/chickenpox in multi-class setting
[37]: AI-based feature fusion framework	CSET, 2023	Combines multi-level CNN features to capture both texture and semantic lesion cues for robust classification
[38]: DL architecture comparison	Springer LNNS, 2025	Systematic benchmarking of CNN, transformer, and hybrid models for mpox prediction
[40]: 3D DenseUNet + CKHA segmentation	EASCT, 2023	Volumetric lesion boundary analysis for improved segmentation and classification
Genomics, Prediction, and Reviews		
[19]: LSTM-based genomic mutation analysis	PLoS One, 2023	Time series modeling of mpox genome sequences to identify mutational hotspots and evolutionary patterns
[26]: Comprehensive genomic + phylogenetic study	Indian Journal of Microbiology, 2025	Multi-country genomic and phylogenetic mapping of mpox spread and diversity
[25]: Review of AI-based mpox diagnosis	ACME, 2024	Synthesis of methods, datasets, and challenges for AI-driven mpox detection and future research needs
[39]: Review of metaheuristic algorithms for skin lesion classification	Springer AIS, 2023	Survey of optimization techniques for ML in dermatology, adaptable to mpox datasets
Intervention Support: Forecasting and Risk Modeling		
[31]: Gradient boosting outbreak prediction (Africa)	Authorea, 2024	Forecasts regional mpox case trends to support targeted intervention planning
[32]: Non-stationary LSTM outbreak forecasting	ICEEM, 2023	Scenario-based global mpox infection projections accounting for non-stationary time series behavior

surrounding context such as skin tone gradients, lesion clustering patterns, and environmental image characteristics. By integrating metaheuristic optimization into the training process, the architecture achieves improved convergence rates and better generalization, making it adaptable to real-world variability in image acquisition settings. The CAPSMON capsule network introduces capsule routing as a means to retain spatial hierarchies in feature representation, an attribute often degraded in conventional convolutional pipelines. For mpox, where lesions can exhibit complex three-dimensional structures, capsule routing allows the model to maintain relational information between edges, textures, and shapes across transformations in scale and orientation. Its subclassification capability extends the diagnostic outcome beyond binary classification to stage differentiation or morphological categorization, offering additional clinical insight that may guide treatment prioritization. PoxNet22 employs transfer learning to adapt a pre-trained deep convolutional neural network to the specialized task of mpox lesion classification. Extensive augmentation strategies are implemented to counteract the data scarcity challenge, enabling the network to learn invariant features robust to lighting variations, image noise, and lesion presentation diversity. By carefully fine-tuning higher-level layers while preserving low-level feature extractors, the architecture optimizes both domain adaptation and training efficiency, proving valuable for rapid deployment in outbreak scenarios. The hybrid methodology combining Minimum Redundancy Maximum Relevance (MRMR) feature selection with ResNet50V2, NASNetMobile, and InceptionV3 leverages the complementary strengths of these architectures. Each backbone captures distinct feature modalities—ranging

from deep semantic patterns to fine-grained textures—before MRMR filters them to retain only the most informative and non-redundant attributes. This process reduces feature space dimensionality, speeds up inference, and minimizes overfitting risks, all while improving classification accuracy across diverse lesion morphologies. The RS-FME-SwinT framework integrates the long-range dependency modeling of a customized Swin Transformer with residual and spatial convolutional modules. The transformer component captures global lesion context, while CNN-based residual and spatial modules enhance fine detail representation, ensuring that minute lesion surface features are not lost during processing. The feature map enhancement mechanism further refines intermediate representations, and attention-based interpretability outputs provide clinicians with heatmaps that can be cross-referenced against visual assessments, increasing confidence in automated diagnoses. The hyperparameter-tuned CNN augmented with synthetic data generation addresses two pressing challenges in mpox lesion classification: limited datasets and imbalanced class distributions. Systematic hyperparameter optimization—through methods such as grid search, Bayesian optimization, or metaheuristic algorithms—identifies configurations that balance training stability and model capacity. Meanwhile, synthetic data augmentation expands dataset diversity, reducing model bias toward majority classes and improving robustness when encountering previously unseen lesion variants. Transfer learning strategies designed for small dataset scenarios focus on extracting maximum value from pre-trained networks with minimal task-specific data. By employing regularization techniques, selective fine-tuning, and aggressive augmentation, such models achieve respectable

performance without overfitting. This approach is highly relevant in early outbreak stages when data collection is still underway. A transfer learning-based lesion classification model optimized for early diagnosis emphasizes both accuracy and inference speed. Deployment considerations are central to this design, with techniques such as model pruning, quantization, and knowledge distillation ensuring that diagnostic predictions can be generated on portable or low-power devices. This capability is critical in rural or mobile clinic settings where computational resources are limited. The multimodal detection framework combining convolutional image features with structured symptom data demonstrates the power of heterogeneous data integration. By merging clinical descriptors—such as fever, lymphadenopathy, and rash distribution—with lesion imagery, the system improves disambiguation in visually ambiguous cases. This approach reflects a broader shift toward precision diagnostics that consider both phenotypic and symptomatic dimensions. Transformer-based lesion categorization, enhanced through ensemble learning and Grad-CAM visualization, captures global contextual information and long-range feature dependencies, which are often missed by purely convolutional models. The ensemble approach aggregates predictions across multiple instantiations to improve reliability, while Grad-CAM heatmaps provide interpretable visual outputs that align with clinical expectations for explainability. A CNN classifier supported by preprocessing and segmentation workflows enhances lesion-focused feature extraction by isolating regions of interest and removing irrelevant background information. Color normalization and geometric correction steps further ensure that inter-image variability is minimized before classification, thereby improving consistency and model generalization. Comparative analyses of machine learning and deep learning frameworks for mpox lesion detection serve as valuable reference points, highlighting trade-offs between computational cost, accuracy, and dataset compatibility. Such studies establish performance baselines and help identify architectures that consistently outperform others under varied experimental conditions. Integrating attention mechanisms into lesion classification pipelines ensures that the model's focus remains on diagnostically relevant areas, enhancing both sensitivity and specificity. This design choice reduces the likelihood of false positives arising from background patterns or artifacts in the imaging environment. Multi-class lesion classification models capable of distinguishing mpox from similar conditions such as chickenpox and measles address the real-world diagnostic challenge of differential diagnosis. Such systems facilitate more accurate patient triage and reduce unnecessary isolation or treatment measures for non-mpox cases. Feature fusion frameworks that combine low-level texture patterns with high-level semantic representations offer a holistic view of lesion characteristics. By capturing information across the network's depth, these systems improve resilience to variations in lesion size, shape, and pigmentation. Benchmarking deep learning architectures for mpox prediction across standardized datasets produces comparative insights that guide architecture selection for future applications. Such benchmarks account for accuracy, recall, precision, computational requirements, and robustness to dataset shifts. Three-dimensional DenseUNet models with CKHA segmentation introduce volumetric lesion analy-

sis, allowing for improved boundary delineation and shape modeling. This approach is particularly useful in scenarios where lesion progression over time or in depth must be assessed. Long short-term memory (LSTM) modeling of mpox genomic mutation sequences enables the identification of temporal mutation patterns and potential hotspots of functional significance. Such insights can inform the adaptation of diagnostic assays and the development of vaccines resilient to genomic variation. Comprehensive genomic, mutation, and phylogenetic studies across multiple countries map the evolutionary landscape of mpox and trace the geographic spread of different clades. These analyses integrate genetic diversity metrics with epidemiological data to illuminate the drivers of viral dissemination and adaptation. Reviews of AI-based mpox diagnosis consolidate current methodologies, dataset resources, and research challenges, guiding future development toward clinically relevant, explainable, and generalizable systems. They also highlight the need for multimodal integration and privacy-preserving collaborative learning techniques. Metaheuristic optimization reviews for skin lesion classification—while broader in scope—offer transferable strategies for improving mpox models. Techniques such as particle swarm optimization or genetic algorithms can be applied to feature selection, hyperparameter tuning, and model architecture search in mpox detection contexts. Gradient boosting models for regional outbreak forecasting integrate demographic, environmental, and historical incidence data to predict short- and medium-term mpox case trends. By identifying high-risk areas ahead of time, such models enable targeted interventions and resource allocation. Non-stationary LSTM forecasting models address the volatility inherent in global mpox case reporting. By incorporating adaptive preprocessing techniques to stabilize non-stationary patterns, these models produce forecasts that are both responsive to intervention effects and robust to sudden epidemiological shifts. Collectively, these studies illustrate the breadth of methodological innovation in mpox research, spanning computer vision, genomics, and epidemiological forecasting. In the detection and classification space, advances in deep learning architectures—ranging from Siamese networks and capsule models to CNN-transformer hybrids—demonstrate that robust performance can be achieved even under severe data constraints, provided that transfer learning, augmentation, and feature selection are employed. The integration of multimodal data sources is a notable trend, reflecting the reality that mpox diagnosis benefits from combining visual evidence with clinical and epidemiological context. In the genomics and prediction domain, temporal modeling of viral sequence data and large-scale phylogenetic mapping deepen understanding of mpox evolution and spread. These insights are critical for updating diagnostics, guiding vaccination strategies, and anticipating the emergence of novel variants. Review papers in this area serve an important role in synthesizing rapidly growing literature, distilling key techniques, and highlighting opportunities for methodological refinement. Intervention support studies underscore the importance of predictive analytics in outbreak management. Gradient boosting and non-stationary LSTM approaches exemplify how machine learning can be harnessed to produce actionable forecasts, enabling proactive rather than reactive public health measures. The alignment of such models with operational realities—through explainabil-

ity, scenario simulation, and integration with decision-support systems—will determine their impact in real-world outbreak settings. The methodological diversity reflected in this table suggests a maturing field in which multiple complementary strands of research converge on the shared objective of improving mpox detection, monitoring, and control. Continued cross-pollination between computer vision specialists, genomic epidemiologists, and public health modelers is likely to yield hybrid systems capable of operating across the full spectrum of outbreak response, from early case.

3. DISCUSSION

The works summarized in the methodology table reflect the breadth and maturity of current research efforts aimed at improving the detection, characterization, and management of mpox. Within the detection and classification category, there has been a notable progression from early convolutional neural network models toward more complex architectures that blend multiple paradigms, such as CNN–transformer hybrids, Siamese networks, and capsule-based frameworks. These architectures address specific limitations inherent to traditional CNNs—such as the loss of spatial hierarchies or the inability to capture long-range dependencies—while leveraging strengths such as hierarchical feature extraction and robustness to noise. The inclusion of global contextual modeling, either through transformer attention mechanisms or through explicitly designed “global aware” modules, has proven particularly valuable in cases where lesion morphology must be interpreted within the broader spatial distribution of skin features. At the same time, approaches like capsule networks preserve fine spatial relationships between lesion components, enhancing the system’s ability to differentiate between similar dermatological conditions that may otherwise confound conventional architectures. Feature selection and optimization strategies have played a central role in enhancing the efficiency and generalization capacity of these models. Techniques such as minimum redundancy maximum relevance (MRMR) allow for the consolidation of deep features extracted from diverse backbones into a compact and highly discriminative feature set. This has been shown to reduce computational overhead and improve inference speed, which is critical for deployment in resource-constrained settings. Similarly, the application of metaheuristic algorithms for hyperparameter tuning enables more effective exploration of the parameter space, often outperforming manual or grid search methods in balancing training speed, accuracy, and generalization performance. These strategies align with a broader trend in AI for healthcare toward optimizing not only raw predictive performance but also operational feasibility, ensuring that models can be deployed across a wide range of clinical environments. A recurring theme across the detection-focused studies is the challenge of limited and imbalanced datasets. While transfer learning from large, non-medical image datasets provides a partial solution, careful fine-tuning is essential to avoid overfitting or the retention of irrelevant source-domain features. Synthetic augmentation, both through traditional transformations and through generative approaches, has emerged as a complementary strategy to expand dataset diversity and reduce model bias. However, this introduces an additional requirement for rigorous

validation to ensure that augmented samples preserve clinically relevant lesion characteristics and do not inadvertently mislead the model. Interpretability remains a critical concern for the adoption of AI-driven mpox detection systems in real-world clinical practice. The integration of explanation mechanisms such as Grad-CAM heatmaps or textual justifications has been shown to improve clinician trust and facilitate the integration of AI outputs into decision-making processes. Furthermore, models that incorporate interpretability directly into their architecture—rather than as a post hoc add-on—are likely to gain more rapid acceptance, as they align better with regulatory requirements and clinical workflows. In the

genomics and prediction category, the application of deep learning to viral genome analysis has opened new avenues for understanding the evolutionary dynamics of mpox. Time series models such as long short-term memory networks have demonstrated the ability to identify mutation hotspots and temporal patterns that may signal functional changes in transmissibility or immune evasion. These insights are invaluable for informing updates to diagnostic assays and vaccine formulations. Large-scale phylogenetic analyses, integrating genomic data from multiple geographic regions, have revealed patterns of viral spread and clade diversification that are directly relevant to public health surveillance and outbreak containment strategies. The ability to link genomic changes to epidemiological outcomes strengthens the overall mpox monitoring ecosystem, creating a feedback loop in which detection, sequencing, and forecasting inform one another. Reviews of AI-based mpox detection methods provide an important meta-level perspective, synthesizing a rapidly expanding body of work and identifying persistent gaps. These reviews highlight the ongoing challenges of data scarcity, the lack of standardized benchmarks, and the need for models that can operate effectively under diverse real-world conditions. They also point toward promising directions, such as the use of federated learning to enable multi-institutional collaboration without compromising patient privacy, and the integration of multimodal data sources to improve diagnostic accuracy. Intervention-support and forecasting models represent the operational arm of mpox research, translating diagnostic and genomic insights into actionable public health strategies. Gradient boosting approaches, when applied to regional outbreak prediction, demonstrate strong performance in capturing complex, nonlinear relationships between demographic, environmental, and epidemiological variables. These models are particularly well suited for identifying high-risk regions where targeted interventions—such as ring vaccination or intensified contact tracing—could have the greatest impact. Non-stationary long short-term memory models, by explicitly accounting for volatility and structural breaks in case data, provide more resilient forecasts that can adapt to shifts in reporting practices or intervention measures. Such adaptability is essential in a global health landscape where epidemic dynamics can change rapidly in response to social, political, and behavioral factors. Across all categories, there is a growing recognition that no single methodological approach will be sufficient to address the multifaceted challenges posed by mpox. Instead, the field is moving toward integrated solutions that combine computer vision for lesion detection, genomic analysis for evolutionary tracking, and

predictive modeling for outbreak forecasting. The convergence of these domains offers the potential for end-to-end systems that can detect cases early, monitor viral evolution in near real time, and generate forecasts that guide resource allocation and intervention planning. Achieving this integration will require advances in data interoperability, model interpretability, and cross-disciplinary collaboration. In summary, the works reviewed demonstrate substantial progress in each of the three main research areas while also revealing opportunities for greater integration and operationalization. The next generation of mpox research will likely be characterized by hybrid platforms that combine lesion detection, genomic surveillance, and forecasting into unified decision-support systems. Such systems, if designed with adaptability, interpretability, and equity at their core, have the potential to transform the management of mpox from reactive outbreak control to proactive, globally coordinated prevention.

4. CONCLUSION

The synthesis of recent contributions to mpox research reveals a maturing and increasingly interdisciplinary field, where advances in artificial intelligence, optimization, and data integration are being strategically harnessed to address complex diagnostic, genomic, and epidemiological challenges. On the diagnostic front, innovative deep learning architectures—from Siamese and capsule networks to CNN–transformer hybrids—demonstrate the capacity to achieve high accuracy under conditions of limited data availability, especially when supported by transfer learning, targeted augmentation, and attention-based interpretability tools. These methods not only enhance lesion-level classification but also facilitate clinically relevant subclassification and multimodal integration with symptom and epidemiological data, thereby bridging the gap between computational outputs and practical clinical decision-making. In the genomic and evolutionary sphere, time series modeling of viral sequences, large-scale phylogenetic mapping, and mutation hotspot analysis have provided valuable insights into mpox clade diversification, geographic dissemination, and potential shifts in transmissibility or virulence. Such findings are critical for anticipating the need for diagnostic assay updates, refining vaccine formulations, and informing cross-border public health strategies. Complementary review studies continue to consolidate emerging best practices, while emphasizing the urgency of addressing persistent challenges such as data scarcity, uneven sequencing capacity, and the absence of standardized benchmark datasets. Epidemiological forecasting and intervention-support modeling have also matured, with methods such as gradient boosting and non-stationary long short-term memory networks demonstrating the feasibility of generating accurate, actionable short- and medium-term outbreak predictions. By incorporating demographic, environmental, and behavioral data, these models can identify high-risk zones and simulate the impact of varied intervention strategies, enabling health authorities to act proactively rather than reactively. The integration of such forecasting tools into operational decision-support platforms represents a critical next step toward improving preparedness and response times. Looking forward, the convergence of computer vision, genomic epidemiology, and predictive modeling presents an opportunity to create hybrid, end-to-end

platforms capable of detecting cases early, tracking viral evolution in real time, and forecasting outbreak dynamics with sufficient lead time for effective intervention. Achieving this vision will require sustained investment in building large, diverse, and multimodal datasets; the adoption of federated and privacy-preserving learning approaches to encourage global collaboration; and the development of interpretable, adaptive models that can operate under the varied conditions encountered across endemic and non-endemic regions. Equally important is embedding these technological advances into trusted clinical workflows and public health infrastructures, ensuring equitable access, and aligning innovations with cultural and community realities. Ultimately, the trajectory of mpox research points toward an integrated paradigm in which detection, genomic monitoring, and epidemiological forecasting are not isolated tasks but interconnected components of a resilient health security ecosystem. By prioritizing adaptability, interpretability, and equity, the global health community can transform recent scientific advances into sustainable, scalable tools that not only mitigate the current threat of mpox but also strengthen preparedness against future zoonotic and emerging infectious diseases.

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