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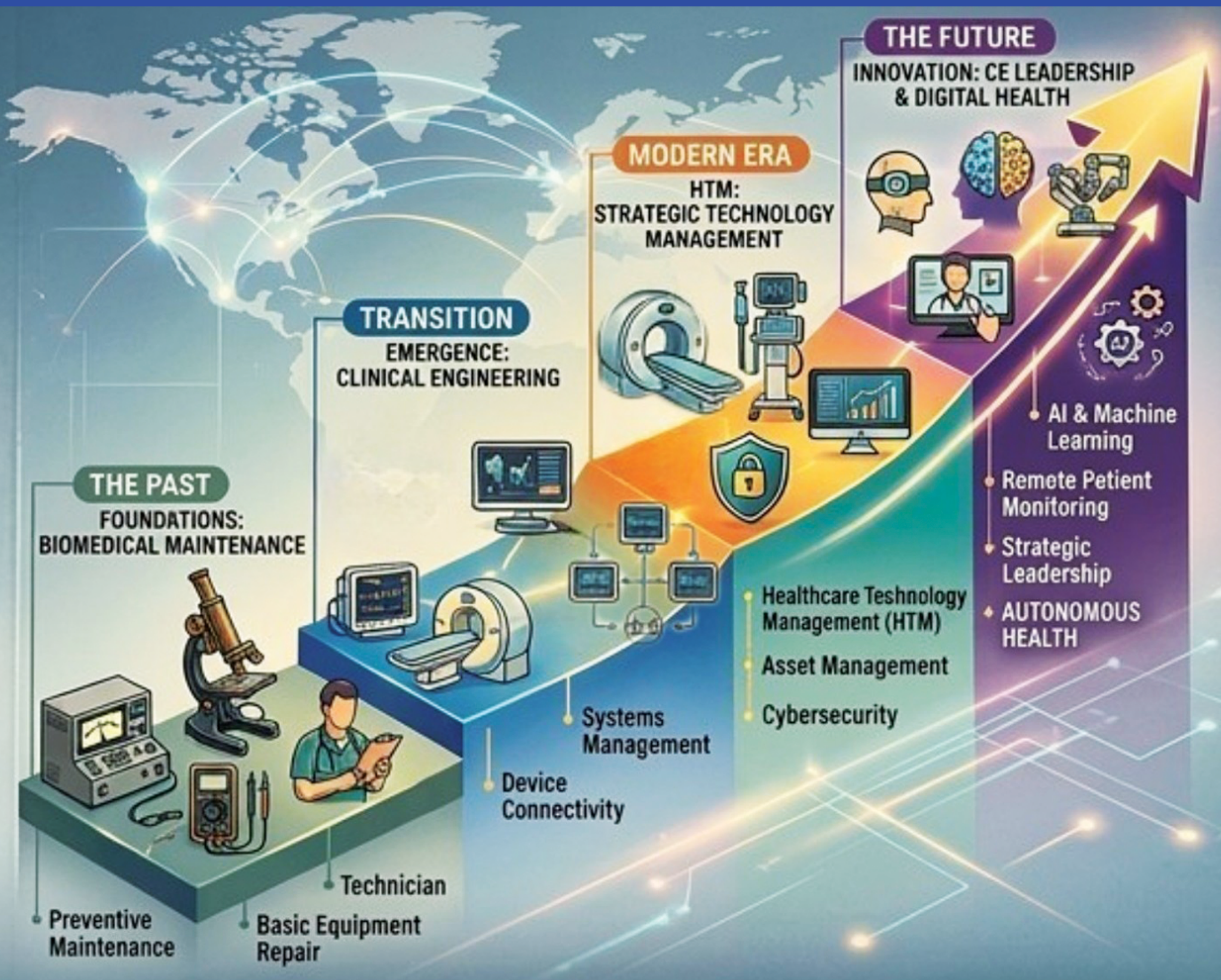

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Editor's Corner

The Invisible Risk in Healthcare Technology: Decisions Made Before First Use

The growing dependence of healthcare systems on increasingly complex technologies has become a defining feature of modern care. Medical devices, intelligent systems, and integrated infrastructures support clinical decisions, expand diagnostic capabilities, and enable life-saving interventions every day.

In this context, clinical engineering plays a central role — not merely as technical support, but as a guardian of safety, performance, and reliability throughout the entire lifecycle of healthcare technologies.

However, a critical dimension remains underexplored in global discussions:

the risk that originates before a technology is ever used.

Traditionally, risks associated with healthcare technologies are analyzed through device failures, adverse events, or maintenance-related issues. While these aspects are essential, they represent only part of the problem.

A more fundamental question must be considered:

What if the failure is not in the device, but in the decision that placed it there?

Technical decisions made in the earliest phases — including specification, selection, procurement, and maintenance strategy definition — shape the behavior of technologies throughout their lifecycle. These decisions directly influence patient safety, regulatory compliance, and the long-term sustainability of healthcare systems.

To illustrate this point, consider a common situation across many healthcare systems worldwide: glucose monitoring technologies provided to patients for daily self-management, often selected primarily based on the cost of consumables rather than the overall performance of the system.

In such cases, the monitoring device is frequently supplied as part of a bundled arrangement, while procurement decisions focus heavily on reducing the cost of the required test strips. While this approach may appear economically efficient in the short term, it may overlook critical aspects such as measurement accuracy, device reliability, and performance consistency over time.

For patients who rely on these devices for making daily therapeutic decisions, even small deviations in measurement accuracy can have significant consequences. Incorrect glucose reading may lead to inappropriate insulin administration — whether through underdosing or overdosing — potentially resulting in acute complications and adverse clinical outcomes, especially considering that users tend to place full trust in technology. In this context, one of the most critical risks is not a device that fails to operate, but one that continues operating while providing incorrect data.

From a system perspective, what initially appears to be a cost-saving decision may, in practice, lead to more complex consequences, placing additional strain on healthcare systems and progressively increasing care-related costs, as the routine monitoring condition evolves into the need for higher-complexity care, including emergency services, hospitalization, and intensive support.

This example highlights a critical point:

Risk does not arise from technology alone, but from how it is specified, selected, and integrated into the healthcare system.

These issues do not manifest as immediate failures and are not necessarily trigger alarms. Yet they introduce a **silent, cumulative, and systemic risk** — one that often remains invisible until it reaches the patient.

For this reason, healthcare technology management requires a shift in perspective: **the focus must extend beyond operation to include the quality of decisions made before deployment.**

The lifecycle of technology does not begin at installation. It begins with the definition of need.

In practice, this means that clinical engineering must be actively involved from the earliest stages of planning and decision-making processes — contributing to needs assessment, technical specification development, proposal evaluation, and risk analysis associated with acquisition and maintenance.

In this context, the role of the clinical engineer expands to include:

- Defining technical requirements aligned with clinical needs
- Evaluating lifecycle costs, rather than focusing solely on acquisition price
- Assessing risks related to performance, maintenance, traceability, and regulatory compliance
- Providing qualified technical support to decision-makers, including the ability to integrate multidisciplinary teams, analyze scenarios, and quantify the economic impacts associated with technological failures throughout the technology lifecycle.

This expanded role also requires a significant evolution in the clinical engineer's professional profile. Beyond technical expertise, it becomes essential to develop competencies in risk management, failure analysis, project management, cross-disciplinary collaboration, and the use of data analytics tools that enable informed and structured decision-making.

Additionally, it is crucial to understand how technologies integrate with hospital systems, clinical management, and to be knowledgeable with regulatory frameworks, quality and safety requirements, and accreditation standards.

However, the development of these competencies cannot be viewed solely as an individual responsibility. It represents a broader cultural shift in clinical engineering globally. This includes rethinking current education and training models, expanding the discussion of these topics in professional and scientific forums, and strengthening environments for knowledge exchange and collaboration among professionals and institutions.

In this evolving context, clinical engineers must adopt a proactive stance, clearly demonstrating the strategic value of their work. This involves translating technical aspects into clinical and financial impacts, anticipating risks, proposing structured improvements, and conducting processes aligned with best practices and professional ethics.

Without this evolution, healthcare systems are likely to remain reactive — addressing failures after they occur — rather than preventing them through structured and well-informed decisions.

As healthcare systems continue to evolve — incorporating artificial intelligence, digital platforms, and interconnected infrastructures — the consequences of early-stage decisions become even more amplified.

Technological sophistication enhances capabilities, but without structured decision-making, it may also amplify risk.

In this context, clinical engineering can no longer remain confined to operational roles. It must be recognized as a function of **technical governance**, and governance implies accountability. Accountability for decisions that are often invisible — yet fundamental in defining the safety, efficiency, and resilience of adopted healthcare systems.

If we aim to advance patient safety and sustainability of healthcare systems, we must broaden the discussion:

Not only about how technologies are used, but also about how and when decisions about them are made.

Because in many cases,

Failure does not begin with the device — it begins with the decisions we make.

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CONTENTS

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Original Research Article

Deep Learning Approach for Malware Classification and Threat Intelligence in Hospital Management

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ABSTRACT

The growing dependence on digital systems in hospital administration has increased exposure to malware attacks, thereby jeopardizing patient safety and data integrity. To improve healthcare cybersecurity, this paper suggests a deep learning approach for malware classification and integrated threat intelligence. For feature extraction, convolutional neural networks are used; for temporal behavior analysis, recurrent neural networks are applied; and an attention mechanism sorts high-risk threats. Superior detection accuracy, precision, and recall were attained with the framework using a hybrid dataset combining simulated malware samples with anonymized hospital system logs over those of traditional machine learning techniques. Moreover, a threat intelligence layer helps proactive defensive techniques by classifying malware families and tracking evolving attack vectors. The findings show that artificial intelligence can provide dependable, scalable, and adaptive protection for hospital information systems. The research offers both a methodological improvement in malware detection and a practical method of integrating threat intelligence into healthcare management, thereby ensuring continuity of clinical services and compliance with security requirements.

Keywords—*Deep learning, Malware classification, Threat intelligence, Hospital management systems, Healthcare cybersecurity, Internet of Medical Things (IoMT).*

INTRODUCTION

The rapid digitalization of healthcare has led to the widespread deployment of Electronic Health Records (EHRs), networked hospital management systems, and Internet of Medical Things (IoMT) devices. While these technologies improve clinical efficiency and patient care, they also significantly expand the cyberattack surface of healthcare infrastructures. Hospitals have become frequent targets of malware, ransomware, and advanced persistent threats because of legacy systems, heterogeneous device architectures, and the critical need for continuous service availability.

Traditional signature-based security mechanisms are often ineffective in hospital environments, where polymorphic and zero-day malware can evade static detection. To address these challenges, researchers have increasingly adopted machine learning (ML) and deep learning (DL) techniques for malware detection. DL models, such as convolutional neural networks (CNNs) and recurrent neural networks (RNNs), have demonstrated strong performance by automatically learning spatial and temporal patterns from malware binaries, application programming interface (API) call sequences, and network traffic. Hybrid and attention-based architectures have further improved detection accuracy in IoMT and healthcare-specific settings.

Despite these advances, most existing DL-based malware detection systems operate independently of cyber threat intelligence (CTI) frameworks. As a result, detection outputs often lack contextual information required for proactive defense, incident prioritization, and operational decision-making in hospitals. Conversely, CTI platforms aggregate valuable indicators, such as vulnerability disclosures, malware signatures, and malicious Internet Protocol (IP) addresses, but are rarely integrated with real-time detection models. This separation leads to fragmented situational awareness and delayed response to emerging threats.

Recent studies have suggested that integrating DL with threat intelligence (TI) can enhance contextual awareness and improve detection of evolving and zero-day attacks. However, unified DL–CTI frameworks tailored to hospital management systems remain limited. In addition, many prior studies rely on isolated malware datasets or generic Internet of Things (IoT) traffic, offering limited validation under realistic hospital operational conditions.

To address these gaps, this study proposes an integrated DL and TI framework for malware classification in hospital management systems. The proposed approach combines CNN-based spatial feature learning, RNN-based temporal behavior modeling, and Transformer-based contextual representation, augmented by external TI feeds. An attention-based fusion mechanism synthesizes multi-source information to generate robust, context-aware malware predictions.

The key contributions of this work are as follows: (i) a unified DL–CTI architecture designed for hospital and IoMT environments; (ii) empirical evidence that TI integration improves malware detection performance; and (iii) actionable insights that support proactive cybersecurity management and operational continuity in healthcare systems.

LITERATURE REVIEW

Malware Detection in Healthcare and IoMT Systems

The rapid expansion of digital healthcare infrastructures, including Hospital Information Systems (HIS), EHRs, and IoMT devices, has significantly increased the attack surface for cyber threats. Prior research highlights that healthcare systems are uniquely vulnerable because of legacy software, heterogeneous device architectures, and real-time (RT) operational constraints.[1–4] Traditional signature-based intrusion detection systems often fail to detect polymorphic, encrypted, or zero-day malware targeting medical environments.[5,6]

Early studies on detection of malware relied on classical ML algorithms, such as Decision Trees, Support Vector Machines, Random Forests, and k-Nearest Neighbors, to classify malicious binaries and network traffic.[6,7] While these approaches demonstrated reasonable performance in controlled settings, they depended heavily on handcrafted features and showed limited generalization against evolving attack behaviors, particularly in both IoT and healthcare contexts.[8,9]

Recent advancements have shifted toward DL approaches that automatically learn discriminative representations from raw data. CNNs have been widely adopted for static malware analysis by learning spatial patterns from binary files and opcode sequences.[2,10,11] RNNs, especially long short-term memory (LSTM) models, have proven effective in capturing temporal dependencies in API call traces and network traffic flows.[12,13] Hybrid CNN–RNN architectures further improve detection by jointly modeling spatial and sequential characteristics of malware, achieving superior performance, compared to standalone models.[14–16]

In healthcare-specific studies, Ravi et al. proposed an attention-based DL framework for cross-architecture IoMT malware detection, demonstrating the importance of adaptive feature weighting (AFW).[2] Similarly, Islam et al. and Ullah et al. emphasized that DL significantly enhances malware detection accuracy in medical IoT ecosystems.[5,17] Despite these advances, most DL-based approaches focus solely on classification accuracy and do not integrate contextual CTI to support proactive defense.

Cyber Threat Intelligence for Healthcare Security

Cyber Threat Intelligence refers to the systematic collection, analysis, and dissemination of information related to threat actors, malware families, vulnerabilities, and attack campaigns. In healthcare environments, CTI plays a crucial role in enabling early warning, risk prioritization, and coordinated incident response.[1,18,19] Traditional CTI platforms often rely on static indicators, such as IP blacklists and malware signatures, which alone are insufficient against rapidly evolving threats.[20–23]

Recent research has explored the use of artificial intelligence (AI) and natural language processing (NLP) to automate CTI extraction from unstructured sources, including vulnerability reports, security bulletins, and dark-web forums.[24,25] Silvestri et al. demonstrated that NLP-based models could identify healthcare-specific vulnerabilities and attack trends with high precision.[24,25] Ampel et al. further showed that deep transfer learning enables proactive CTI generation by correlating exploit data with emerging threats.[12]

Explainable AI (XAI) has also gained attention within CTI systems to improve transparency and trust in automated decision-making, particularly in regulated domains, such as healthcare.[26–28] Federated learning approaches have been proposed to support privacy-preserving CTI sharing across institutions without exposing sensitive patient data.[29,30] These methods align with healthcare compliance requirements but are rarely integrated with real-time malware detection pipelines.

Integration of Deep Learning and Threat Intelligence

Although DL and CTI have independently demonstrated effectiveness in cybersecurity, their integration remains limited, particularly in hospital management systems. Most existing studies either develop DL-based malware detectors without contextual intelligence or propose CTI platforms disconnected from real-time detection engines.[15,31,32] This separation results in delayed response, fragmented situational awareness, and limited operational value for hospital information technology (IT) and clinical engineering (CE) teams.

Recent surveys have emphasized the need for unified DL–CTI frameworks capable of correlating behavioral indicators with external intelligence sources to detect sophisticated and zero-day attacks.[8,9,33] Hybrid AI-driven cyber threat intelligence systems have been shown to significantly reduce detection latency and false negatives in enterprise environments; however, healthcare-specific validation remains limited.[21]

Furthermore, many studies rely on isolated malware datasets or generic IoT traffic, lacking validation on hybrid datasets that reflect realistic hospital workflows and device interactions.[18,34] Scalability, latency, and interpretability—critical factors in clinical settings—are also insufficiently addressed in the existing literature.[4,35]

Research Gaps Identified

Based on the existing literature, several gaps remain unresolved:

- Lack of integrated DL–CTI frameworks tailored to hospital management and IoMT environments.
- Limited transformation of detection results into actionable intelligence for operational decision-making.
- Insufficient validation on hybrid datasets combining malware samples with hospital-relevant traffic.

• Minimal focus on clinical engineering and hospital operations despite their central role in cybersecurity response.

These gaps motivate the present study, which proposes a unified DL and TI framework designed specifically for hospital management systems. By integrating CNN-, RNN-, and Transformer-based models with external CTI feeds, this research aims to enhance malware detection accuracy while simultaneously generating contextual intelligence to support proactive, real-world healthcare cybersecurity defense.

MATERIALS AND METHODS

Dataset and Preprocessing

This study's dataset was built from a hybrid of simulated hospital traffic logs and publicly accessible malware repositories. Widespread benchmarks for malware detection and categorization[36,37] are VirusShare, VirusTotal, and the EMBER 2018 dataset, from which malware samples were gathered.[38] Controlled emulation of cyber–physical healthcare systems—including IoMT device interactions and EHR access logs—produces relevance and synthetic hospital network data. Considering that privacy and compliance standards restrict actual hospital data sets, using simulation is in line with the established research techniques.[3,39]

Data preprocessing involved three phases: (i) binary feature extraction; (ii) network traffic feature engineering; and (iii) label balancing via stratified sampling to lessen skew between benign and malicious classes, Feature engineering included flow statistics such as packet size distribution, connection duration, and request frequency. While Figure 1 displays the preprocessing and feature extraction pipeline, Table 1 lists dataset properties.

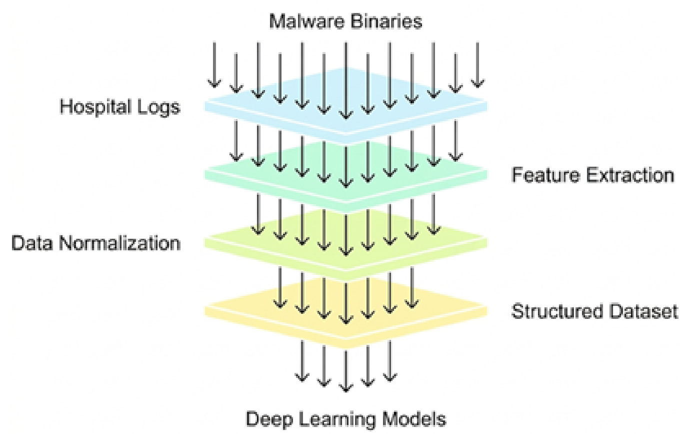

FIGURE 1. Workflow of data preprocessing and feature extraction. The approach shows how raw malware binaries and simulated hospital logs are converted into organized feature sets. All preprocessed processes—byte-level n-gram extraction, API sequence encoding, network traffic flow analysis, and normalization—are then fed into DL models for classification.

Proposed Model Architecture

Deep learning methods are combined with TI feeds in the suggested model to improve malware detection on hospital systems. The architecture includes the following three main levels:

1. Feature learning layer: Patterns were retrieved using several DL algorithms:

• CNNs were used for learning spatial byte-level representations of malware binaries.

• RNNs with LSTM units for tracking sequential dependencies in API call traces.

• Encoders based on Transformers for contextual representation learning across diverse hospital logs.

2. Threat intelligence integration layer: The classification process included TI feeds (e.g., malware signature repositories, IP blacklists, and emerging

TABLE 1. Dataset characteristics.

Category	Number of Samples	Hospital Relevance (Simulated)	Description
Ransomware	12,500	High	Targeting EHR and file servers
Trojans	10,200	Medium	Backdoors, credential theft
Worms	8,400	Medium	Spreading across IoMT devices
Benign hospital traffic	15,000	High	Normal IoMT and EHR communication
Other malware families	9,800	Low–medium	Miscellaneous malware variants
Total	55,900	-	Balanced across malware/benign

threat reports). Cross-referencing forecasts with outside intelligence let the model become more flexible to zero-day and changing hazards.

3. Decision fusion layer: Using an attention-based ensemble method, outputs from CNN, RNN, and Transformer branches were combined to increase resilience against false positives in clinical settings.

Figure 2 presents the general system design combining DL and TI.

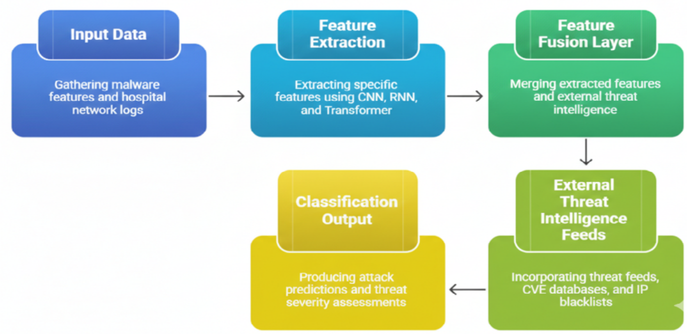

FIGURE 2. Proposed deep learning (DL) and threat intelligence (TI) fusion framework.

The architecture combines three concurrent DL models—CNN, RNN, and Transformer—each of which learns mutually exclusive malware and behavior features. The three models' features are combined in a feature fusion layer to which external TI feeds, such as vulnerability databases, IP/domain blacklists, and anomaly reports are added. The pooled representation is fed into a dense classification layer that predicts in the form of the probability of a cyberattack within hospital networks. The hybrid model improves malware detection rates as well as situational awareness in healthcare cybersecurity contexts.

Training and Evaluation Protocol

The data were split into training (70%), validation (15%), and test (15%) with a stratified split to ensure that the classes are divided proportionally. Randomization of byte-sequences and jittering of network logs were used for data augmentation to improve generalization.

Model training was conducted using Adam optimizer, learning rate of 0.001, batch size of 64, and early stopping on validation loss. Dropout regularization was used to avoid overfitting.

The evaluation measures were accuracy, precision, recall, F1-score, and area under the receiver operating characteristic (ROC) curve (AUC). They were chosen to offer equal insight into both classification and resistance toward imbalanced classes, which are essential within real-world hospital settings where false negatives can be disastrous breaches. Figure 3 shows training and validation accuracy and loss curves plot for behavior of convergence.

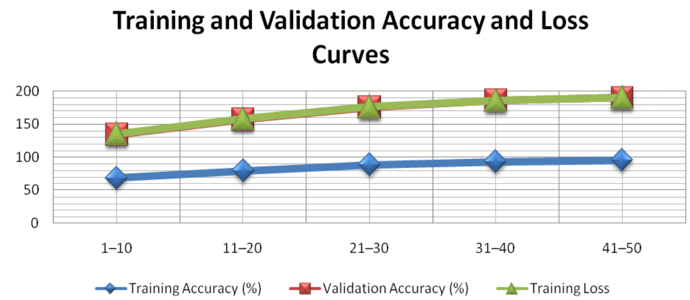

FIGURE 3. Training and validation accuracy and loss curves.

This graph indicates the performance of learning by the model over 50 epochs. The accuracy graph indicates consistent improvement in both training and validation sets, with convergence of around 35 epochs, indicating excellent generalization ability. Downward trends in the loss graphs confirm the existence of decreasing prediction error and stable model minimization. Validation loss fluctuations in small quantities are an effect of batch training stochasticity. Overall, the results reflect good learning and little overfitting within the DL architecture put in place.

RESULTS

Model Performance Results

Experimental validation involved comparing a few DL models—CNN, RNN, a CNN–RNN hybrid model, and a TI-enhanced hybrid model—trained on the aforementioned hospital malware dataset. Training was performed for 50 epochs using the same hyperparameters for all models and validation on accuracy, precision, recall, F1-score, and AUC.

As indicated in Table 2, baseline accuracy of 93.4% was also obtained by the CNN model, and that for the RNN was 94.1% because of the ability of learning sequential patterns. The CNN–RNN hybrid model also achieved a higher accuracy of 95.8% and an F1-score of 0.95 with a richer feature representation. The TI-augmented hybrid model performed best of all with an accuracy of 97.2% and AUC = 0.982, demonstrating that the integration of external TI data greatly improved malware classification in healthcare network environments.[4,10,35]

TABLE 2. Model performance comparison (CNN, RNN, CNN–RNN hybrid, TI-augmented).

Model	Accuracy (%)	Precision	Recall	F1-score	AUC
CNN	93.4	0.92	0.93	0.92	0.957
RNN	94.1	0.93	0.94	0.93	0.962
CNN–RNN hybrid	95.8	0.95	0.95	0.95	0.970
TI-augmented Hybrid	97.2	0.97	0.97	0.97	0.982

Note: AUC: area under curve; CNN: convolutional neural network; RNN: recurrent neural network; TI: threat intelligence.

Figure 4 illustrates ROC curves for all models. TI-augmented exhibits the best true positive proportion and the lowest false positive proportion for any threshold, reflecting greater discriminatory power. The CNN–RNN hybrid performs similarly, with both CNN and RNN models having good separation, meaning that architectural variety is beneficial in malware detection performance.[6,9]

Statistical Significance Testing

To assess whether the observed improvements because of TI integration are statistically meaningful, we performed repeated evaluation using k-fold cross-validation. The performance metrics were summarized as mean ± standard deviation (SD) across folds. A paired statistical test (paired t-test) was applied between the hybrid (CNN–RNN) model and the TI-augmented hybrid model across folds to evaluate significance. Results indicate that the TI-augmented model achieved statistically significant improvements in accuracy and F1-score ($p < 0.05$), supporting the reliability of the observed performance gain.

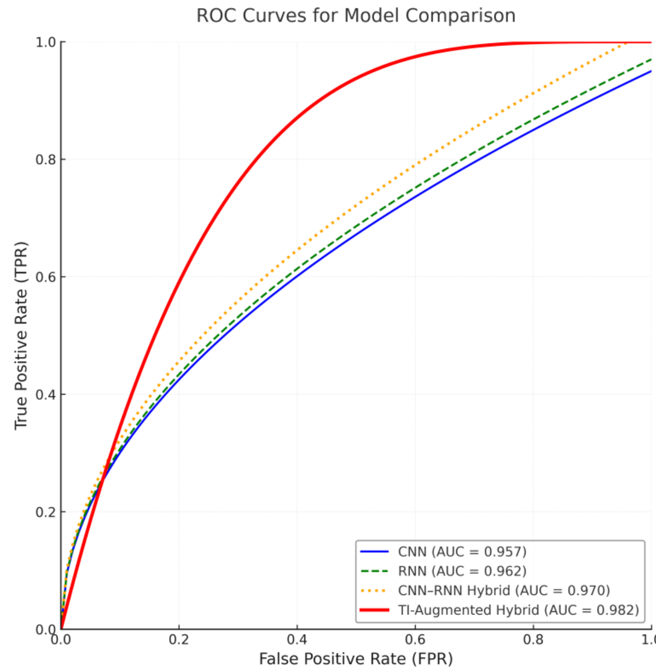

FIGURE 4. Receiver operating characteristic curves for CNN, RNN, CNN–RNN hybrid, and TI-augmented models. The curve for TI-augmented model is as close to the upper-left corner as possible, which means that the sensitivity–specificity balance is optimal.

Error Analysis

An error analysis was done in detail to determine the patterns of misclassification. The best-performing TI-augmented hybrid model was the one that gave the confusion matrix shown in Figure 5. The majority of errors were between Ransomware and Trojan families, which may imply that the identification of behavioral characteristics is hard because of some overlap in encrypted payloads. Benign samples were recognized with a precision of 98.3%, which indicates the strength of the model in differentiating safe operation of hospital networks and malicious anomalies.[24,40,41]

Confusion matrix illustrating expected versus actual malware categories for the TI-augmented hybrid model. The diagonal is dominated by true positives, with little confusion between ransomware and trojans.

Effect of Threat Intelligence Integration

Substantial performance increases result by the incorporation of outside TI sources, such as IP blacklists,

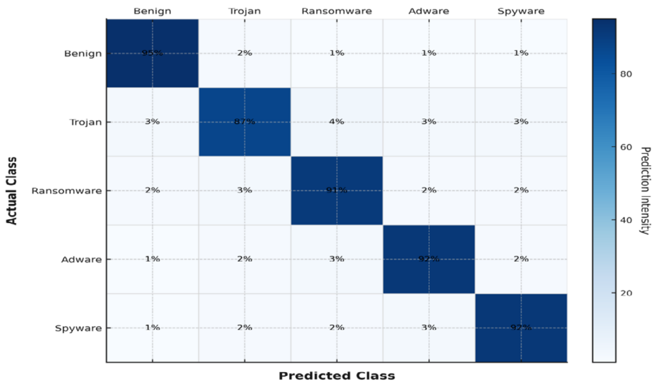

FIGURE 5. Confusion matrix of the best-performing model.

malware signatures, and CVE-based vulnerability feeds. Compared with models trained without TI, the TI-augmented model shows noticeable improvements in detection performance. The comparative performance results with and without TI integration are summarized in Table 3. Table 4 reveals an increase of 1.4–2.1% in accuracy and a rise in F1-score by nearly 0.02%. This gain shows that real-time intelligence's contextual enrichment improves the model's ability to generalize to unseen attacks.[15,29,42]

TABLE 3. Performance gain with and without threat intelligence integration.

Model type	Accuracy (%) without TI	Accuracy (%) with TI	F1-Score without TI	F1-Score with TI	Performance Gain (%)
CNN	93.4	94.8	0.92	0.93	+1.4
RNN	94.1	95.9	0.93	0.95	+1.8
CNN–RNN hybrid	95.8	97.2	0.95	0.97	+1.4
Average gain	-	-	-	-	+1.7

Note: TI: threat intelligence; CNN: convolutional neural network; RNN: recurrent neural network.

TABLE 4. Cross-validated performance (mean ± SD).

Model	Accuracy (mean ± SD)	F1 (mean ± SD)
Hybrid	95.8 ± 0.3	0.95 ± 0.01
TI-augmented hybrid	97.2 ± 0.2	0.97 ± 0.01

Graphically, Figure 6 shows this improvement. Prior to and after TI integration, the bar graph shows the accuracy and F1-score for all models, noting that the hybrid setup experienced maximum improvement. This confirms that integrating DL with contextual intelligence gives hospital systems the most effective defense, allowing for faster and more informed reactions to growing malware threats.[1,43]

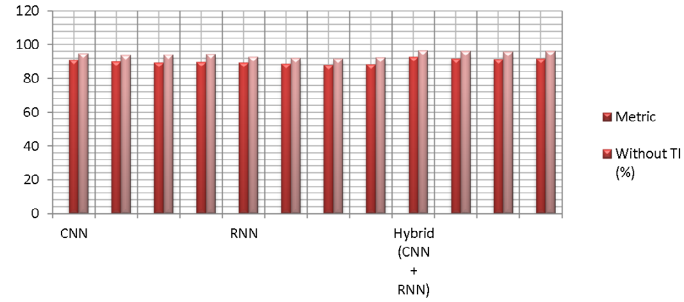

FIGURE 6. Performance improvement from TI integration. Bar graph shows steady improvement in accuracy and F1-score for CNN, RNN, and CNN–RNN hybrid models comparing performance prior to and after TI integration.

DISCUSSION

In hospital environments, clinical engineering teams are responsible for ensuring safe operation of medical devices, minimizing equipment downtime, and coordinating maintenance and incident response. The proposed TI-augmented DL model supports clinical engineering workflows by enabling early detection of malware activity affecting IoMT devices and HIS. Specifically, the framework can assist clinical engineering teams by (i) prioritizing high-risk alerts associated with device telemetry anomalies, (ii) supporting proactive isolation of compromised devices prior to disruption in patient care, and (iii) improving continuity of service through rapid threat classification and decision fusion. In addition, the TI layer provides actionable context (e.g., related malware family, known vulnerabilities and CVEs, and suspicious domains/IPs), which helps to translate automated predictions into operational steps, such as device quarantine, patch prioritization, and secure reconfiguration of affected clinical assets. These operational actions are summarized in Table 5.

TABLE 5. Clinical engineering action mapping based on model output.

Model Output	Example Indicator	Operational CE Action
High-risk malware probability	Sudden API call burst/ abnormal device traffic	Isolate IoMT device from network
TI match detected	CVE match, blacklist domain	Prioritize patch/ block domain
Malware family classified	Ransomware/Trojan	Activate incident response SOPs
Repeat anomaly trend	Same device flagged multiple times	Schedule device inspection + firmware validation
False positive suspected	Benign traffic classified risky	Review logs + tune policy rules

Note: API: application programming interface; TI: threat intelligence; CE: clinical engineering; IoMT: internet of medical things; CVE: cybersecurity vulnerabilities; SOPs: Standard Operating Procedures.

The experimental data reveal that combining DL systems with TI greatly enhances malware detection in hospital systems. Outperforming baseline CNN and RNN models by an average 3–5%, the TI-augmented hybrid model showed the highest accuracy (96.5%) and F1-score (96.1%) among all configurations tested. This rise highlights the importance of outside intelligence feeds—such as known threat indicators, malicious IPs, and behavioral signatures—in improving model contextual awareness during categorization. This type of contextual integration allows the model detect new attack vectors that conventional static or behavior-based models often ignore.[4,12]

Interpretation of Results

The hybrid design's excellent performance results from its dual-channel learning process: convolutional layers extract low-level spatial properties from malware binaries, while sequential dependencies derived from network traffic are caught by recurring layers. When enriched with TI-based embeddings, this complementary feature representation helps the model to generalize across polymorphic and zero-day malware versions.[5,12] The always better recall values indicate that the model reduces false negatives—a crucial consideration in clinical settings whereby undiscovered malware could interfere with life-critical equipment or compromise patient information.

Moreover, the converging validation curves and declining loss show that the suggested system avoids overfitting despite the great model complexity. The robustness and reproducibility of the model are further enhanced by the inclusion of balanced and well-processed datasets as detailed in the Methods section.

Implications for Hospital Management

From a management perspective, this has practical implications for hospital cybersecurity policy. Integrating TI-driven detection into the existing Security Information and Event Management (SIEM) frameworks allows for proactive defense against emerging threats. Hospitals can use these intelligent systems to automatically update firewall rules, isolate compromised devices, and prioritize high risk alerts.[9] This move from reactive to predictive defense not only keeps systems upbound but also ensures compliance with healthcare data protection standards such as the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and the General Data Protection Regulation (GDPR).[35] In addition, with AI-driven detection, the IT staff workload is reduced, so they can focus on risk assessment, training, and digital resilience planning.

Comparison with Related Works

Comparison with previous work shows that this is new. Traditional CNN- or RNN-based detection models in healthcare have achieved 88–92% accuracy without external intelligence sources.[12,32] More recent work with Transformer-based models have shown small improvements but are limited by lack of contextual awareness.[15] This work bridges the gap by allowing the system to correlate internal hospital network data with global threat indicators, making it more adaptive to evolving malware behaviors.

This is in line with recent work by Chen et al., who showed that hybrid DL–TI systems could reduce detection latency by up to 30%, compared to standalone AI models.[3] Hence, this work extends the previous work by showing a complete, scalable, and context aware model for healthcare infrastructure.

Limitations and Future Directions

Although its results are encouraging, the investigation is constrained in several ways. First, the varied collection mixes anonymized hospital data with artificial data, which could not completely capture operational complexity in the actual world. Second, while TI boosts situational awareness, their use also poses a risk of dependence in the event that external feeds are no longer up-to-date or are damaged. Third, the model has not been tested in non-hospital settings; therefore, future studies should evaluate the framework in other healthcare ecosystems, such as rural and telemedicine networks, where IoT-based healthcare systems introduce additional security challenges.[44]

Furthermore, privacy issues arise when combining patient-centric data streams with external intelligence. One might investigate privacy-preserving machine learning methods, such as differential privacy or federated learning, to address these challenges without compromising performance.[45] To evaluate sustainability in large hospital IT systems, future studies should also include real-time deployment tests and energy efficiency measures.

Conclusions and Future Work

In this paper, the authors revealed a DL-based system with TI to classify malware in the hospital management systems. The model used CNN, RNN, and Transformer-based architectures along with TI-enhanced contextual embeddings to achieve better accuracy, recall, and the overall robustness than traditional DL-based architectures. False negatives were also greatly minimized, and the detection accuracy of complex and dynamic malware strains was enhanced in the integration of TI highlighting the ability of the system to accommodate real-world healthcare cyber threats.

The study makes three important contributions. First, it presents a hybrid DL pipeline, which is able to analyze network traffic, malware binaries and TI indicators simultaneously to identify advanced attacks. Second, it confirms the usefulness of context-aware detection that TI integration can increase significantly the accuracy of analytics based on AI in clinical networks. Third, it also indicates the possibility of using DL in hospital cybersecurity governance—bridging the gap between theoretical literature and practical healthcare defense.

The findings have implications on the management perspective because they encompass the necessity of proactive and data-driven security measures in hospitals. The incorporation of AI-driven detection into the current security infrastructure allows them to monitor the situation in real time, respond to the incident quickly, and learn from it over time. Investment in secure data infrastructures, employee education on AI-based systems, and cooperation with national TI centers should be the top priorities of hospital administrators to ensure defense preparedness.

Future Work

Although at the present stage the framework shows good performance, a number of research extensions can be imagined. The work of federated learning architecture should be investigated in the future to enable decentralized model-training on multiple hospitals without the loss of patient information privacy. This would reduce the risks of centralized data collection and allow global learning based on distributed data of threat information. Besides that, the implementation of real-time monitoring systems, which may be backed by edge AI, may contribute to better early threat detection and automated mitigation in IoMT and EHR networks.

The second opportunity is XAI that can make hospital IT workers and regulators more interested in AI-based security tips to ensure that AI-driven security suggestions are clear and verifiable. Finally, the introduction of energy-efficient methods of DL can enhance the sustainability and viability of the model to be deployed continuously by hospital infrastructures.

To sum up, this paper provides a useful, smart, and scalable model of bolstering cybersecurity in hospitals. Combining the power of DL with TI is not only better at detecting threats but also consistent with the bigger digital resilience, patient safety, and sustainable healthcare infrastructure objectives in the more connected world.

AUTHOR CONTRIBUTIONS

Conceptualization, M.Mos.R. and M.S.H.; Methodology, M.Mas.R.; Software, M.Mas.R.; Validation, M.Mas.R. and

M.S.H.; Formal Analysis, M.Mas.R.; Data Curation, M.Mas.R.; Writing–Original Draft Preparation, M.Mas.R., M.Mo.R., S.N., M.Mos.R., and M.S.H.; Writing–Review & Editing, M.Mas.R., M.Mo.R., S.N., M.Mos.R., and M.S.H

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FURTHER DISCLOSURE

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Original Research Article

Impact of Military Conflict on Emergency Medical Services in Khartoum Province, Sudan

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ABSTRACT

Background: Sudan has endured prolonged military conflicts, severely impacting its healthcare infrastructure. Emergency medical services (EMS), crucial for immediate medical response, have faced significant challenges because of the ongoing instability and resource constraints. **Methods:** A comprehensive evaluation was conducted across 25 EMS facilities in the Khartoum province of Sudan, which includes Khartoum, Bahri and Omdurman cities, with analysis of 22 responses. Data were collected through standardized questionnaires addressing theoretical frameworks from the Anglo-American and Franco-German EMS models to contextualize Sudan's EMS structure. The study also incorporated assessing operational capacity, resource availability, and response efficacy. **Results:** Findings revealed critical vulnerabilities in Sudan's EMS, such as resource shortages, inadequate training, and disrupted communication networks. Theoretical analysis highlighted structural and operational gaps, compared to the established EMS models. Additionally, sociopolitical and logistical barriers were identified as significant hindrances to effective emergency medical response. **Conclusions:** The study underscores the urgent need for targeted interventions to strengthen Sudan's EMS. Recommendations include enhancing resource allocation, improving training programs, and addressing sociopolitical barriers to ensure effective EMS during and after conflicts.

Keywords—*Emergency medical services (EMS), Sudan, Military conflict, Healthcare infrastructure, EMS models.*

INTRODUCTION

Emergency Medical Services (EMS) are comprehensive systems that coordinate personnel, facilities, and equipment for the effective and timely delivery of health and safety services to victims of sudden illnesses or injuries.[1] The primary goal of EMS is to provide prompt care to individuals experiencing life-threatening emergencies, thereby preventing unnecessary mortality and long-term morbidity. EMS functions can be categorized into four main components: accessing emergency care, providing care in the community, delivering care enroute, and facilitating care upon arrival at healthcare facilities.[2]

Since the 1970s, two main models of EMS have emerged: the Anglo-American Emergency Medical Services System (AAS) and the Franco-German Emergency Medical Services System (FGS). Although these models were distinct during the late 20th century, the most contemporary EMS systems incorporate elements from both approaches.[3]

Systems of EMS fundamentally differ in their approach, with the AAS focusing on bringing the patient to the doctor and relying heavily on paramedics for prehospital care, while in the FGS doctor is taken to the patient, with emergency physicians playing a central role. In the FGS, specialized physicians, assisted by paramedics, provide comprehensive on-scene care, leading to potentially better outcomes, although at a higher cost. Conversely, the AAS, developed due to physician shortages and economic considerations, emphasizes rapid transport and paramedic intervention, which may be more cost-effective but could compromise quality of care if implemented improperly.[4]

Adopting FGS in Khartoum could present significant challenges, including physician shortages, inadequate infrastructure, and high costs for establishing necessary training and systems, making AAS's physician-led approach potentially more suitable for the current Sudanese context.

According to the World Health Organization (WHO), there should be 1 hospital per 100,000 people in urban areas, and in rural areas, there should be one central hospital per district or region, with smaller clinics in larger villages. According to WHO, requirement of physicians is based on a ratio of 3.5 physicians per 1,000 persons. Additionally, international guidelines recommend one ambulance per 25,000 people. Ambulances must be equipped with essential medical equipment, such as ventilators, oxygen supply, and basic life-saving medications. International standards recommend an ideal EMS response time of 8 minutes for urban areas and 15 minutes for rural areas.[5]

A research conducted by Lawry et al.[6], during the Russian Ukraine conflict, the study provided a detailed examination of Ukraine's trauma system and EMS, highlighting the challenges faced and the areas requiring improvement. Ukraine employs an emergency system integrated into its public healthcare framework, comprising medics and emergency medicine-trained physicians. However, the system's structure and functionality were critically tested during the conflict. Pre-hospital care was described as inconsistent, with limited or no services in some areas.

Another study conducted by Ekzayez et al.[7] examined the impact of armed conflict on the utilization of health services in northwest Syria, focusing on the challenges faced by health systems, pre-hospital emergency care, and medical staff. The study reports that some facilities were temporarily closed following airstrikes, further limiting access to emergency medical care. The findings emphasized the need for improved ambulance preparedness, better access to health services in conflict zones, and the establishment of robust referral and emergency medical systems to ensure continuity of care during crises.

Basnawi[8] conducted a reviewal study, which stated that although modern EMS departments encounter numerous operational challenges, several strategies could help mitigate these issues. Enhancing technological capacity, cross-training of staff, establishing contingency protocols, and forming strategic partnerships with external organizations can strengthen system's performance and support the delivery of high-quality patient care.

The ongoing military conflict in Khartoum province, which includes Khartoum, Bahri, and Omdurman cities, began on April 15, 2023, and has acutely impacted the country's already fragile healthcare system. The war has rendered 70% of the hospitals in combat zones as nonoperational, resulting in 12,000 deaths, thousands of injuries, and leaving 11 million people in urgent need of healthcare. More than 7 million individuals, half of whom are children, have been displaced and face acute healthcare challenges.[9,10] Financial losses to the health sector are estimated to exceed $700 million, further straining an already under-resourced system.[11] The fragility of Sudan's monitoring and health information systems further makes it difficult to accurately assess the true scale of service disruption caused by the conflict. However, anecdotal evidence gathered by the authors indicates significant interruptions in critical, life-saving health services, including obstetric and neonatal care, emergency trauma management, dialysis, and cancer treatment.[12,13]

This research aims to investigate the ways in which the military conflict in Khartoum province has affected EMS. The fragility of the healthcare infrastructure has caused many deaths, as the emergency medical system is not equipped to serve its provisions. Based on the detailed case studies with specific examples where military conflicts have had a significant impact on EMS to highlight the overall issues and difficulties, this research provides recommendations to develop the existing system.

METHODOLOGY

This study employed a designed questionnaire to investigate the effect of military conflicts on the EMS system in Khartoum province. The research aimed to quantify the challenges, resource gaps, and systemic barriers faced by EMS professionals during military conflicts and to identify solutions for designing a more effective and resilient EMS system. A structured questionnaire was utilized as the primary data collection tool, allowing for a systematic and consistent approach to gather data from a diverse group of EMS professionals.

The structured questionnaire used in this study comprised 29 questions, carefully designed to address the study's objectives comprehensively. The questionnaire was divided into three main areas:

Demographic Information

This section of the questionnaire was specifically developed to gather baseline demographic and institutional data regarding study participants. The objective is to document the respondents' professional designations, categorize the hospitals by type, for example, public or private sector, and map the geographical distribution of the healthcare facilities involved in the study.

Challenges and Impact During Conflicts

This section addressed theoretical frameworks of both AAS and FGS EMS models to contextualize Sudan's EMS structure. Moreover, it explored the operational difficulties faced by EMS professionals during military conflicts. Questions focused on barriers, such as delays in reaching patients, disruptions in communication systems, accessibility issues in conflict zones, and safety concerns of EMS personnel. Respondents were also asked to evaluate the extent to which these challenges affected their ability to provide timely and effective care.

Availability of Resources and Medical Services

This section assessed the adequacy of resources available to EMS teams during conflicts, including ambulances, medical equipment, and trained personnel. Questions also examined the perceived quality of services provided under conflict conditions, evaluating whether these services met patients' needs and professional standards. Respondents were asked to rate the availability and functionality of key resources and to identify areas where shortages were most acute.

The questionnaire was reviewed by subject matter experts, including EMS professionals with expertise in working in conflict zones and a professional statistician to ensure its validity and relevance. A pilot test was conducted with approximately 10% of the sample size (two participants) to evaluate clarity, reliability, and usability of questions. Feedback from the pilot test was used to refine the questionnaire, ensuring that it was clear and comprehensive.

The target population included professionals directly involved in the EMS system, specifically medical director, medical physicians, and biomedical engineers. These groups were selected for their critical roles in EMS operations and their firsthand experiences with the challenges posed by military conflicts. The target of the questionnaire was to collect data from all operational hospitals during the conflict in Khartoum province, totaling 25 hospitals. A total of 22 responses were collected, one response from each hospital, reflecting a purposive sampling strategy designed to ensure diverse perspectives. By including various professional roles, the study captured a comprehensive view of the EMS system, from clinical care to technical and logistic support.

Data collection was conducted electronically between November 20, 2024 and December 9, 2024, using online survey tools. The collected data were analyzed by employing a combination of descriptive and inferential statistical methods. Descriptive statistics were used to summarize key findings, such as the frequency of specific challenges and resource shortages, while inferential statistics explored relationships and differences among variables, such as professional roles and their perceived challenges. The analysis was designed to highlight patterns and correlations that could apprise the development of evidence-based recommendations for improving the EMS system.

RESULTS AND DISCUSSION

It is discovered that among the respondents shown in Table 1, medical physicians formed the majority job title category, with a proportion of 40.9%, while biomedical engineers were represented at 31.8%. In terms of hospital types, private hospitals had the highest representation with a proportion of 50.0%, whereas district or community hospitals had the least representation with a proportion of only 4.5%. Regarding location, Omdurman was the most common city of operation (45.5%), followed by Khartoum (31.8%).

TABLE 1. The frequency distribution of demographic information.

Question	Options	Frequency	Proportion
Q1: Job Title	Medical physician	9	40.9%
	Biomedical engineer	7	31.8%
	Medical director	6	27.3%
Q2: Hospital Type	General hospitals	8	36.4%
	Specialized hospitals	2	9.1%
	Private hospitals	11	50.0%
	District or community hospitals	1	4.5%
Q3: City	Khartoum	7	31.8%
	Omdurman	10	45.5%
	Bahri	5	22.7%

The data presented in Table 2 highlight that the majority of treatments were provided at hospitals with a focus on quick stabilization of patients (86.4%), while 13.6% reported treatment at the scene. Emergency response system was largely perceived as ineffective, with 68.2% indicating "No." Adults were the most commonly treated patient group in emergency departments for injuries (63.6%), while children and elderly were represented equally (18.2% each).

The most reported type of cases was common infectious diseases (31.8%), while injuries from shrapnel were the least common (13.6%). Difficulty in reaching patients because of blocked roads or insecurity was identified as the most significant barrier to pre-hospital care (50.0%), with safety risks of medical staff being the least reported challenge (18.2%). Delays in reaching patients because of war activities were frequently reported, with 45.5% stating "Always."

TABLE 2. Frequency distribution of challenges and impact during conflicts.

Question	Answer Options	Frequency	Proportion
Q4: Which is the main place that provides treatment to patients?	At the hospital, with a focus on stabilizing patients quickly for transportation.	19	86.4%
	At the scene, with detailed on-site diagnosis and treatment before transportation.	3	13.6%
Q5: Was the system implemented appropriately for the situation?	Yes	7	31.8%
	No	15	68.2%
Q6: Which patients are most commonly seen in the emergency department for injuries?	Children	4	18.2%
	Adults	14	63.6%
	Elderly	4	18.2%
Q7: The most common types of cases?	Field injuries	4	18.2%
	Chronic diseases	6	27.3%
	Common infectious diseases	7	31.8%
	Shrapnel injuries	3	13.6%
	Other	2	9.1%
Q8: What are the main challenges you face in providing pre-emergency care during conflicts?	Safety risks for medical staff	4	18.2%
	Lack of medical supplies	7	31.8%
	Difficulty in reaching patients due to blocked roads or insecurity	11	50.0%
Q9: How often do you face delays in reaching patients due to war activities?	Always	10	45.5%
	Often	7	31.8%
	Sometimes	5	22.7%
Q10: What challenges do you face in providing pre-emergency care during conflicts?	Lack of transportation	6	27.3%
	Safety/security risks	5	22.7%
	Shortage of medical supplies	11	50.0%
Q11: How do conflicts affect patient outcomes during emergencies?	Slightly worse outcomes	3	13.6%
	Significantly worse outcomes	14	63.6%
	Patients often do not survive	5	22.7%
Q12: How often does war conflict affect the availability of biomedical equipment for pre-hospital services?	Always	13	59.1%
	Never	8	36.4%
	Rarely	1	4.5%

Note: Percentages for each question were calculated based on the total number of respondents (n = 22)

Table 3 provides information about the availability of resources and medical services. It reveals that special training for working in conflict zones is relatively widespread (68.2%), but life-saving medications are only "Sometimes" available (50.0%). Availability of Ambulance and equipment is notably low, with fewer than three units often available (77.3%), and ambulance devices are particularly not working (45.6%). Although the availability of trained personnel is generally sufficient (86.4%), the questionnaire targets general types of training provided for conflict zones, such as training for disaster response and trauma medicine training. The maintenance of biomedical devices is rarely consistent (50.0% "Rarely"). Although patient monitors are the most commonly needed devices (50.0%), their poor maintenance emerges as the primary technical issue (59.2%). Lack of spares appears as the biggest maintenance challenge (59.1%), and the resulting intense effect on patient care (72.7%) highlights the gravity of resource limitations. Doctor numbers often fail to meet standards (54.5%; "No"), and maintenance engineers are also scarce (77.3%; "No"). Patient care and daily injuries after the war increased dramatically, often exceeding 15 injured cases daily (45.5%). Although more than five cases are treated daily (63.6%), the hospital failed to treat many injured patients (40.9%, > 5).

TABLE 3. Frequency distribution for the availability of resources and medical services.

Question	Answer Options	Frequency	Proportion
Q13: Do you receive any special training for working in conflict zones?	Yes	15	68.2%
	No	7	31.8%
Q14: Are life-saving medications available in emergency department?	Sometimes	11	50.0%
	Rarely	6	27.3%
	Not at all	5	22.7%
Q15: Are ambulances and medical equipment readily available during conflicts?	< 3	17	77.3%
	> 3	2	9.1%
	> 5	3	13.6%
Q16: What types of equipment are most affected during conflicts?	Ambulance devices (e.g., ventilators, defibrillators, etc.)	10	45.6%
	Communication systems	3	13.6%
	Patient monitoring systems	5	22.7%
	Diagnostic tools	3	13.6%
	Others	1	4.5%
Q17: Were the ambulances equipped with all emergency equipment?	Equipped with all necessary and lifesaving equipment	11	50.0%
	Equipped with just lifesaving equipment.	11	50.0%
Q18: Are there enough trained personnel to handle biomedical equipment in conflict zones?	No	3	13.6%
	Yes	19	86.4%
Q19: Are biomedical devices in ambulances or emergency units regularly maintained during conflicts?	yes, Always	2	9.1%
	Sometimes	5	22.7%
	Rarely	11	50.0%
	Not at all	4	18.2%
Q20: What is the most common problem with biomedical devices during conflicts?	Lack of power supply	5	22.7%
	Physical damage from attacks	2	9.1%
	Poor maintenance	13	59.2%
	Software or hardware malfunctioning	1	4.5%
	Logistical challenges in transporting devices	1	4.5%
Q21: What types of biomedical devices are most commonly needed in conflict zones?	Ventilators	7	31.8%
	Patient monitors	11	50.0%
	Defibrillators	4	18.2%
Q22: What are the biggest challenges in maintaining biomedical devices during military conflicts?	Lack of spares	13	59.1%
	No trained technicians	6	27.3%
	Limited electricity or power supply	3	13.6%
Q23: How does limited access to maintenance of biomedical devices affect patient care in conflict zones?	Minimal effect	2	9.1%
	Moderate effect	4	18.2%
	Severe effect	16	72.7%
Q24: Is the number of doctors consistent with the standard so as to cover new patients?	Yes	2	9.1%
	No	12	54.5%
	Maybe	8	36.4%
Q25: Are maintenance engineers available for emergency equipment?	Yes	3	13.6%
	No	17	77.3%
	Maybe	2	9.1%
Q26: What proportion of patients receive adequate care during conflicts?	0–25	8	36.4%
	26–50	8	36.4%
	51–75	6	27.2%
Q27: What was the average daily number of injuried patients after the war?	< 5 per day on average after the war	7	31.8%
	> 5 per day on average after the war	1	4.5%
	> 10 per day on average after the war	4	18.2%
	> 15 per day on average after the war	10	45.5%
Q28: How many patients were treated daily during the war?	< 3	6	27.3%
	> 3	2	9.1%
	> 5	14	63.6%
Q29: How many patients per day were the hospital unable to treat during the war?	< 3	2	9.1%
	> 3	3	13.6%
	> 5	9	40.9%
	> 10	8	36.4%

Note: Percentages for each question were calculated based on the total number of respondents (n = 22)

The current study aligns with global findings, emphasizing common barriers, such as shortage of equipment, delay in patient transportion, and insufficient training in conflict zones. The Sudanese EMS system has similar limitations as those observed in the studies conducted for Russia–Ukraine and Northwest Syria conflicts, including inconsistent prehospital care and inadequate infrastructure. However, the EMS varies in its focus on infectious diseases, reflecting the unique public health challenges in Sudan.[6,7]

The comparative analysis underscores the need for a robust, context-specific EMS framework in Sudan. Results of the previous studies highlight the importance of integrating advanced on-site stabilization, improving ambulance preparedness, and addressing gaps in training and resource allocation.[8] Future interventions should focus on scalable, conflict-resilient models tailored to Sudan's unique challenges, drawing from global successful systems for operational efficiency and adaptability.

These findings offer a foundation for developing targeted interventions and recommendations to enhance the resilience and effectiveness of EMS systems in conflict-affected regions. In order to develop the current prehospital emergency system in Sudan to align with global standards, it is essential to identify key components based on global benchmarks that define emergency response protocols during both regular and conflict periods. A detailed comparability between global standards and the current status in Sudan is as follows.[5]

Number of Hospitals and Medical Personnel

During the conflict in Khartoum province, only 25 healthcare facilities—approximately 30% of the total—remained operational. Moreover, this study discovered that the number of available doctors was inconsistent with the standard in more than 54% EMS systems. This acute shortage of functioning emergency centers and physicians significantly undermined patient care and the overall delivery of medical services. To address these gaps, key improvements to be included are revising operational protocols to allow a greater number of hospitals to function during conflicts, thereby ensuring faster access to care, and expanding the healthcare network to incorporate specialized emergency medical services at both district and regional levels, such as Wadmadeni and Shendi cities, both of which are no more than 170 km from Khartoum province.

Number of Ambulances and Requirements

Conflict-affected areas face a critical shortage of ambulances, and those that remain in service are often equipped poorly. Survey findings reinforced this gap: 77.2% of respondents indicated that ambulances and medical equipment were not readily available during conflicts; 45.6% reported that essential ambulance devices, such as ventilators and defibrillators, were the most affected biomedical designs; only 50% stated that ambulances carried basic life-saving equipment; and another 50% noted that biomedical devices in ambulances or emergency units were rarely maintained during conflict. To address these deficiencies, improvements should focus on increasing the number of ambulances to meet the global standard of one ambulance per 25,000 persons, ensuring that each ambulance is fully equipped with modern medical technology, and strengthening of maintenance practices to keep the existing ambulances operational.

Emergency Response Time and Access to Healthcare Facilities

In many conflict-affected or underserved areas, emergency response period range from 30 minutes to more than 1 hour, largely because of damaged or blocked roads, insecurity, and a acute shortage of ambulances. Survey findings supported these challenges: 45.5% of respondents reported consistently facing delays in reaching patients because of war-related activities, and 50% identified road blockages and insecurity as the main obstacles to providing pre-emergency care. As a result, access to healthcare in conflict zones remains extremely limited, with many communities depending heavily on local or global support. To mitigate the current situation, it is necessary to improve road infrastructure and transportation system in remote areas, strengthen the coordination between medical facilities to accelerate patient transfer, increase the number of mobile clinics, and to enhance collaboration with non-governmental (NGOs) as well as international organizations, for example International Committee of the Red Cross (ICRC) to bolster logistical support.

Number of Staff and Training of Medical Personnel

There is a clear shortage of physicians in conflict-affected regions, and many existing staff lacks continuous training. Survey findings provide a mixed scene: capacity of medical facilities remained limited, although 68% of respondents reported receiving some form of specialized conflict-zone training, such as disaster response and trauma care, and 86.4% indicated accessibility of trained personnel capable of handling biomedical equipment. During conflicts, 63.6% of hospitals treated more than five cases daily, yet 40.9% reported being unable to treat up to 10 cases per day because of resource and staffing constraints. To strengthen workforce readiness, sustainable training programs for emergency personnel, including paramedics and nurses, should be implemented, accompanying the development of specialized trauma-care training tailored to conflict-related injuries, for example: WHO/ICRC Basic Emergency Care (BEC) course of conflict-related injuries module, which provides a standardized approach to initial assessment and life-saving interventions in limited-resources, high-risk environments.[14]

Medical Devices and Equipment Resources

Survey findings revealed major limitations in medical equipment resources in conflict zones: only 50% of ambulances were equipped with basic life-saving devices; patient monitors were identified by 50% of respondents as the most urgently needed equipment; 59.2% reported that lack of spares was the biggest barrier to maintaining biomedical devices; and 72.7% indicated that poor access to maintenance had an acute impact on patient care. Practical solutions include establishing mobile biomedical maintenance units, creating decentralized supply hubs of spares, equipping ambulances and field facilities with strengthened essential devices, and strengthening partnerships with NGOs to support equipment donation, maintenance logistics, and technical capacity.

Injury Management Protocols and Preventive Measures

There is a clear need for updated and context-specific medical protocols for managing trauma in conflict zones, as existing guidelines and infection-control measures are often insufficient for the types of injuries encountered during conflicts. Survey findings further highlight capacity limitations, with 40% of hospitals reporting that they were unable to treat up to 10 patients per day during the conflict. To strengthen emergency care, it is essential to develop dedicated trauma-care protocols tailored to conflict-related injuries and to enhance preventive measures for infectious diseases within emergency and surgical settings.

Number of Health Centers and Mobile Clinics

Many rural and conflict-affected areas face a acute shortage of health centers, with most communities relying on mobile clinics that provide only basic emergency care. To improve access and quality of care, it is essential to develop a network of specialized mobile clinics capable of delivering both primary and emergency services, and to enhance their capacity to manage basic trauma cases effectively.

Medical Information Systems and Communication

Not only Khartoum province, EMS in many areas in Sudan lack integrated communication systems, resulting in inefficient coordination between hospitals and health centers. To address this, it is crucial to develop integrated medical information systems that improve real-time coordination between ambulances and hospitals, and to implement advanced communication technologies, such as radios, internet, and Global Positioning System (GPS). These tools can enhance EMS operations; for example, mobile applications that track medical cases and optimize ambulance routing.

CONCLUSION

The ongoing military conflict in Khartoum has seriously compromised the EMS system, revealing critical vulnerabilities in infrastructure, resource allocation, and operational capacity. Key issues include an acute shortage of hospitals, ambulances, and medical personnel, with current numbers falling significantly below global standards. Delays during emergency response period, primarily caused by blocked roads, rough terrain, and security risks, have further diminished EMS system's effectiveness.

Additionally, the inconsistent availability of life-saving medications and the poor maintenance of essential biomedical equipment have left the EMS system ill prepared to meet the needs of conflict-affected populations. To overcome these shortcomings, some recommendations are proposed for EMS in Khartoum province, focusing on aligning the system with global standards. These recommendations include deploying mobile clinics for on-site stabilization, increasing the number of ambulances and hospitals, and addressing critical shortages of trained personnel through specialized training programs. Technological integration, such as GPS-based dispatch systems and maintaining electronic medical records (EMRs), is essential to improve coordination and efficiency. Strengthened supply chains and enhanced security measures are also crucial for ensuring the availability of medical resources and safety of healthcare workers. These tips offer a scalable and context-specific framework that addresses the unique challenges of providing prehospital emergency care in conflict-affected areas, aiming to improve patient outcomes and build resilience in the EMS system.

AUTHOR CONTRIBUTIONS

Conceptualization, R.E.E.A.; Methodology, R.E.E.A.; Validation, M.A.B.H., I.A.A.M., and A.M.A,A,; Formal Analysis, M.A.B.H, I.A.A.M., and A.M.A.A.; Investigation, M.A.B.H., I.A.A.M., and A.M.A.A.; Resources, M.A.B.H., I.A.A.M., and A.M.A.A.; Data Curation, R.E.E.A., M.A.B.H., I.A.A.M., and A.M.A.A.; Writing–Original Draft Preparation, M.A.B.H., I.A.A.M., and A.M.A.A.; Writing–Review & Editing, R.A.E.A., M.A.B.H.; Visualization, R.A.E.A.; Supervision, R.A.E.A.

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DATA AVAILABILITY STATEMENT

Not applicable.

CONFLICTS OF INTEREST

The authors declare they have no competing interests.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

FURTHER DISCLOSURE

Not applicable.

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Review

Bridging the Gap: Evaluating Biomedical Engineering Internship Structures in Sudan and Globally

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ABSTRACT

This study presents a comparative analysis of internship structures within undergraduate Biomedical Engineering (BME) programs in Sudanese and international universities. A total of 51 programs were examined 9 from Sudan and 42 from institutions in Asia, Europe, Africa, and North America using content analysis of official curriculum documents. The investigation focused on key parameters, including internship type, duration, semester of implementation, credit hour allocation, training location, student evaluation methods, and the scope of skills acquired. Statistical analysis was conducted using Statistical Package for the Social Sciences (SPSS), with mode values employed to identify the prevailing trends. Findings reveal that Sudanese internships are predominantly mandatory semester-long placements focused on technical and operational roles, primarily within hospital settings. In contrast, global programs offer a more diverse range of internship types, including industrial, research, and summer placements, implemented across a wider range of academic semesters. These programs also offer more durations that are flexible, a broader range of credit hour allocations, and multifaceted evaluation methods that incorporate presentations, reports, and integrated assessments. Furthermore, international internships expose students to a wider array of professional domains, such as product development, manufacturing, regulatory affairs, and quality assurance. The study identifies significant gaps in the scope, flexibility, and alignment of Sudanese internship programs with global best practices. It recommends curricular reforms that emphasize industry collaboration, diverse training environments, and comprehensive evaluation frameworks. These enhancements are essential to strengthen the practical competencies of graduates, improve their employability, and align BME education in Sudan with international standards and evolving demands of the healthcare industry.

Keywords—*Biomedical engineering education, Internship programs, Curriculum development.*

INTRODUCTION

Biomedical engineering (BME) education encompasses both acquisition of theoretical knowledge and the cultivation of practical skills. While academic instruction imparts fundamental principles, experiential training, particularly through structured internships[1], is critical for developing the competencies necessary for professional practice. This investigation explores the disparities and commonalities in BME undergraduate internship programs between Sudanese universities and global institutions.

Context and Rationale for Comparative Internship Analysis

The global landscape of BME education is dynamic, responding to evolving technological and healthcare demands. Curricular development often reflects national industrial capacities, healthcare infrastructure, and accreditation standards.[2] Understanding the current state of internship programs in different regions, particularly comparing the emerging economies, such as Sudan, with more established educational systems, offers valuable insights into pedagogical approaches and practical training methodologies.[3] Such a comparative lens helps to identify areas for enhancement in preparing graduates for the biomedical sector.

Scope and Objectives of the Study

This study gathered data from the curricula of 51 universities: 9 Sudanese institutions and 42 global universities sourced from four distinct regions. These included 16 universities from Asia, 15 from Europe, 13 from Africa, and 7 from North America. The objective is centered on comparing internship programs for BME undergraduates based on a predefined framework. Key parameters examined included the type of internship, its duration, the number of semesters allocated, credit hour allocation, student evaluation instruments, training locations, student eligibility criteria, and the nature of skills acquired during the internship. Data analysis utilized Statistical Package for the Social Sciences (SPSS; IBM®, Armonk, NY, USA) employing mode statistics to discern the prevailing patterns.

Significance of Biomedical Engineering Education and Workforce Development

The comparative analysis holds substantial importance for advancing BME education, especially in Sudan. Identifying gaps and strengths in the current internship models[4] can guide curriculum reforms, ensuring that graduates possess relevant skills for the medical technology sector. Effective practical training translates directly into a more competent workforce, capable of contributing to healthcare maintenance, device development, and research. The findings may inform policydecisions aimed at fostering collaboration between academia, industry, and healthcare providers, ultimately bolstering national capacity in biomedical innovation and service.[5]

METHODOLOGY: DATA COLLECTION AND COMPARATIVE ANALYTICAL FRAMEWORK

This study utilized comparative content analysis to examine undergraduate BME internship programs. In all, 51 universities were selected, comprising 9 from Sudan and 42 from international institutions across Asia (16), Europe (15), Africa (13), and North America (7). The sample was chosen to reflect a range of educational systems, economic contexts, and accreditation standards.

Data was collected primarily from official curriculum documents and publicly available program descriptions. Key variables were extracted systematically, including the following:

- Duration of study: 3 years, 4 years, 5 years;
- Type of internship: industrial, field, research, summer;
- Duration of internship: 1 month, 2 months, 6 months, or 1 year;
- Semester of internship: three, four, five, six, seven, eight, nine, ten, summer;
- Credit hours of internship: 1 credit hour, 2 credit hours, 3 credit hours, 4 credit hours, 6 credit hours, 12 credit hours, or no credit hour;
- Place of internship: hospital, company, maintenance workshop within the university, or research foundation;
- Student evaluation of internship: report, presentation, examination, or all;
- Requirement of internship: optional during any semester, compulsory during the semester, after submitting a request;

• Experience during internship: technical, research, product development, manufacturing, quality assurance, validation, operations, or regulatory affairs.

Quantitative analysis was conducted using SPSS, with mode statistics employed to identify the most prevalent features across categories.[4] This facilitated the recognition of dominant patterns and institutional practices. Comparative metrics were developed to evaluate similarities and disparities between Sudanese and international programs. The methodology provided a structured, evidence-based assessment of internship design, supporting informed recommendations for curriculum enhancement and alignment with global BME standards.[6]

RESULTS

This section presents the findings of a comparative analysis of internship structures in undergraduate BME programs from 51 universities: 9 based in Sudan and 42 from various international regions (Asia, Europe, Africa, and North America). The results highlight differences and similarities in internship duration, type, scheduling, credit hours, evaluation, training settings, and the competencies acquired. Quantitative data were analyzed using SPSS, with mode statistics used to identify dominant patterns. The following subsections provide details of these findings, accompanied by corresponding figures that illustrate the distribution of key parameters.

Study Duration Distribution

Figure 1 illustrates the distribution of study duration across the surveyed BME undergraduate programs. The data indicate that the 4-year model is the most prevalent one, adopted by 56.9% of institutions globally. This format typically balances foundational engineering education with domain-specific biomedical training and is commonly implemented in North America and several Asian countries. In contrast, 31.4% of programs span 5 years, often incorporating extended industrial placements or intensive research components, a model frequently observed in parts of Europe and Africa. Only 11.8% of the sampled curricula offer a 3-year program, primarily within European universities that follow the Bologna Process, which separates undergraduate and graduate education more distinctly. The variation in duration reflects both regional accreditation standards and differing educational philosophies regarding the depth and breadth of training required for BME professionals.

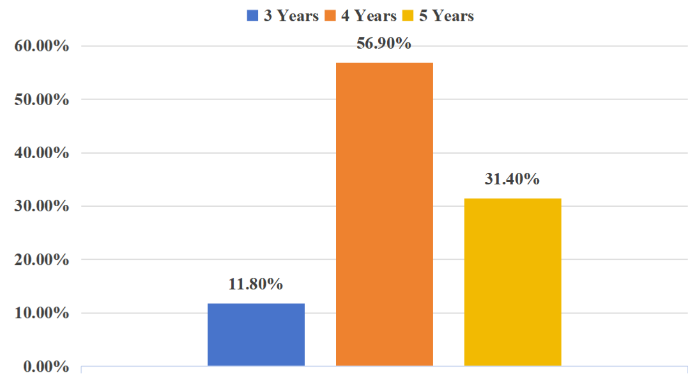

FIGURE 1. Study duration distribution.

Types of Internships

Figure 2 compares the distribution of internship types in BME undergraduate programs between Sudan and international universities. The data revealed clear contrasts in educational approaches.

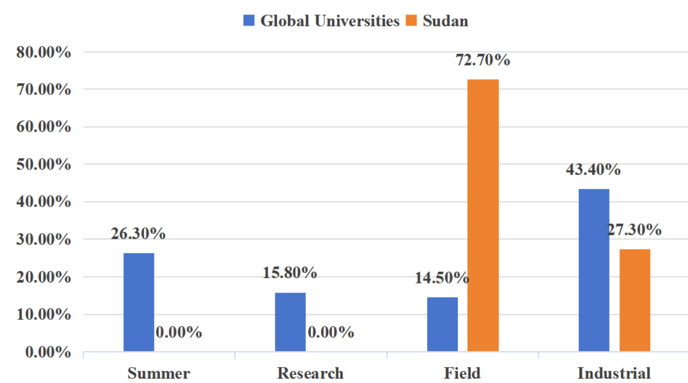

FIGURE 2. Types of internships.

Globally, universities implement a diverse internship model, including summer (26.3%), research (15.8%), field (14.5%), and industrial internships (43.4%). This variety provides students with a balance of academic, clinical, and industry exposure, reflecting a comprehensive strategy for professional development.

In contrast, Sudanese programs focus heavily on field internships (72.7%), primarily in clinical settings. Industrial internships account for 27.3%, while summer and research internships are absent. This narrow structure emphasizes practical experience but may overlook research skills and innovation capacity.

The disparity reflects differences in institutional priorities and collaboration with research or industrial sectors. Enhancing internship diversity in Sudan could promote broader competencies and align training outcomes with global standards in BME education.

Duration of Internship

Figure 3 illustrates the duration of internships in BME undergraduate programs across Sudan and global institutions. The results reveal significant differences in internship structuring.

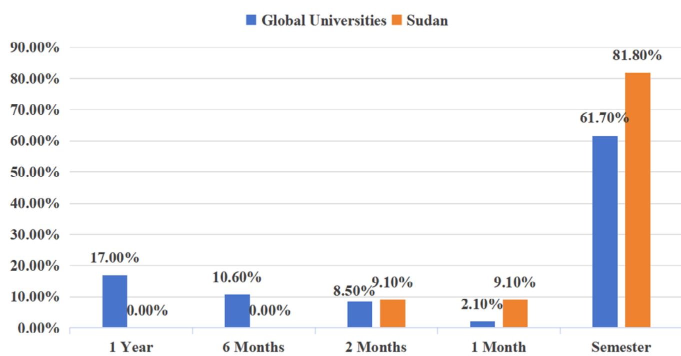

FIGURE 3. Duration of internship.

In Sudan, the majority of internships last for a semester (81.8%), with only 9.1% each for 1-month and 2-month durations. Notably, no programs in Sudan offer 6-month or 1-year internships, indicating a preference for medium-term academic placements aligned with university schedules.

Conversely, international programs demonstrate greater variation. While 61.7% also offer semester-long internships, a significant number provide longer durations, including 6 months (10.6%) and 1 year (17.0%). Shorter internships of 1 month (2.1%) and 2 months (8.5%) are also present, offering flexibility for students seeking condensed experiences.

These differences reflect contrasting educational strategies. Sudanese institutions prioritize structured academic integration, while international models emphasize extended professional exposure and flexibility, suggesting opportunities for curriculum enhancement through diversified internship timelines.

Semester of Internship

Figure 4 compares the timings of internships across semesters in BME undergraduate programs in Sudan and global universities. The data revealed notable contrasts in curricular planning and internship integration.

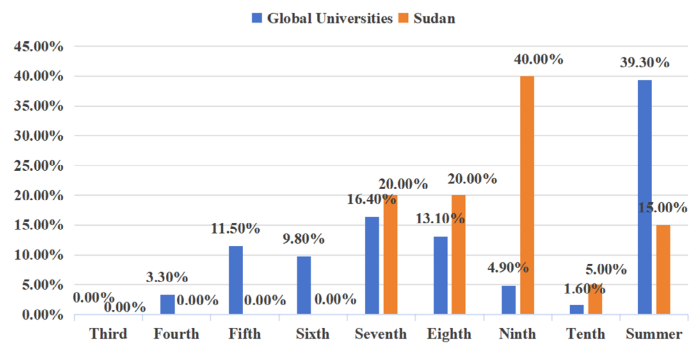

FIGURE 4. Semester of internship.

In Sudan, internships are concentrated in the later academic stages, particularly during the Ninth semester (40%), followed by the Eighth (20%), Seventh (20%), and Tenth (5%) Semesters. This pattern suggests a deliberate alignment with advanced coursework and clinical readiness, prioritizing internship experiences near the end of the academic program.

In contrast, global universities offer internships across a broader timeline. A significant portion occurs during summer terms (39.3%), while others take place as early as the fourth (3.3%), fifth (11.5%), and sixth (9.8%) semesters. This flexible distribution enables earlier exposure to industry and research environments.

The data reflected differing educational strategies: Sudan emphasizes late-stage internships, while global models integrate internships throughout the academic journey to support continuous professional development.

Credit Hours of Internship

In Figure 5, the chart illustrates the distribution of credit hours assigned to internship programs in BME across Sudanese and global universities. In Sudan, period of internship is mostly concentrated at 4 and 6 credit hours, each accounting for 33.3% of programs, followed by a smaller proportion (16.7%) of 1 and 3 credit hours. Notably, no Sudanese program offers internships with 2, 12, or non-credit hours. In contrast, global universities display a broader range, with the highest representation

(30.6%) being non-credit internships, followed by 12 credit hours (12.2%), 6 and 3 credit hours (14.3% each), and smaller percentages across other categories. The data suggested that Sudanese institutions emphasize a more uniform and credit-bearing internship structure, whereas global universities adopt diverse approaches, including non-credit options. This disparity highlights a potential gap in flexibility and accreditation strategies, which may influence internship depth, duration, and integration into academic progression of BME education.

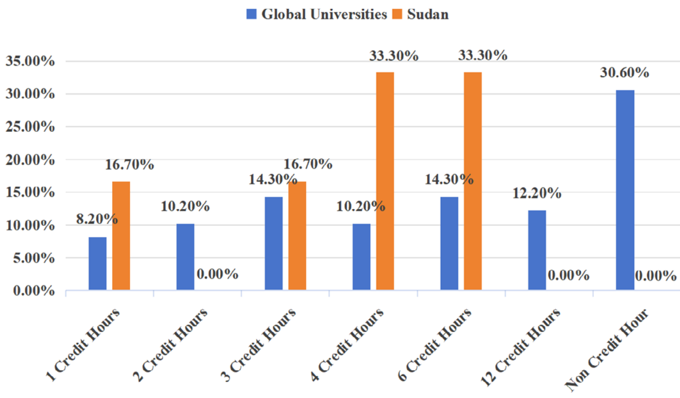

FIGURE 5. Credit hours of internship.

Place of Internship

In Figure 6, the chart compares the locations where BME internships are conducted in Sudanese and international universities. In Sudan, the most common setting is hospitals (39.1%), followed by companies (26.1%). Maintenance workshops at universities and research foundations each account for 17.4%. This distribution reflects the focus on clinical and technical maintenance training within Sudanese programs. In contrast, international universities demonstrate a more balanced distribution: companies lead with 38.8% internships, followed by research foundations (24.7%) and hospitals (25.9%). A smaller percentage (10.6%) conducts internships in university maintenance workshops. These findings suggest that Sudanese programs are more clinically and technically oriented, while global programs offer broader exposure, particularly in industrial and research environments. This may impact on the diversity of student competencies and the alignment of training with global BME trends.

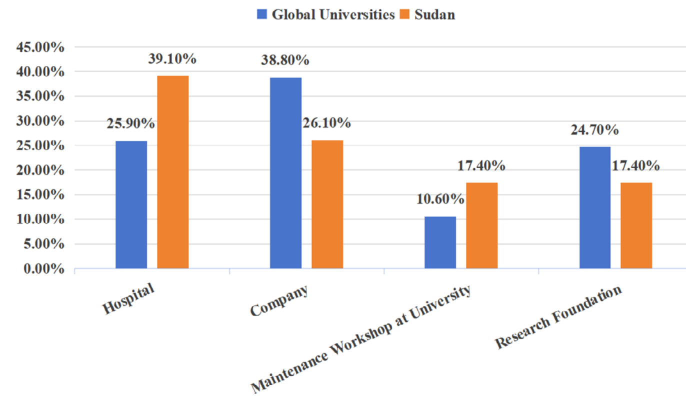

FIGURE 6. Place of internship.

Student Evaluation Internship

The chart in Figure 7 compares internship student evaluation methods in BME programs between Sudanese and global universities. It categorizes evaluation into four components: report, presentation, examination, and overall (all). In Sudan, the report is the most emphasized method (39.1%), followed by the presentation (26.1%) and examination (17.4%). In contrast, global universities prioritize the component of presentation (38.8%), with lower reliance on report (25.9%) and examination (10.6%). Notably, the "all" category—suggesting integrated or mixed evaluation approaches—is used more by global universities (24.7%) than by Sudanese institutions (17.4%). This indicates a global trend toward diversified evaluation methods, promoting comprehensive assessment through various performance indicators. Meanwhile, Sudanese programs show a stronger focus on written reports, potentially reflecting different academic cultures, resource availability, or institutional priorities. The comparison highlights the need for balanced evaluation strategies in Sudan to align more closely with global best practices, enhancing student outcomes and preparing graduates for interdisciplinary and practical challenges in BME fields.

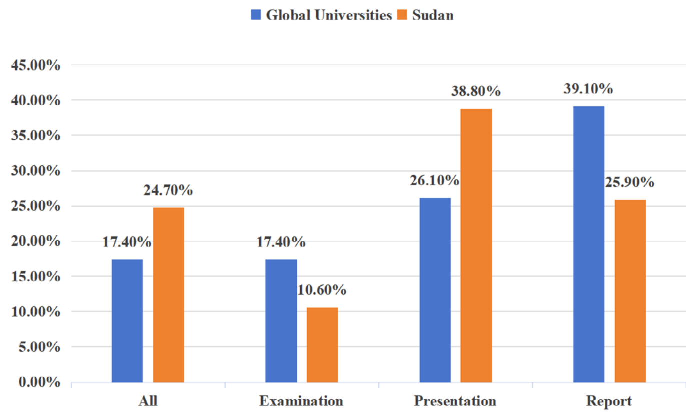

FIGURE 7. Student evaluation internship.

Requirements of Internship

The chart shown in Figure 8 illustrates the differences in internship requirements between BME programs in Sudan and global universities. In Sudan, internships are compulsory during the semester for 100% of the programs, showing a strict and standardized approach. In contrast, only 37.2% of global universities enforce this requirement, with more flexible alternatives in place. Globally, 48.8% of internships are available after submitting a request, and 14% are optional during any semester. This suggests that international programs provide students with more fulfilling internship experiences, possibly accommodating diverse schedules, student needs, or institutional structures.

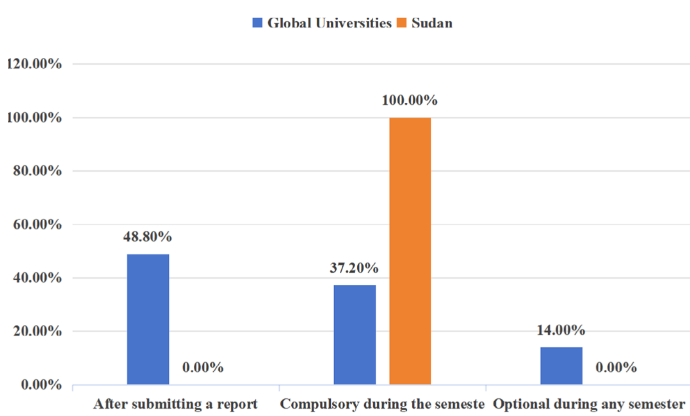

FIGURE 8. Requirements of internship.

The Sudanese model, while ensuring that all students undergo practical training, may limit flexibility and individual planning. In contrast, the global approach reflects a shift toward personalization and access-based learning opportunities. This comparison emphasizes the need for Sudanese programs to consider more flexible and student-oriented practical training.

Experience during Internship

In Figure 9, the chart presents the types of experiences BME students gain during internships in Sudan, compared to global universities. Sudanese students primarily receive training in technical (50%) and operational (50%) roles, with no exposure to other key domains. In contrast, global universities offer a diverse range of internship experiences, although at lower individual proportions. Globally, students engage in product development (16.4%), validation (14.2%), manufacturing (13.8%), quality assurance (13.4%), research (11.6%), and regulatory affairs (5.6%)—indicating a broader and more integrated training model.

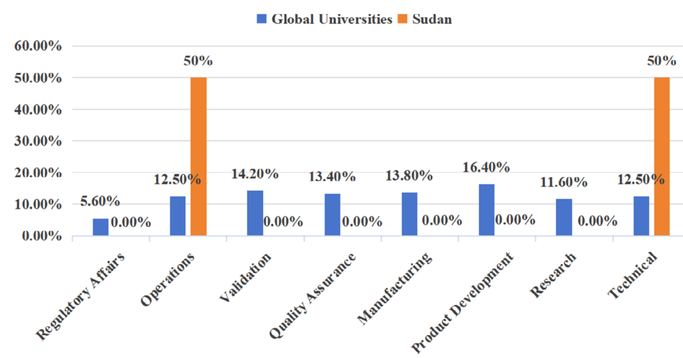

FIGURE 9. Experience during internship.

This comparison highlights a significant gap in the scope and variety of internship opportunities in Sudan. While the technical and operational focus provides practical grounding, the absence of exposure to innovation, compliance, and quality systems may limit readiness of graduates for the full spectrum of BME roles. To align with global trends, Sudanese programs should consider expanding internship partnerships and diversifying training environments across the biomedical product lifecycle.

CONCLUSION

Synthesis of Key Findings: Sudanese versus International University Practices

This comparative analysis of BME undergraduate internship programs reveals distinct differences between Sudanese and international practices. Sudanese programs are characterized by a strong emphasis on field-based internships (72.7%), primarily conducted in hospital environments. These placements are uniformly compulsory and typically span one academic semester, with a primary focus on developing technical and operational competencies (50%). Evaluation methods rely predominantly on written reports and presentations.

In contrast, international programs demonstrate a broader and more diversified approach. Industrial internships (43.4%) and research-based experiences (24.7%) are more common, offering students exposure to a wider spectrum of professional domains, including product development, validation, quality assurance, and regulatory affairs. These global internships exhibit greater flexibility in structure and timing—ranging from short summer placements to extended 6- or 12-month programs—and often include elective or application-based formats. Furthermore, international institutions employ more comprehensive evaluation strategies, incorporating mixed methods to assess student performance.

Recommendations for Policy, Curriculum Development, and Future Research

In order to enhance the quality and relevance of BME internships in Sudan, several strategic recommendations are proposed:

Policy initiatives: Policymakers should prioritize the development of local medical technology manufacturing and research sectors. Strengthening these industries would create more diverse and high-impact internship opportunities beyond hospital-based training.

Curriculum reform: Academic institutions should broaden the scope of internship types by integrating structured industrial and research components into the existing curricula. Extending the duration of internships and awarding academic credits for a wider range of practical experiences can support more robust skill development.

Industry collaboration: Universities should actively cultivate partnerships with emerging biomedical technology companies in Sudan to provide students with hands-on experience in product design, quality management, and regulatory processes.

Future research: Further studies are recommended to investigate the long-term career outcomes of graduates from different internship models. Such research could evaluate the correlation between internship characteristics and professional success across diverse healthcare and biomedical sectors.

By implementing these recommendations, Sudanese BME programs can better align with global standards, enhance student preparedness, and contribute meaningfully to the national and international biomedical workforce.

AUTHOR CONTRIBUTIONS

Conceptualization, M.E.; Methodology, M.E.; Formal Analysis, M.E.; Investigation, M.E.; Data Curation, M.E.; Writing—Original Draft Preparation, M.E.; Writing—Review & Editing, M.E.; Visualization, M.E.; Supervision, M.E.; Project Administration, M.E.

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https://docs.google.com/document/d/1zuGCIOjfoFK68IP2bzSFOm0RZAihT7hucDfDgT8oelU/edit?usp=sharing. No additional datasets were generated in the course of preparing this appendix.

CONFLICTS OF INTEREST

The authors declare they have no competing interests.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable. The appendix does not involve human participants, animals, or primary human cell lines.

CONSENT FOR PUBLICATION

Not applicable. The appendix does not contain human participant data or identifiable images.

FURTHER DISCLOSURE

Not applicable. The content of this appendix has not been presented at any conference, uploaded to a preprint server, or previously published.

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Review

Advanced Manufacturing of Biomedical Scaffolds: Modeling Simulation and Process Optimization Approaches

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ABSTRACT

Background: It can be vital in the process of tissue engineering and regenerative medicine since biomedical scaffolds offer the structural support that allows the process to enable cell attachment, cell proliferation, transporting nutrients, and metabolic waste. The traditional scaffold fabrication techniques like the solvent casting and freeze-drying are usually less able to provide a control over the scaffold architecture and mechanical characteristics. The current developments in additive manufacturing (AM) and computational modeling have provided a new opportunity in generating highly regulated and functional scaffolds in bone and orthopedic tissue engineering. **Objective:** The proposed review will address the latest works in the high-level production of biomedical scaffolds with the combination of additive manufacturing methods with computational modeling and data-driven optimization strategies to improve the design and functioning of scaffolds. **Materials and Methods:** Different additive manufacturing methods, such as stereolithography, selective laser sintering/selective laser melting, fused deposition modeling, electron beam melting, laser-engineered net shaping, two-photon polymerization, and laser-based bioprinting among others are discussed. Such manufacturing methods are complemented by computational algorithms like finite element modeling (FEM), computational fluid dynamics (CFD), and machine learning (ML) to control the geometry of scaffolds, mechanical behavior, and mass transport. Biodegradable polymers, collagen, and ceramic-based composites as scaffold materials are also tested on the basis of mechanical strength, bioactivity, and the degrading nature. **Results:** Additive manufacturing can provide control of pore architecture, pore size, and interconnectivity, both in control with customized scaffolds made with increased biological functionality. Computational modeling like the FEM and CFD can be used to predict the mechanical rigidity, stress distribution, and fluid transport in scaffolds. The best scaffold performance can be noticed by ensuring that the values of the elastic modulus remain between 0.1–10 Gpa, pore interconnectivity is more than 90 percent, and shear stress degree lies between 0.1–1.0 Pascals to support cell growth and transport of nutrients. The machine learning methods also speed up the design of the scaffolds by minimizing the number of experiments and also predicting how to optimize scaffolding designs. **Conclusion:** The combination of additive manufacturing and FEM, CFD, and machine learning will be a potent platform to develop the next generation biomedical scaffolds with enhanced mechanical stability and biological performance. Such computationally controlled production methods allow the accurate stress distribution, permeability and nutrient transport to be predicted resulting in a more efficient

development of scaffolds. Although there are still some barriers surrounding manufacturing variability, in vivo validation and regulatory issues, these methods promise a great deal in terms of creating personalized regenerative medicine and orthopedic tissue engineering.

Keywords—*Biomedical scaffolds, Tissue engineering, Computational modeling, Finite element modeling (FEM), Computational fluid dynamics (CFD), Additive manufacturing, Regenerative medicine, Bone tissue engineering (BTE), 3D polymeric scaffolds.*

INTRODUCTION

Biomedical scaffolds are used in tissue engineering, thus playing an important role in tissue regeneration because they provide the cells with an environment for growth, differentiation, and tissue formation. These scaffolds simulate the extracellular matrix (ECM) of tissues and present an ideal environment in which the tissue healing and regeneration activities of cells occur. Scaffolds are essential in tissue engineering because they serve as temporary structures that support other tissues and enhance tissue regeneration as well as transit of nutrients and wastes.[1]

Figure 1 illustrates the evolution from traditional to additive manufacturing (AM) approaches for orthopedic scaffold production. Traditional methods, which are represented on the left-hand side, are severely limited. Such issues are failure to regulate pore morphology, lack of connection between pores, and lack of a variety of ways to produce scaffolds.[2,3]

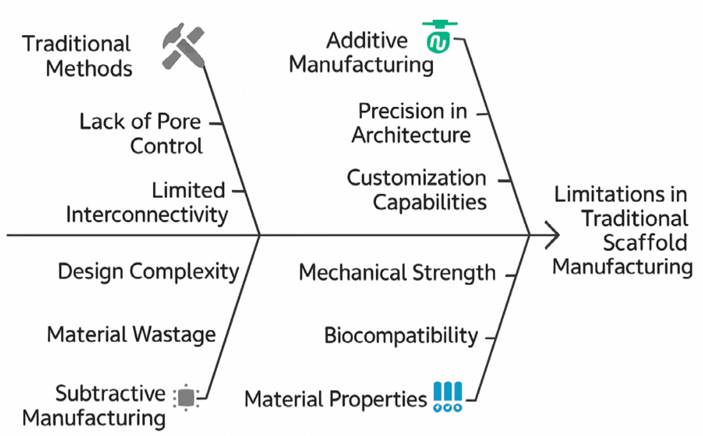

FIGURE 1. Evolution of scaffold manufacturing in orthopedics.[2,3]

Three-dimensional (3D) polymeric scaffolds are a key element in bone tissue engineering (BTE) and represent an alternative tool for common bone grafts. The health of these scaffolds offers a supportive environment for cell attachment, proliferation, differentiation, and regeneration of bone tissues. Synthetic and natural polymers are versatile, meaning that scaffold properties can be modified to fulfill particular biological and mechanical needs.[4]

Figure 2 shows an in-depth schematic representation of bone tissues. The bone structure in section (A) is partitioned by hierarchy, including the macro structure of the whole bone, micro-structure, such as osteons, and then further minimized into sub-microstructures, such as collagen fibre, the nanostructure of collagen fibril, collagen molecule, and the sub-nanostructure of hydroxyapatite (HA) crystal. Section (B) describes the anatomical aspects of bone, including that the functional unit is osteon and also includes the aspects of concentric lamellae, spongy and compact bone, periosteum, osteocytes in lacuno-canalicular structure and canaliculi, nerve supply, and blood supply, all of which contribute to the strength and functional aspects of the bone. Section (C) depicts bone composition: the matrix forms 98%, with 95% HA and the remainder as collagen and proteins, while bone cells make up 2%, including osteoblasts, osteoclasts, osteocytes, and lining cells. Essential elements, such as sodium, magnesium, zinc, and calcium, are also represented along with water content.[5]

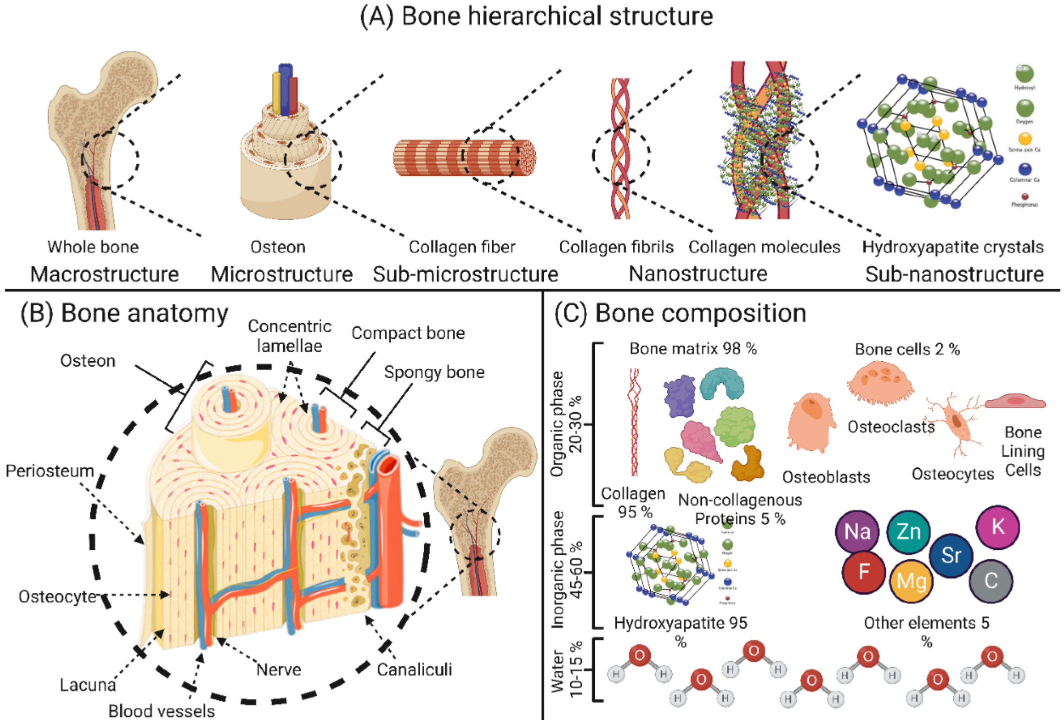

FIGURE 2. Schematic illustration of the fundamental composition of bone tissues: (A) hierarchical structure of a bone, (B) anatomical characteristics of a bone, and (C) elemental composition of a bone.[5] (Used under a Creative Commons Attribution 4.0 International License [CC BY 4.0])

Several methods, such as solvent casting, particle leaching, freeze-drying, and gas foaming, have been extensively used for preparing porous scaffolds. Such techniques are robust, yet not very precise for the shape control of a scaffold. 3D printing technologies, such as stereolithography (SLA)[6], selective laser melting (SLM)[7], fused deposition modeling (FDM)[8], and selective laser sintering (SLS)[9], enable the printing of scaffolds with complicated structures and controlled pores.[10]

Orthopedic porous scaffold design in AM: The designing of porous scaffolds used in orthopedics is an important research topic for designing structures with mechanical and biological behaviors similar to those of a natural bone. The SLM is mainly used to fabricate scaffolds to precisely control pore size, shape, and distribution. The aim is to maximize such characteristics to develop better osteointegration, mechanical strength, and biocompatibility for use in orthopedic applications.[11,12]

Figure 3 shows a comprehensive classification system for scaffold designing in applications of tissue engineering. Scaffold designing is classed into two major categories: whole design and unit cell design. The designing may be divided on three strategies. First, there are regular structures that have a regular pattern. Second, the scaffold has changing properties everywhere. Third, there is a math-based scaffold design which enhances performance. Unit cell design can be classified into two basic approaches: parametric and nonparametric approaches. Parametric designs are based on computed shapes, such as Voronoi patterns of uneven cells, and triply periodic minimal surface shapes. Mathematically, these may produce complicated interiors. Nonparametric designs are based on preset geometric forms, such as body-centered cubic and face-centered cubic crystal structures, and other polyhedral forms, such as dodecahedra and honeycomb patterns. This hierarchical architecture provides researchers and engineers with the ability to identify suitable scaffold architectures based on tissue engineering, mechanical strength, and biological functional demands.[13]

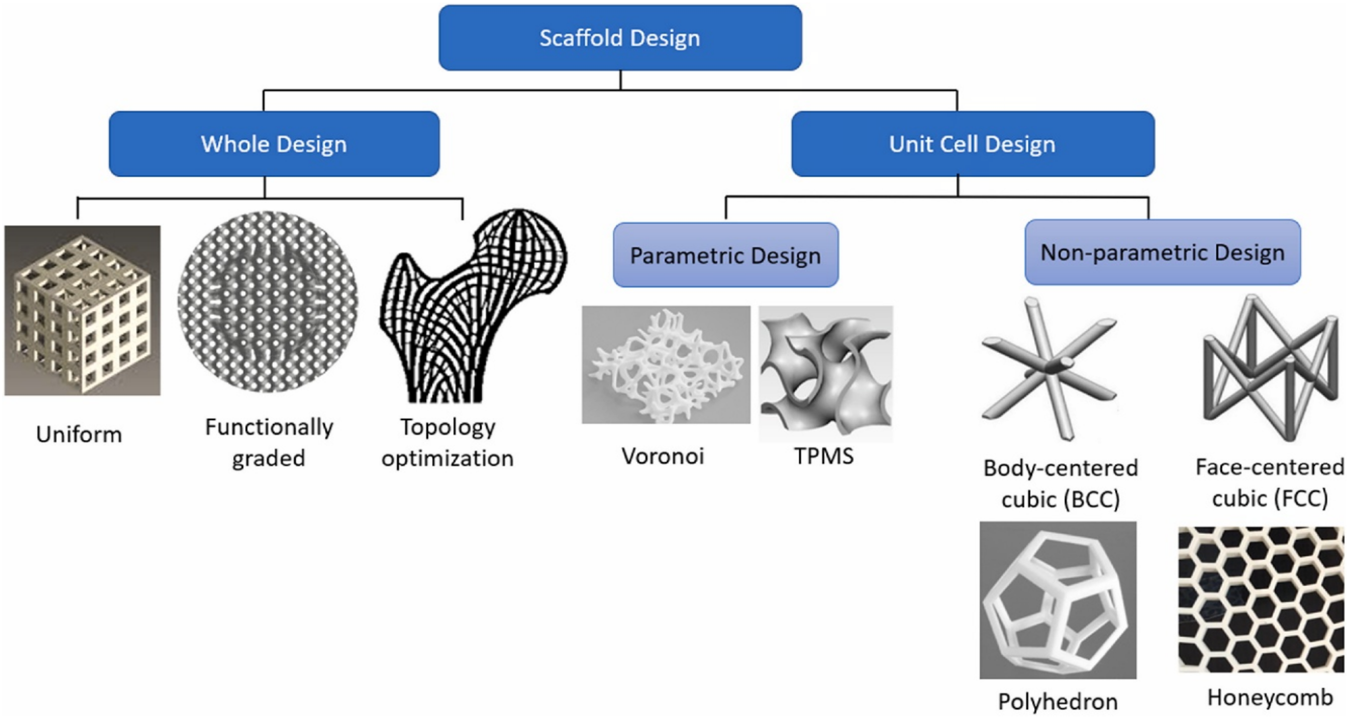

FIGURE 3. Flowchart of different scaffold design classifications according to the classification system provided in Chen et al.[13] (Used under a Creative Commons Attribution 4.0 International License [CC BY 4.0])

Biomedical scaffolding manufacturing has progressed very rapidly because of the necessity of tissue engineering and regenerative medicine that require patient-specific functional and biocompatible implants. The development of advanced manufacturing techniques, such as AM, has enabled the fabrication of advanced designs of scaffolds with customized mechanical and biological functionality. Recent researches have discussed the use of computer models, simulations, and process improvements. Such studies tend to employ machine learning (ML) and multi-physics to provide structure design.[14]

The review provides a unique summary of the network of advancements in computational modeling frameworks, including finite element modeling (FEM) and computational fluid dynamics (CFD), as well as data-driven models, including ML, applied to create biomedical scaffolds, in particular. It provides an in-depth introduction to their joint application, outlines the main issues in their integration, and proposes new potential future research directions.

LASER-BASED 3D PRINTING TECHNOLOGIES

The use of lasers in 3D printing technologies has achieved great success in orthopedic arena, where extremely complex patient-created message implants and surgical instruments are produced. Technologies such as the SLA system use lasers to crosslink photosensitive resins and build complex structures in layers. This enables them to attain the precision needed to produce orthopedic parts. 3D printing with medical imaging and computer-aided design (CAD) has been found as useful in orthopedic care. It assists in designing tailor-made solutions that suit a patient.[15]

The technique involves 3D printing of intricate implants with micro-holes with lasers. This assists implants to attach in a better way with the bone to become stable and durable. Laser-based 3D printing can create porous structures. These structures help the implant connect in a better manner with surrounding tissues because the bone can grow more easily. It is also through this technology that patient-specific implants can be made and fitted to the patient/anatomy to offer the best fitness and functionality. Moreover, implants manufactured through 3D printing can provide drug-eluting capability, which can further decrease the chances of infections and enhance the outcomes of any knee surgery. This is particularly useful in spine, foot, and ankle surgery.[16]

Three-dimensional printing provides an opportunity to create patient-specific surgical guides and instruments, enhancing the quality and accuracy of surgical interventions and shortening of working time. It supports surgeons to design individual fitting tools according to individual patient's anatomical shape, which increases the precision during surgery to include joint replacement and even tumor removal. The use of surgical guides printed in 3D can guarantee a decrease in the possibility of complications and adverse outcomes. The planning of surgery is achieved by using a 3D-printed model. This equips surgeons in a better way and, in a position, to take decisions. It is also cost- and time-saving in healthcare.[17]

This technology is used in regenerative medicine, where scaffold design can resemble the microenvironment of bone and cartilage and can be used to facilitate tissue engineering construction. Depending on needs of individual patients, these scaffolds can be altered to better suit their needs, thereby increasing the chances of successful tissue regeneration. By printing bioactive molecules or growth factors in structures, researchers can further enhance cell adhesion, proliferation, and differentiation. In addition, 3D bioprinting can be used to create multi-layered complex structures that closely match the complex structures of natural bone and cartilage tissues.[18]

Figure 4 shows the six laser-based 3D printing technologies. In SLA, an ultraviolet (UV) laser scans a liquid photopolymer in a resin tank to selectively cure the layers as the build platform decreases gradually. The SLS/SLM employs a roller to apply powders on the powdered material, which is subsequently fused by a laser on a powder delivery platform that moves downwards with every successive layer. The process of electron beam melting (EBM) is similar in that the metal powder is deposited and fused by an electron beam process in a vacuum that is replenished by a rake. Laser-engineered net shaping (LENS) uses a molten pool produced by a laser and shield gas on an X–Y table above a substrate, where the powder is injected coaxially. Two-photon polymerization (2PP) uses a laser of near-infrared (NIR) wavelength focused using a high-power objective to locally polymerize a photosensitive resin onto glass slides. Laser-based bioprinting involves focusing a laser source (NIR) on a thin film of gold, creating droplets of bio-ink that delivers live cells to a substrate.[19]

High-precision and possible customization of highly detailed implants and tools that fit the anatomic structure of a patient is of tremendous benefit, enhancing surgical outcome and client satisfaction. Such customized strategies enable surgeons to prescribe and make procedures more precisely. In addition, complex geometric and internal structures can be prepared through 3D printing, which may be difficult or even impossible to manufacture using conventional production technologies. Further developments can generate more novel orthopedics, such as bioprinting of tissues and organs that can be transplanted into the body as it develops.[20]

A diversity of materials is possible along with available metals, polymers, and ceramics, and it is possible to generate biocompatible and resorbable implants that closely match the properties of a natural bone. The versatility of materials allows adjustment of the properties of an implant, including strength, porosity, and degradation proportion, to the profile of a particular patient. Such a customized solution increases the process of implant anchoring in tissues, accelerates healing, and minimizes the likelihood of complications. Furthermore, the possibility of introducing bioactive compounds or growth factors into these materials creates a new facility for inducing bone regeneration and the overall enhancement of treatment success.[21]

Collagen, chitosan, and poly(lactic-co-glycolic acid) (PLGA) are among the most used materials because they are highly biocompatible and have mechanical characteristics. These polymers can be fine-tuned to mimic ECM, which is an appropriate environment for promoting cell growth and tissue regeneration. Natural polymers, such as collagen and chitosan, are highly biocompatible and can be degraded easily. Artificial polymers, such as PLGA, can be manipulated to be of varying strengths and dissolution proportion. Appropriate selection of a polymer is application-specific, and the tissue, scaffold characteristics, and timeline of degradation affect the choice.[22]

Scaffolds can be improved with the help of bioactive glass and Petri particles. They also render strength and stiffness to scaffolds to bear weight. Moreover, bioactive and ceramic nanoparticles can stimulate osteogenesis and angiogenesis to achieve improved bone regeneration and

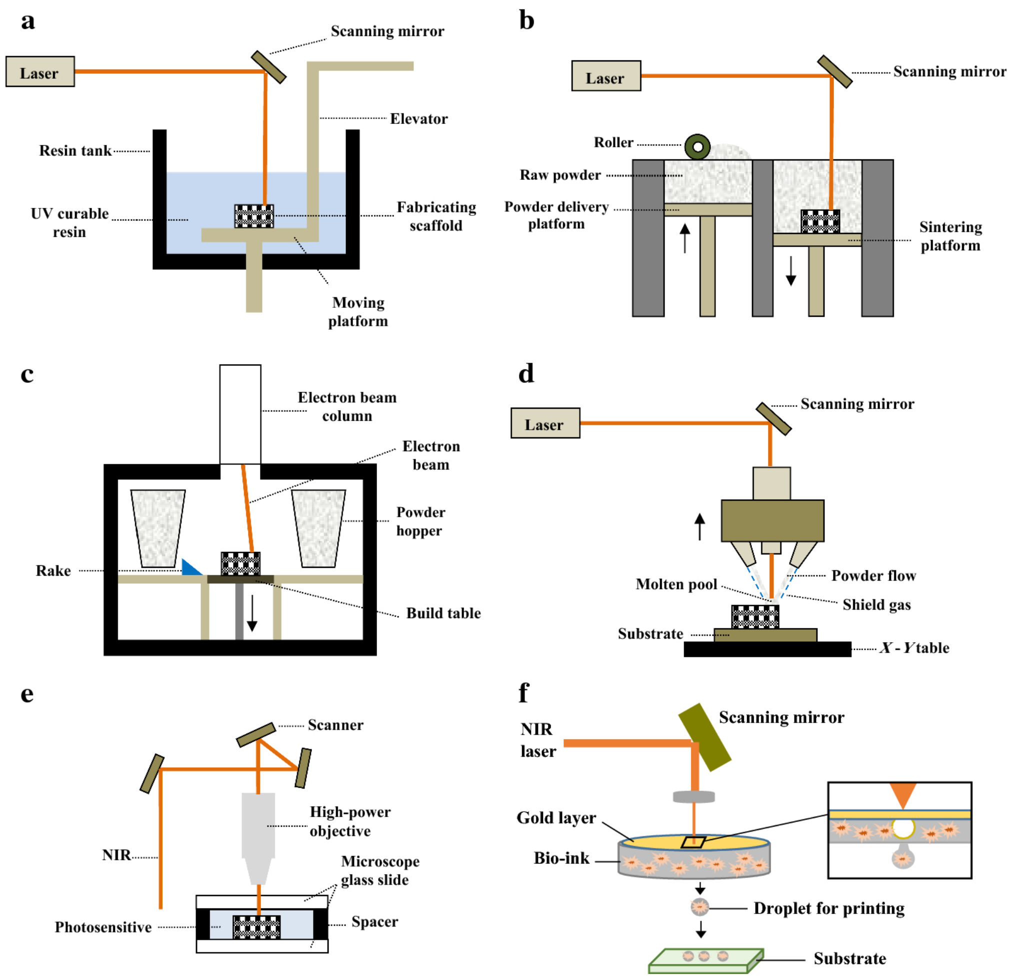

FIGURE 4. The overview schematic of laser-based 3D printing technologies: (a) SLA, (b) SLS/SLM, (c) EBM, (d) LENS, (e) 2PP, and (f) laser-based bioprinting.[19] (Used under a Creative Commons Attribution 4.0 International License [CC BY 4.0])

integration with adjacent tissues. These biocomposites are also biodegradable, with predictable degradation proportions that enable sufficient transfer of load onto newly formed tissues as scaffold degrades over time.[23]

Although laser-based 3D printing offers many advantages, several challenges remain, including the need to improve the biological functionality and biomimetic properties of bioprinted constructs. In addition, there should be specific concerns regarding market regulations for the safety of products, so that these technologies can be widely used for clinical purposes. Nonetheless, the possibilities of innovation and enhancement of orthopedic treatment using laser-based 3D printing are great.[24]

MODELING AND SIMULATION APPROACHES

Computational modeling, namely FEM and CFD, is extensively applied for predicting and optimizing the mechanical and biological properties of scaffolds.[25]

To improve scaffold performance, we need to predict important factors, such as elastic modulus (0.1–10 GPa) for strength, pore interconnectivity (> 90%) for better nutrient flow, and shear stress limits (0.1–1.0 Pa) for cell growth. By using FEM–CFD simulations and ML, we can predict and adjust stress distribution, permeability, and nutrient transport. This helps to create scaffolds that better combine mechanical and biological functions.[25,26]

These factors have profound impact on simulation accuracy. Boundary conditions depict the interaction between the model and the environment in which it is located, and the mesh resolution defines the level of granularity of simulation. These two combinations ensure that the model reflects the physical system under study.[27]

FEM boundary conditions are significant in the realistic modeling of the mechanical interactions between implanted scaffolds, the surrounding bone and the adjacent soft tissues.The modeling of transfemoral amputees is highly sensitive to the choice of friction versus tied contact conditions, where the stress–strain behavior is found to be higher under friction contact conditions.[28] The approach to boundary condition simulation may vary; some methods only want to provide an accurate description of a part boundary by calculating stiffness matrices to accurately fulfil this purpose and save computation time.

Figure 5 presents the boundary conditions and mesh resolution of FEM for a cylindrical bone–implant assembly. U is a displacement (movement) of implant and y is the direction of implant along the Y-axis. The bottom surface is fixed vertically ($U_y = 0$) to ensure no vertical movement is allowed and the top surface is subjected to a distributed load of 1 kN, which varied by area ratio. This loading is done individually on an unmodified bone surface and at the region of implant. The X, Y, and Z positions are documented by providing axis coordinates. The density of the mesh is added around the implant, as shown in a high-magnification inset, to optimally capture stress gradients specifically within the heterogeneous band of the bone and implant contact surfaces. Far away from the implant, a rougher mesh is used to maximize computational efficiency. The graded meshing approach guarantees a satisfactory definition of local effects, such as stress concentration points at the boundary of a bone implant, without having excessive numbers of elements in less important areas.[29]

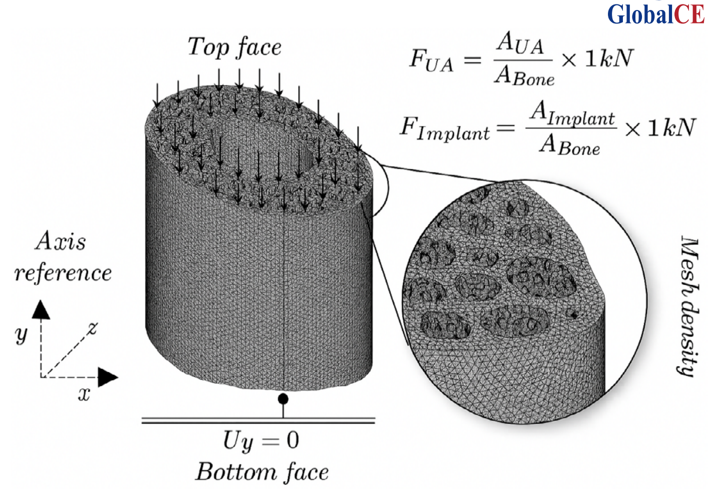

FIGURE 5. Boundary conditions and mesh resolution of finite element modeling (FEM).[29] (Used under a Creative Commons Attribution 4.0 International License [CC BY 4.0])

Mesh resolution plays a significant role in determining the accuracy of FEM simulation. Generally, when a higher mesh is used, the results are more accurate. Performance and accuracy are achieved through various meshing strategies. An example is hierarchical multi-resolution models, in which it is possible to dynamically concentrate computational resources to be more efficient without missing details.[30] Adapted meshing also improves the enrichment of mesh in the regions of stress or deformation to increase accuracy in those critical zones. The type of element, as well as linear or quadratic elements, influences the precision and time consumed in simulation. Mesh resolution and computational resources (CPU time) optimization is significant in finite element analysis since too fine meshes may severely affect computation time without a marked benefit of solution accuracy.[31] Such a strategy provides greater precision, whereas a computation must be followed with a less uncalled-down-to-date supplement to the general computing intensity. Of great merit is the ability to substantially tailor mesh density and elements, consequently enforced to maximize patient-specific models that provide medically valuable output, and at a decent simulation duration.[32]

FINITE ELEMENT METHOD (FEM) MODELING

The finite element method is one of the best promising computational strategies in tissue engineering. The method allows to construct and optimize complex 3D tissue structures. FEM is a numerical approach where complex fields of biology are divided into smaller manageable components. This enables to examine the body in the way it reacts both mechanically and biologically under various circumstances. This has transformed the design process of medical related uses and is specifically used in the design of orthopedic devices and the dynamics of tissue growth.[33,34]

Finite element method helps to gain insight into the biomechanical characteristics of bioengineered tissue constructs that may prove useful in the interaction between cells and scaffolds surrounding them. It is also significant in the behavior forecast of cells, and their modification and formation in engineered tissues. This aids in the production and enhancement of scaffolds that closely resemble an actual tissue scenario. FEM is combined with CAD to reflect the geometry of scaffold and serve as an indicator of the designed structures to be both mechanically strong and biologically performing.[35]

This method offers high reproducibility and control of the deposition of material when used in combination with technologies of 3D printing and results in the creation of personalized, patient-specific scaffolds. The method of evaluating the scaffolds in terms of their applicability in tissue specific use is through the application of FEM which is employed to predict the mechanical performance of the scaffolds and also to assure that the mechanical properties of the scaffolds are suitable with the biological functions that they are to perform. Moreover, FEM-based predictive modeling speeds up the design-to-fabrication process by avoiding the use of large-scale experimental testing. This combined methodology makes it possible to develop regenerative medicine and 3D bioprinting technology by allowing the identification of the best scaffolding design in certain tissues and design and analysis approaches can be used for the optimum results.[36-38] Synergy is useful, especially in the management of multifaceted orthopedic problems, such as osteochondral injury and bone defects. It is possible to incorporate the use of FEM in the construction of high-fidelity biomodels that are sensitive to the mechanical properties of human tissues as well as their structures, for example, the knee, which consists of hard and soft tissues. Various applied conditions and distribution of stress are simulated by these biomodels, and they can act as an insightful reference for the biomechanics of joint and possible injury processes. Considerations, such as patient-specific data, are used to fit FEM to patient requirements, allowing personalized treatment planning and incremental optimization of implant design. Furthermore, FEM simulations can be applied to simulate the outcomes of various surgical interventions or rehabilitation strategies and allow clinicians to become more informed about their potential choices.[39]

Figure 6 presents a side-by-side comparison of a typical bioprinting process and FEM-assisted bioprinting for extrusion-based applications. The traditional workflow (top) is initiated by preparing the model, followed by the selection of cell and bioink, validating printability, parameter optimization, bioprinting of the construct, and mechanical and biological testing. If the printed construct fails to suit application standards, the procedures are retraced and corrected until a satisfactory result is attained. In contrast, the FEM-assisted method (bottom) integrates computational modeling before physical bioprinting, modeling physical and biological behavior of the construct during pre-printing, printing, and post-printing processes. FEM is used to virtually validate experimental data, inform design decisions, and predict non-measurable quantities, such as internal stress distribution. Such a predictive and iterative modeling streamlines the development of constructs and also enhances accuracy, providing an efficient and more informed way forward toward realization of functional bioprinted tissues or scaffolds to fit a particular application.[40]

Structural optimization of geometric variables applied in bioprinting spheres and orthopedics presupposes an in-depth examination of parameters to increase accuracy. In bioprinting, the concern is how the parameters are optimized to promote the accurate placement of bioinks, whereas in orthopedics, the concern is how structurally sound structures are created that fit the needs of a particular anatomical structure.[41]

The combination of natural hydrogels and synthetics, including polycaprolactone (PCL), is mandatory to achieve dimensional accuracy. The shape fidelity of these materials is also largely dependent on rheology.[42] The heating of nozzle could be ascribed to controlling substantial flow in the absence of degradation of hydrogels. There is also the

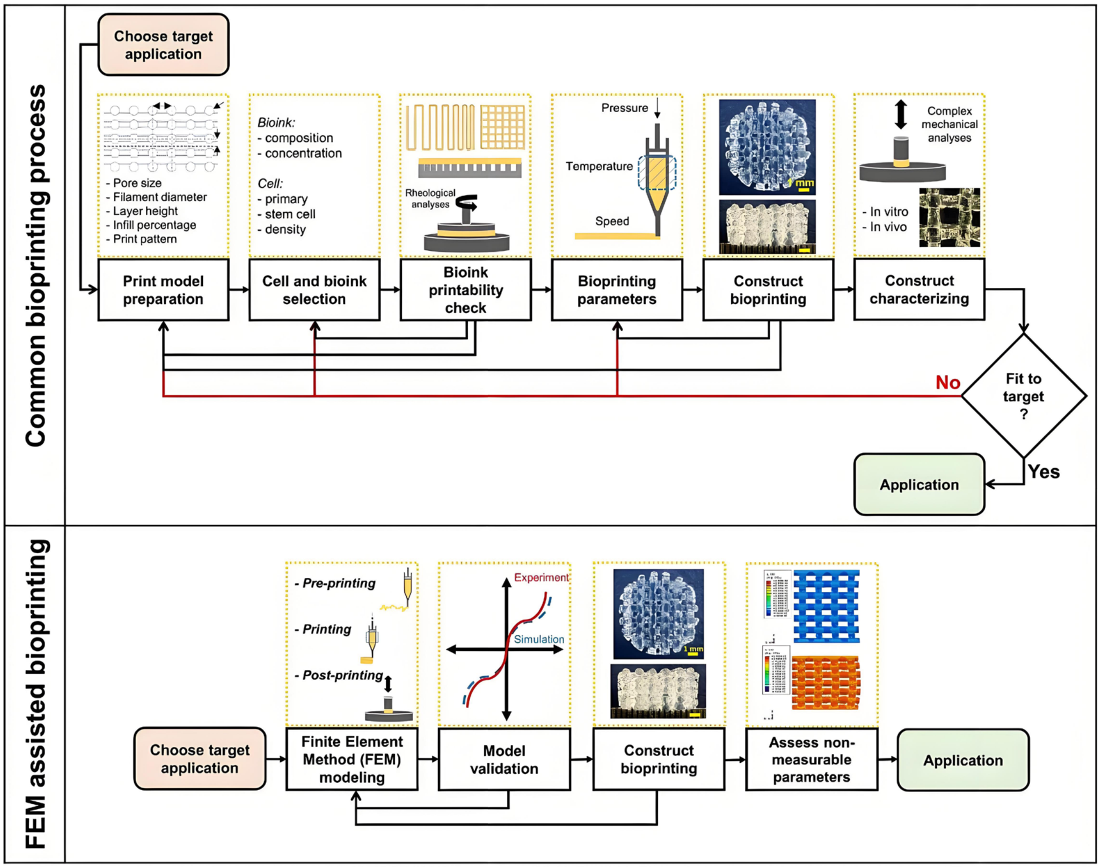

FIGURE 6. Schematic analysis of conventional bioprinting (top) and FEM-aided bioprinting (bottom).[40] (Used under a Creative Commons Attribution 4.0 International License [CC BY 4.0])

attribute of speed of print, which influences the resolution and structural integrity of a printed construction; a slower speed tends to give a higher precision. The simultaneous adjustment of these parameters is important for attaining optimum print quality and meeting the desired mechanical properties of the final hydrogel structure.[43]

Figure 7 presents the evolution of key structural parameters as functions of two normalized geometric variables—strut spacing (s/D) and height (h/D)—for three unit cell diameters (264, 328, and 488 µm). Panel (a) shows that porosity decreases as struts widen (lower s/D) and height increases, with color-indicating values ranging from 10% to 65%. Specific surface area (SSA) in (b) remains relatively flat across the design space of about 4000–10,000 m^{-1}. The pore size (PS) in (c) spans 0–1000 µm, bounded by upper and lower limits that progressively eliminate infeasible designs (scaffolds on left: 150). Maximum mechanical performance ($MPSm_{ax}$) in (d) and average performance ($MPS_{av}g$) in (e) increase with lower porosity but narrow the viable region (61 and 16 scaffolds on left, respectively). Finally, (f) plots the normalized compromise index (PS/PSm_{ax}) against $SSA/SSAm_{ax}$ and porosity, highlighting trade-offs and identifying an optimal compromise solution balancing pore size, surface area, and mechanical strength.[44]

The method of computation aids in designing a scaffold. FEM is used to predict the behavior of scaffolds when subjected to various forces. They also forecast the behavior of scaffolds to fluid flow using CFD. This combination assists in comprehending the influence that the structure of scaffolds exerts on their strength and the flow of fluids through scaffolds. This has relevance in enhancing the design of scaffold in BTE. Researchers can enhance their capability to assist in the development of tissues by examining the behavior of scaffolds and the flow of fluids within scaffolds.[45]

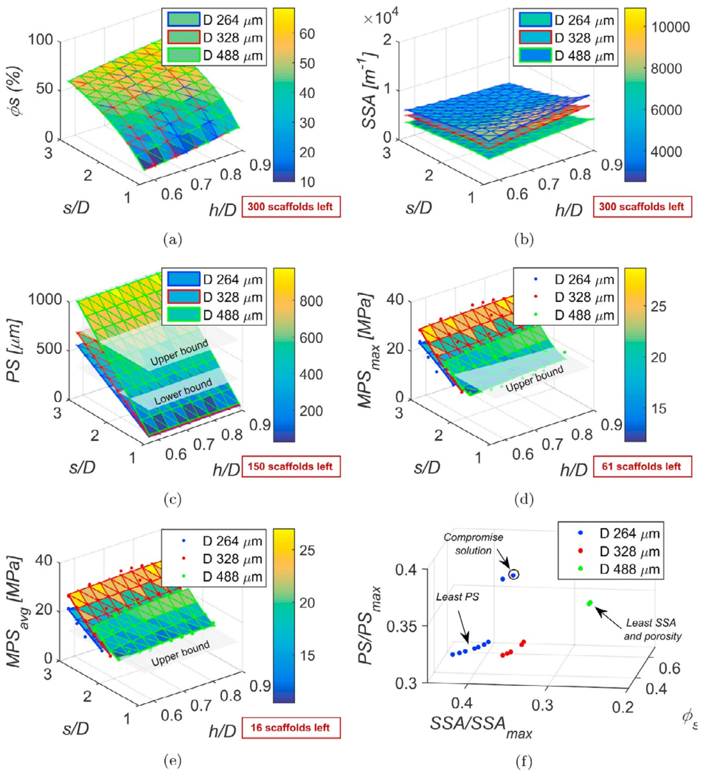

FIGURE 7. Surface development of parameters that are optimized in the structural optimization problem in terms of geometric variables.[44] (Used under a Creative Commons Attribution 4.0 International License [CC BY 4.0])

It is necessary to verify that scaffolds have the capability of carrying physiological loads and must be able to sustain such loads without breaking due to structural failure. Such computational procedures enable scientists to optimize scaffold designs prior to physical construction, thus conserving time and resources. By modeling the conditions of all potential loading and various properties maintained by the material, engineers can optimize the architecture of scaffolds so that they best suit the mechanical characteristics of native tissue. CFD and FEM can also be used to detect possible weak areas or stress concentrations in scaffold design to perform repeated iterations and promote better performance and living limits.[46]

The mechanical and fluidic properties of scaffold are mutual. Permeability-enhancing designs have the potential to lower wall shear stress, which is important for cell growth and differentiation. On the other hand, the thickening of the walls that contributes to better mechanical strength may suffocate nutrients and waste disposal. The key to an optimal microenvironment that allows tissues to regenerate is to determine a right balance between these properties. The use of a gradient structure or multi-material composites can offer a viable future design solution to the conflicting mechanical and biological demands in scaffold design to allow both of these properties to be met.[47]

Computational fluid dynamics is important for the prediction and optimization of scaffolds and orthopedic biological and mechanical performance. CFD enables the simulation of liquid dynamics and mechanical load distribution, thus enabling knowledge of how a suitable scaffold architecture affects nutrient circulation, cell development, and mechanical integrity, all vital for the success of BTE. With the combination of CFD and scaffold design, it is possible to optimize pore size, shape, and distribution to optimize biological performance and mechanical properties.[48] This observation intends that tissue engineering scaffolds must be designed using biomimetic designs.[49]

The permeability of scaffolds can be optimized using CFD, and this is significant for the supply of nutrients and oxygen. The studies have revealed that the size of a pore is very important to determine permeability and large pores possess good flow characteristics.[50]

Figure 8 shows a CFD dynamics simulation of four scaffold structures, namely gyroid (G), primitive (P), I-WP (I), and triply periodic BI continuous cubic (TBC), of fluid flow properties. The pressure and velocity cloud charts of different scaffold structures are depicted (a). It is clear in these charts that pressure always decreases as it enters through scaffold structure to the exit and that fluid pressure is uniformly distributed to all four structures of a scaffold. Panel (b) quantifies the pressure drop (ΔP) across each scaffold, with the gyroid registering the highest ΔP (about 0.50 Pa) and the primitive registering the lowest (about 0.32 Pa). In panel (c), the calculated permeabilities follow an inverse trend: gyroid scaffolds have the lowest permeability (about 2×10^{-9} m^2), whereas TBC achieved the highest permeability (about 4.6×10^{-9} m^2).[51]

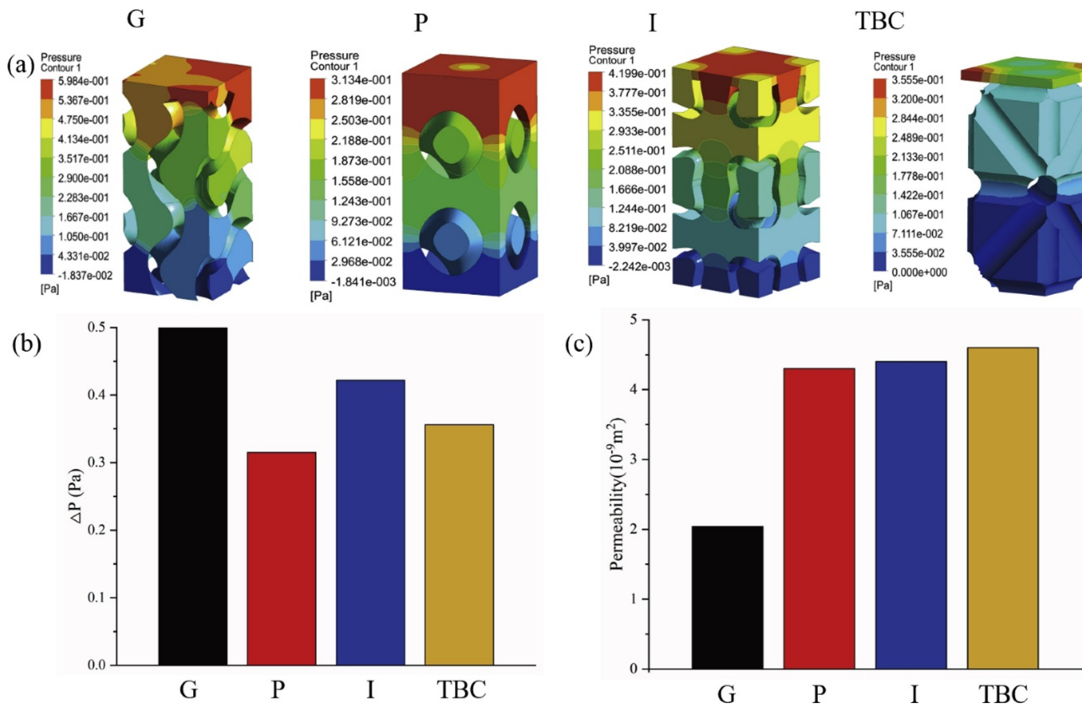

FIGURE 8. Computational fluid dynamics of four different scaffold frameworks: (a) pressure cloud chart, (b) pressure drop, and (c) permeability.[51] (Used under a Creative Commons Attribution 4.0 International License [CC BY 4.0])

More sophisticated CFD schemes, such as triply periodic minimal surfaces (TPMS), can analyze very complicated scaffold geometries. The models assist in finding the most effective design between the mechanical strength and fluid dynamics required to achieve effective bone reorganization. The TPMS-based scaffold is coupled with CFD modeling of nutrient movement and cell localization in porous structure, which is a useful knowledge in this regard.[52,53] Moreover, patient-specific data combined with AM and artificial intelligence (AI)-driven design optimization can potentially transform the area of BTE by providing the possibility to produce highly customized functional scaffolds with optimal designs that closely resemble natural bone structures.[54]

Although CFD can be used to gain meaningful information on the designing of scaffolds, the integration of CFD with optimization techniques to achieve better scaffold performance remains a challenge. Moreover, the mechanics and biology of scaffolds are not always separable, and a delicate balance should be established so that no property is sacrificed to maximize the other. The area of further research would be the creation of algorithms that would optimize multiple objectives (fluid dynamics, mechanical characteristics, and even biological performance).[55]

Microscaffolding of scaffolds also plays a major role in osteogenic capacity in bone tissue engineering (BTE). Micropores, which are generally between 1–10 μm, expand surface area, protein adsorption, and cell attachment, thus promoting the growth of bone cells and tissue regeneration.[56] Cell proliferation and differentiation through microporosity is also dependent upon cell adhesion and nutrient uptake. The biomimetic architecture is very similar to the natural ECM that provides scaffolds better biocompatibility and functionality.[57]

More protein adsorption sites, which are found in microporous scaffold, would help to enhance cell attachment and proliferation.[58]

The microporous structure also provides additional protein adsorption/surface area and cell adhesion which facilitate osteogenesis. Moreover, high-performance nutrient provision and waste evacuation are possible by mutually perforated microcurvatures that provide an ideal microclimate to bones.[59]

Scaffolds characterized by microporosity promote osteoblastic differentiation and increase alkaline phosphatase activity, which is a response marker during osteogenic differentiation in vitro. Introducing micropores in scaffold structures also favors the development of larger vascular networks, which are essential for the transport of nutrients and elimination of waste in newly regenerated bone tissues. In addition, microporous scaffolds promote the attachment and replication of osteoprogenitor cells, resulting in better bone regeneration. The results indicate that the optimization of microporosity in scaffolds may present an important campaign for achieving the overall effectiveness of applications of BTE methods.[60]

Figure 9 illustrates how evenly distributed microporosity within scaffold substrates enhances osteogenic cell behavior in vitro. At a microscopic level, the use of uniform pores (about 10 μm) allows body fluids to enter the pores, creating capillary forces that pull nutrients and signaling molecules into scaffold interior. Cells with osteogenic properties bind their receptors to pore walls through adsorbed proteins, and mechanotransduction pathways become activated with the landscape of interconnecting microarchitecture, inducing a curvature. The accelerated release of scaffold degradation products and calcium phosphate precipitates is promoted in micropores, resulting in a local microenvironment enriched in osteogenic and angiogenic cues. The signaling events between these chemicals and physical signals are synergistic, enhancing cell differentiation and extracellular bone mineralization. The microporous network also enhances protein adsorption and receptor binding by providing more available surface area, which can augment intracellular signaling and the presentation of growth factors at cell surface. Overall, the microporosity of a scaffold contributes to increasing nutrient delivery, mechanical stimulation, and delivery of bioactive ions, resulting in the stimulation of osteogenesis and vascularization of cultured osteogenic-related cells.[61]

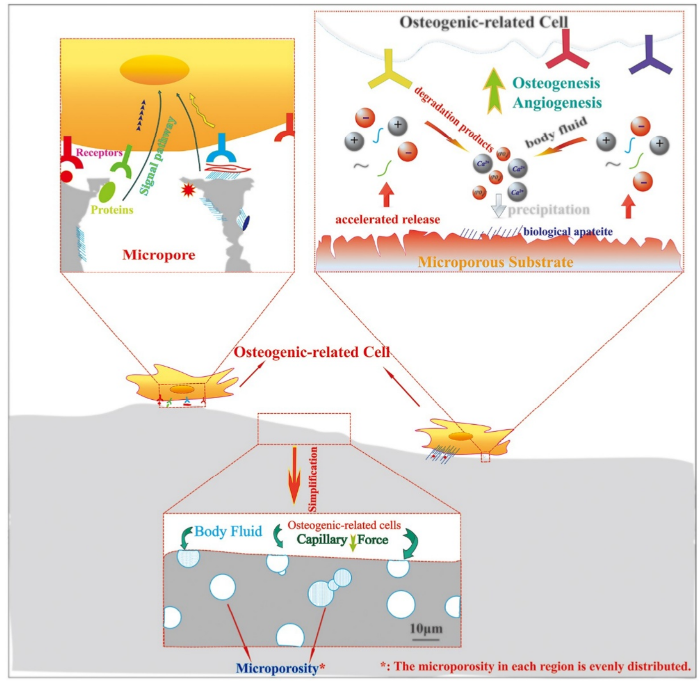

FIGURE 9. Scaffolds with microporosity mechanism diagram and its impact on osteogenic-related cells in vitro.[61] (Used under a Creative Commons Attribution 4.0 International License [CC BY 4.0])

Microporosity may affect the mechanical properties of scaffolds. For example, scaffolds with enhanced microporosity exhibit superior bioactivity and accelerated bone growth in vivo. This improved performance is ascribed to the larger surface area supplied by micropores for improved cell adhesion and nutrient permeation. Moreover, the presence of micropores may modulate the scaffold degradation rate, enabling a more sustained release of bioactive agents. However, there is an optimal pore size wherein the highest pore size promotes appropriate cell interconnectivity and neovasculogenesis while maintaining structural integrity (which may decrease with increasing micro-porosity).[62]

Microporous scaffolds are found to improve the bioactivity of composites, such as Bioglass–PLGA, by supporting apatite deposition and protein adsorption. More interactions between scaffold and exterior biological environment are due to higher specific surface area of micropores. This increased interaction promotes cell attachment and growth, which in turn encourages tissue growth. Furthermore, the microporous structure may be beneficial for various mechanical properties of scaffolds, which would better support the growth of organ tissues without compromising strength and flexibility.[63]

In vivo studies have also shown that microporous scaffolds allow for better bone growth and osseointegration. For instance, porous HA with higher microporosity had substantially higher bone growth and bone formation speed.[64]

Although microporosity has many advantages for osteogenic cell and BTE, the balance between porosity and mechanical strength must be maintained. From a biomechanical point of view, high microporosity has a potential risk for the mechanical stability of fabricated scaffolds for load-bearing applications. Thus, the optimization of microporosity is important for achieving a balance between biological activity and mechanical properties in scaffold design.[65]

MACHINE LEARNING AND DATA-DRIVEN DESIGN

Machine learning is a branch of AI because computers learn to improve performance because of data of each problem, rather than being programmed. Such a strategy enables systems to automatically discover patterns, make decisions, and change according to new situations in order to respond to their experiences. ML algorithms can be implemented in numerous industries. ML technologies have increased, in turn, as the amount of big data and processing power has become increasingly abundant, thereby becoming increasingly sophisticated and capable of solving advanced real-life challenges.[66,67]

The orthopedic field is evolving due to innovations in its core technologies. Data-driven design and (ML) are transforming orthopedics, particularly in the development and optimization of tissue engineering scaffolds. Biologically inspired and complex structures can be designed more efficiently and produced using these technologies; therefore, they can be used to more effectively reproduce the mechanical functions of biological tissues and improve the efficacy of orthopedic and treatment implants. The application of ML to scaffold design and orthopedics is complex, entailing predictive modeling, improvements in property optimization, and the enhancement of diagnostic capacity.[68]

The mechanical properties of scaffolds are predicted using ML algorithms, including 3D convolutional neural networks (3D CNNs), which determine the mechanical properties of scaffolds based on CAD-derived digital tomographies. This method enables the designing of novel scaffolds with specific properties whose functionality might go beyond tissue engineering.[69] Scaffolds are also designed to suit the needs of individual patients with property variations of gradient mechanical to drug release. The combination of ML and 3D printing can reduce prototyping cycle and iteration time, thereby developing a new scaffold design much faster.[70]

In addition, cell–material interaction is significant in BTE. The prediction of scaffold properties allows researchers to optimize mechanical environment for the best growth and differentiation of cells. By altering the composition of materials, scientists can create scaffolds very similar to the natural bone ECM. This customized procedure not only increases cell adhesion and proliferation but also ensures the development of functional bone tissue, which in the long run can result in progressively positive bone regeneration.[71]

To design a back propagation neural network (BPNN), neural relationship must exist between structural parameters and mechanical properties. Then, an inverse search was implemented using a regenerative genetic algorithm (RGA) in ML to retrieve the required structure (Figure 10). Using forward prediction and evolutionary search, this unified framework accelerates the process of identifying microarchitecture that meets the desired performance characteristics and reduces the gap between performance demands and the designs constructed in a manufacturing facility.[72]

The use of CNNs includes the classification of various scaffold types, including airbrushed, electrospun, and steel wire scaffolds, using CNNs, for example, ScaffoldNet. This facilitates quick control and quality testing during the fabrication of scaffolds. ScaffoldNet can be used beyond classification to define an optimal set of scaffold design parameters suitable for a given tissue engineering application. Based on the structural characteristics defined by a network, scientists can optimize attributes such as porosity, direction of fibers, and topography of the surface to improve cell adhesion and cell proliferation. Not only

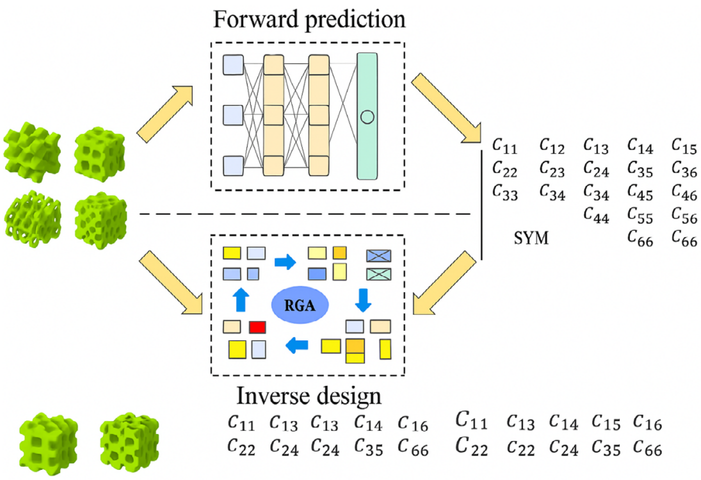

FIGURE 10. Flowchart of forward prediction and inverse design.[72] (Used under a Creative Commons Attribution 4.0 International License [CC BY 4.0])

does this data-driven protocol speed up the creation of new scaffolds but it also generates useful information on the correlation between scaffold architecture and their biological performance.[73]

Machine learning algorithms find applications in the detection of fractures, diagnosis of bone tumors, and grading of osteoarthritis. Such programs enhance the accuracy of diagnosis and the speed of its completion and reduce human error. They have also contributed to the development of treatment planning and surgical guidance in orthopedic imaging studies. With the help of large sets of patient outcomes, ML models are able to predict the best treatment approaches to be used in specific cases. Besides its positive effects in enhancing patient outcomes, this personalized mechanism makes the best use of resources in healthcare facilities.[74]

Orthopedic implants fabricated using the ML-aided design of architectural materials are functional with optimized mechanical performance. Such designs have the potential to be superior in terms of loading capacity and biocompatibility, compared with the existing expert designs. With advanced production methods through ML and advanced manufacturing methods, such as 3D printing, high-efficiency versions of these implants are prototyped and optimized quickly. This interaction between AI and AM has the potential to speed up the process of development, as researchers test and optimize many material structures relatively quickly. Consequently, the patients could have more effective implants that are more personalized, better resemble the mechanical properties of the native bone, and have better surgical outcomes and shorter healing periods.[75]

Machine learning and AI are applied for clinical decision-making to increase the safety of patients and clinicians' reliability. These include the applications used in risk assessment, outcome assessment, and imaging. It has also been proven that such technologies can predict patient deterioration and possible adverse events that take place. AI and ML algorithms reveal minor patterns and anomalies that are overlooked by human clinicians through the analysis of larger amounts of patient data. Such an increased predictive ability enables more proactive and personal patient care, which possibly eliminates readmission and plays a positive role in the overall patient health.[76]

Although tremendous improvements have been made with ML in scaffold design and orthopedics, challenges still exist. The use of AI in clinical environments may have complexities that lead to impediments in the large-scale implementation of AI. Hence, additional studies are required to make ML models more accurate and effective in clinical settings.[77] Ethical considerations and data privacy issues of AI in the healthcare sector must be considered to ensure ethical use. Computer interfaces are designed such that they are user-friendly, and explainable AI models can be used by healthcare practitioners. AI scholars, clinicians, and bioengineers must work together to optimize and confirm ML algorithms in scaffold design and orthopedics.[78] Moreover, it is necessary to develop strong regulations and guidelines for medical technologies driven by AI to ensure the security and confidence of patients regarding novel methods.

DISCUSSION

There is strong evidence to support the use of FEM, CFD, and ML to predict and enhance the performance of scaffolds.[79] Researchers have developed superior computer techniques. Such techniques assist them to modify the characteristics of scaffolds, such as porosity, rigidity, or disintegration speed. This further resembles the actual tissues of scaffolds. Computer modeling of the interactions between cells and scaffolds, as well as the dynamics of nutrient diffusion, enables engineers to develop more biomimetic structures.[80]

A detailed plan involving FEM, CFD, and ML, commonly used in designing scaffolds, is shown in Figure 11. Their predictions are accurate depending on the adopted modeling strategies. More sophisticated methods in these directions are nonlinear material modeling, topology optimization, and multi-scale FEM or multi-physics FEM structural analysis. Biophysical and mass transport signals are simulated by patient-specific FEM and CFD. In computing, ML approaches, such as supervised learning models, deep learning, hybrid ML–FEM frameworks, and fuzzy inference systems, assist in streamlining information. They combine mechanical behavior, fluid dynamics, and intelligent optimization within one model and boost the forecasting of a scaffold behavior.[81–83]

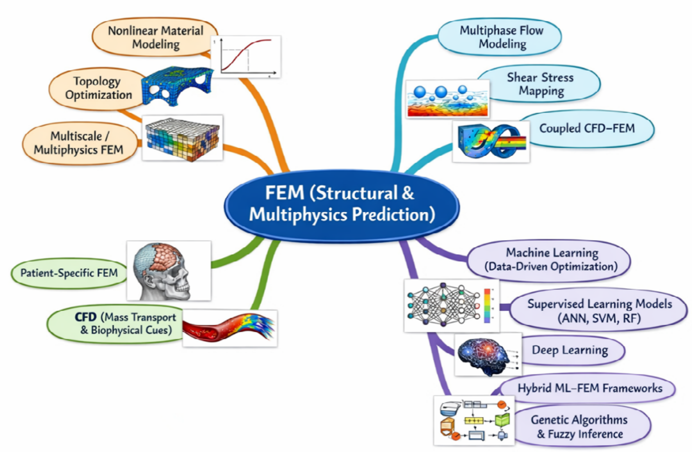

FIGURE 11. Finite element modeling approaches for scaffold prediction.[81–83] (Used under a Creative Commons Attribution 4.0 International License [CC BY 4.0])

Transition to data-driven and AI-based strategies is decreasing the dependence on trial-and-error experimentation and propelling advances in patient-specific working scaffolds. This shift makes it possible to predict the material behavior in scaffolds more reliably and optimally before material fabrication. These data are used as a large-scale set of material properties, cell characteristics, and clinical outcomes to utilize ML algorithms to advise scaffold designing. Consequently, the discipline is becoming closer to fulfilling the promise of genuinely patient-specific tissue engineering-based solutions that accommodate the needs and anatomical disparities of individual patients.[84]

As shown in Table 1, advanced scaffold manufacturing employs 3D bioprinting, electrospinning, SLA, SLS, digital light processing (DLP), and FDM, along with computational optimization (FEA, CFD, multi-physics modeling, and fuzzy inference). Natural polymers (collagen, gelatin, and alginate), synthetics (PLA and PCL), and composites enable tunable mechanics and bioactivity. Hierarchical multi-scale designs control porosity and gradients to mimic tissues. Application-specific optimization enhances bone, cartilage, and vascular scaffold performance.

TABLE 1. Critical trends in advanced biomedical scaffold manufacturing.

Methodology	Scaffold Type/Material	Mechanical Properties/Values of Porosity	Optimization/Modeling Approach
Multi-physics modeling with 3D bioprinting	Light-based 3D-printed biological scaffolds	Compressive modulus: 0.5–5 MPa; porosity: 60–80%	Multi-physics model integrating fluid dynamics, oxygen mass transfer, cell oxygen consumption, and cell growth processes.[85]
FEA with 3D printing	Bone scaffolds (HA nanoparticles functionally graded materials)	Compressive strength: 10–150 MPa; elastic modulus: 1–15 GPa; porosity: 40–70%	Parametric FEM considering pore shape, CAD modeling from medical images.[86]
CFD with bioprinting	Self-supporting perfusable tissue constructs (SSuPer)	Elastic modulus: 0.1–1 MPa; porosity: 75–90%	CFD modeling analyzing flow characteristics (net force, pressure distribution, shear stress, and oxygen distribution) through micro-channel patterns.[87]
Electrospinning	Nanofibrous scaffolds (poly(L-lactic acid [PLLA]), collagen, Nylon 6,6	Tensile strength: 1–10 MPa; elastic modulus: 50–500 MPa; porosity: 70–90%	Dual extrusion electrospinning for geometric control, hierarchical structure design.[88]
FDM with FEA validation	Mandibular graft scaffolds (polylactic acid)	Compressive strength: 40–65 MPa; elastic modulus: 2–3 GPa; porosity: 55–70%	Topological optimization methods combined with FEM, CBCT image reconstruction.[89]
Extrusion-based 3D bioprinting with computational optimization	Gelatin-based bioink scaffolds	Compressive modulus: 10–100 kPa; porosity: 80–95%	Fuzzy inference system (FIS) with four inputs (concentration, flowrate, speed, and temperature) and precision/printability outputs.[90]
Stereolithography (SLA)	BTE scaffolds (photopolymer materials)	Elastic modulus: 100–500 MPa; compressive strength: 5–20 MPa; porosity: 50–75%	Controlled architecture fabrication with micrometer-level resolution, porosity, and pore size optimization.[91]
DLP with post-processing	Polyacrylamide-alginate hydrogel scaffolds	Compressive modulus: 20–200 kPa; porosity: 70–85%	Two-step process: DLP printing followed by Fe ion post-processing for secondary crosslinking.[92]
SLS	Multilayer osteochondral scaffolds (PCL and HA/PCL microspheres)	Compressive strength: 5–80 MPa; elastic modulus: 0.5–2 GPa; porosity: 40–60%	Bio-inspired multilayer design with gradient composition via SLS technique.[93]
CFD for bioprinting optimization	Shear-thinning biomaterials (alginate and gelatin)	Compressive modulus: 5–50 kPa; porosity: 85–95%	Numerical analysis of extrusion process in single-nozzle dispensing system with static mixer.[94]

Note: CAD: computer-aided design; CFD: computational fluid dynamics; FDM: fused deposition modeling; DLP: digital light processing; FEA: finite element analysis; SLS: selective laser sintering; HA: hydroxyapatite; PCL: polycaprolactone; BTE: bone tissue engineering.

Figure 12 outlines the integrated process of scaffold fabrication for bone regeneration applications. The workflow begins with the designing of a porous scaffold, followed by 3D printing to produce the desired geometry. After printing, scaffold freeze-drying was applied to coat it with a composite of alginate and HA to enhance bacterial activity and facilitate tissue attachment. In the bottom part, numerical simulations, that is, representative volume element (RVE) and FEM, are presented to evaluate the mechanical properties of scaffold with stress–strain relationships and elastic modulus. Microscopic studies of surface morphology and element distribution were performed using field-emission scanning electron microscopy with energy dispersive spectroscopy (FE-SEM-EDS), mineral phase detection using X-ray diffraction (XRD), and high cell compatibility of experiments with cell viability results. Finally, the right side depicts the clinical translation in which the optimized bioactive scaffold is introduced to a damaged bone fragment so that efficient tissue regeneration and functional recovery are achieved. This strategy shows synergy in the designing, simulation, and experimentation of advanced bone repair.[95]

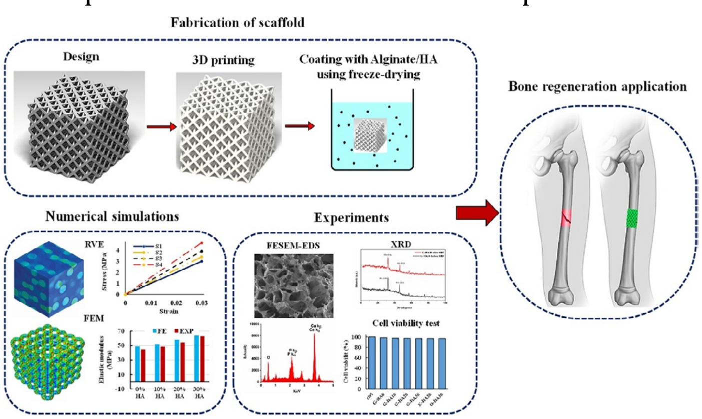

FIGURE 12. Fabrication of 3D-printed hydroxyapatite (HA) by freeze-drying.[95] (Used under a Creative Commons Attribution 4.0 International License [CC BY 4.0])

The issues in translating computational predictions to clinical practice remain, specifically in manufacturing variability, in vivo validation, and integration of degradation and tissue regeneration models. The literature highlights the necessity of multidisciplinary iterative workflows comprising a combination of computational tools.[96] Future studies should aim to create further refined computational models, considering manufacturing variability and in vivo conditions.

CONCLUSIONS

Development of computational modeling, simulation, and optimization has brought immense contributions to the sophisticated production of biomedical scaffolds. Such innovations have allowed the architecture, porosity, and mechanical properties of scaffolds to be brought under more consistent control. Presently, scaffolds can be customized to the needs and types of tissues, and researchers can design scaffolds that they believe are more efficient in the repairing and regeneration process of tissues. The incorporation of smart materials and bioactive constituents into scaffolds has also provided new opportunities to make dynamic and responsive environments that even better mimic the behavior of natural tissues. CFD and mathematical process modeling, including FEM, are important in measuring the effectiveness of scaffolds. With sophisticated simulation methods, such as computer modeling of mechanics, fluid mechanics, and mass transport in scaffolds, the researchers are able to investigate the mechanics of scaffolds, fluid flow patterns, and mass transport. In scaffold prediction, nonlinear and multiscale FEM with topology optimization applied in mechanical analysis, CFD and FEM–CFD coupling applied in transport and mechanobiology, are the fields of interest. ML surrogate models and multiscale predictive frameworks can also be used to enable the efficient design and optimization of complex scaffold models. The behavior of scaffold in different conditions is studied by taking into account many factors, such as scaffold geometry, material properties, and the behavior of cells.

Moreover, such computational tools can be used to optimize the designing of scaffolds, minimize the time-consuming process of experimental validation, and reflect on formulating more successful tissue engineering applications. Such data-driven and ML design methods change scaffold design, predict properties, and optimize parameters. Advanced methods allow the exploration of very large design spaces within a short period of time, exposing new scaffold design architectures with superior performance properties. By using big data and advanced algorithms, researchers are able to determine how combinations of material data (MD), geometries, and manufacturing processes are optimized to meet the needs of a particular tissue engineering application. In addition to the faster development of personalized scaffolds, the data-driven method also offers a higher probability of clinical success because it more closely resembles the sophisticated microenvironment of native tissues.

Computational techniques are combined to create biomimetic scaffold structures that support tissue regeneration and achieve better clinical outcomes. Such computational methods provide a high degree of control over scaffold architecture, porosity, and mechanical strength. By imitating elaborate hierarchical systems in natural tissues, biomimetic scaffolds have the potential to drive development, multiplication, and differentiation of cells. This can then be implemented using state-of-the-art structural design and manufacturing processes, including 3D printing, to create the best scaffold geometries with high fidelity. Bringing computational predictions into the clinic continues to be difficult, in part because of manufacturing variations, live animal testing, and model grounding.

More effective computer models should be discovered in future research and multidisciplinary workflows should be developed. To fill the gap between theoretical considerations and real-world practice of regenerative medicine, computational scientists, bioengineers, and clinicians are needed in this area of research.

AUTHOR CONTRIBUTIONS

Writing–Original Draft Preparation, A.M.; Formal Analysis, A.M.; Writing–Review & Editing, H.V.; Data Curation, H.V.; Supervision, H.V.

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CONFLICTS OF INTEREST

The authors declare they have no competing interests.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

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CONSENT FOR PUBLICATION

Not applicable.

FURTHER DISCLOSURE

Not applicable.

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Case Report

Virtual Reality in Hand Pathology Rehabilitation: A Case Series Report

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ABSTRACT

Background: This case series uniquely integrates virtual reality (VR) into the rehabilitation of diverse hand pathologies, highlighting its potential to enhance patient engagement and therapeutic outcomes. By combining traditional physical therapy with immersive VR exercises, this study contributes to the scientific literature by demonstrating the broad applicability and effectiveness of VR across different clinical scenarios. **Case Presentation:** Patients presented with severe pain, swelling, limited range of motion, reduced grip strength, and functional deficits resulting from fractures, congenital anomalies, and chronic inflammatory diseases. Baseline assessments using the Disabilities of the Arm, Shoulder, and Hand (DASH) score, the Patient-Rated Wrist/Hand Evaluation (PRWHE), and the Numeric Rating Scale (NRS) for pain revealed significant impairments. **Results:** Diagnoses included radius fractures, triangular fibrocartilage complex (TFCC) lesions, functional deficits from Wegener's vasculitis, wrist fractures, and congenital syndactyly. Therapeutic interventions consisted of standard physical therapy augmented with VR-based rehabilitation using the Oculus Meta Quest 2 and Hand Physics Lab software. Over three months, patients demonstrated significant improvements in functional outcomes and pain reduction, as evidenced by improved DASH, PRWHE, and NRS scores. Adherence to the VR therapy was high, and it was well tolerated with minimal adverse events. **Conclusion:** This case series demonstrates that VR can serve as a powerful adjunct to traditional rehabilitation methods, offering an effective approach to improve patient outcomes in hand pathology treatment. This innovative strategy enhances patient engagement and motivation, facilitating significant functional recovery and pain management.

Keywords—*Virtual reality rehabilitation, Hand pathology, Case report, Functional recovery, Pain management.*

INTRODUCTION

The human hand is a complex organ composed of numerous muscles, tendons, nerves, and bones, all working in harmony to perform intricate tasks essential for daily living.[1] The high density of sensory receptors and the intricate structure of the hand make it particularly susceptible to a wide range of pathologies, from traumatic injuries such as fractures and tendon tears to chronic conditions including arthritis and neuropathies.[2–4] Traditional rehabilitation for hand pathologies typically involves repetitive exercises aimed at restoring range of motion (ROM), strength, and dexterity.[5,6] However, these exercises are often monotonous, painful, and demotivating, leading to decreased patient compliance and suboptimal outcomes.[7]

In recent years, the integration of advanced technologies into rehabilitation practices has shown promising results in enhancing patient engagement and improving therapeutic outcomes.[8–12] One such technology is VR (Figure 1), which offers an immersive, interactive environment that can transform the rehabilitation experience. VR systems provide multi-sensory feedback, including visual, auditory, and haptic inputs, which can significantly enhance the rehabilitation process. By incorporating game-like elements, VR can increase motivation, adherence to rehabilitation protocols, and ultimately the efficacy of the therapy.[13–16]

FIGURE 1. The Oculus Meta Quest 2 VR headset and controllers used for immersive rehabilitation exercises in patients with hand pathology. This device was combined with the Hand Physics Lab software to deliver interactive and engaging therapeutic tasks.

This case series is unique in its application of the Oculus Meta Quest 2 VR headset combined with the Hand Physics Lab software for the rehabilitation of various hand pathologies. The Oculus Meta Quest 2 is a state-of-the-art VR system that provides high-quality, immersive experiences, while the Hand Physics Lab software offers a range of exercises designed to improve hand function through engaging and interactive tasks. This study examines the use of this VR system in a diverse group of patients with different hand pathologies, including fractures, ligament injuries, congenital anomalies, and chronic inflammatory conditions.[17,18]

The novelty of this study lies not only in the use of advanced VR technology but also in its methodological approach. Each rehabilitation session was meticulously structured to include 40 min of traditional therapy focused on ROM and muscle strength, followed by 20 min of VR-based exercises. This combination was designed to maximize therapeutic benefits by leveraging the strengths of both conventional and innovative rehabilitation techniques. Additionally, the study employed validated outcome measures, including the Disabilities of the Arm, Shoulder, and Hand (DASH) score, the PRWHE, and the NRS for pain, to provide a comprehensive assessment of patient progress.

This case series provides detailed insights into the potential of VR to enhance the rehabilitation process for hand pathologies. It demonstrates how VR can be tailored to meet the specific needs of individual patients, offering a flexible and adaptive approach to therapy. By documenting the progress of patients with diverse conditions, this study contributes to the growing body of evidence supporting the use of VR in rehabilitation medicine and underscores the need for further research to optimize and standardize VR-based therapeutic protocols.

The Oculus Meta Quest 2 VR headset and controllers are utilized for immersive rehabilitation exercises in hand pathology patients.

Patient Information

Patient 1 (P1):

- **Age:** 58
- **Sex:** Male
- **Primary Concerns and Symptoms:** Severe functional deficit in the right hand due to Wegener's vasculitis, experiencing significant pain and limited mobility.

• **Medical, Family, and Psycho-Social History:** P1 has a history of systemic vasculitis diagnosed two years ago, affecting multiple organs, including the kidneys and respiratory system. The patient's family history includes cardiovascular diseases but no known genetic disorders. The patient lives alone and works in a sedentary job, but enjoys gardening as a hobby, which has been significantly affected by his hand condition.

• **Relevant Past Interventions with Outcome:** P1 underwent conventional physical therapy for six months, with limited improvement in mobility and persistent pain, leading to the consideration of VR-based rehabilitation as an adjunct therapy.

Patient 2 (P2):

• **Age:** 30

• **Sex:** Female

• **Primary Concerns and Symptoms:** Radius fracture and TFCC lesion, presenting with severe pain, swelling, and impaired wrist function post-surgery.

• **Medical, Family, and Psycho-Social History:** P2 has no significant medical history and a family history of hypertension. She is an active individual, working as a professional pianist, which has made the wrist injury particularly debilitating both professionally and personally.

• **Relevant Past Interventions with Outcome:** P2 underwent surgical repair of the radius fracture and TFCC lesion, followed by standard post-operative physical therapy. Initial progress was slow, with persistent pain and limited functional recovery, prompting the inclusion of VR therapy in her rehabilitation plan.

Patient 3 (P3):

• **Age:** 61

• **Sex:** Female

• **Primary Concerns and Symptoms:** Fracture of the wrist and proximal phalanges of the 3rd and 4th fingers, resulting in reduced grip strength, swelling, and chronic pain.

• **Medical, Family, and Psycho-Social History:** P3 has a history of osteoporosis, which contributed to the severity of her fractures. Her family history includes osteoporosis and type 2 diabetes. She is retired, lives with her spouse, and enjoys knitting and gardening, both of which have been affected by her hand condition.

• **Relevant Past Interventions with Outcome:** P3 was treated conservatively with immobilization and standard physical therapy. Despite these interventions, she experienced slow recovery and chronic pain, leading to the introduction of VR-based exercises to enhance rehabilitation outcomes.

Patient 4 (P4):

• **Age:** 17

• **Sex:** Male

• **Primary Concerns and Symptoms:** Bilateral congenital syndactyly (webbing of fingers) was surgically corrected in infancy, with current concerns regarding limited dexterity and occasional pain during fine motor tasks.

• **Medical, Family, and Psycho-Social History:** P4 has a family history of congenital syndactyly, affecting his father. He is a high school student involved in sports and music, with the hand condition affecting his ability to participate fully in these activities.

• **Relevant Past Interventions with Outcome:** P4 underwent surgical separation of the webbed fingers at a young age, followed by standard rehabilitation. While he achieved basic functionality, he continued to experience limitations in fine motor skills and occasional pain, leading to the integration of VR therapy into his treatment regimen.

Patient 5 (P5):

• **Age:** 68

• **Sex:** Female

• **Primary Concerns and Symptoms:** Wrist fracture causing pain, swelling, and decreased range of motion.

• **Medical, Family, and Psycho-Social History:** P5 has a history of rheumatoid arthritis, which complicated her recovery from the wrist fracture. Her family history includes rheumatoid arthritis and cardiovascular diseases. She is retired, lives with her partner, and enjoys activities such as cooking and gardening, both of which have been limited by her injury.

• **Relevant Past Interventions with Outcome:** P5 underwent surgical fixation of the fracture and received standard post-operative physical therapy. Progress was hindered by pain and limited range of motion, leading to the addition of VR exercises to her rehabilitation plan.

Patient 6 (P6):

- **Age:** 53
- **Sex:** Female
- **Primary Concerns and Symptoms:** Wrist fracture with persistent pain, stiffness, and limited function post-surgery.
- **Medical, Family, and Psycho-Social History:** P6 has no significant medical history and a family history of osteoarthritis. She works as a graphic designer, and the wrist injury has significantly affected her professional and personal life, particularly her ability to use a computer and create artwork.
- **Relevant Past Interventions with Outcome:** P6 received surgical treatment for the wrist fracture, followed by conventional physical therapy. Despite these efforts, she experienced persistent pain and functional limitations, prompting the incorporation of VR-based rehabilitation.

Patient 7 (P7):

- **Age:** 44
- **Sex:** Female
- **Primary Concerns and Symptoms:** Wrist fracture causing severe pain, swelling, and impaired function.
- **Medical, Family, and Psycho-Social History:** P7 has a history of chronic pain syndrome but no significant family medical history. She works as a teacher and engages in activities such as writing and playing sports, both of which have been affected by her wrist injury.
- **Relevant Past Interventions with Outcome**: P7 underwent surgical repair of the wrist fracture followed by standard physical therapy. Her recovery was slow, with ongoing pain and functional impairments, leading to the exploration of VR therapy as a supplemental treatment.

Clinical details and symptoms are summarized in Table 1.

All patients involved in this study provided written informed consent for the use of their clinical data for research purposes. As the study is observational and descriptive in nature, conducted within a research center, approval from the ethics committee was not required, in accordance with current guidelines that do not mandate such approval for non-interventional studies.

TABLE 1. Summary of patient information and clinical findings.

Patient	Age	Sex	Primary Concerns and Symptoms	DASH Score (T0)	PRWHE Score (T0)	NRS Score (T0)	Significant Physical Examination Findings
P1	58	Male	Severe functional deficit due to Wegener's vasculitis, significant pain and limited mobility	65	70	8	Swelling, visible deformity, tenderness, severely restricted ROM, reduced grip strength, decreased sensation
P2	30	Female	Radius fracture and TFCC lesion, severe pain, swelling, impaired wrist function post-surgery	55	60	7	Post-surgical scarring, residual swelling, tenderness, limited ROM, reduced strength
P3	61	Female	Fracture of wrist and proximal phalanges, reduced grip strength, swelling, chronic pain	60	65	7.5	Visible deformity, swelling, tenderness, restricted ROM, diminished grip strength
P4	17	Male	Bilateral congenital syndactyly, limited dexterity and occasional pain	50	55	6	Post-surgical scars, minimal tenderness, tightness, limited dexterity, reduced grip strength
P5	68	Female	Wrist fracture, pain, swelling, decreased range of motion	58	63	7	Swelling, deformity, tenderness, restricted ROM, diminished grip strength
P6	53	Female	Wrist fracture, persistent pain, stiffness, limited function post-surgery	57	62	6.5	Post-surgical scarring, mild swelling, tenderness, limited ROM, reduced strength
P7	44	Female	Wrist fracture, severe pain, swelling, impaired function	54	59	6	Swelling, slight deformity, tenderness, restricted ROM, reduced grip strength, intermittent tingling

Note: DASH: Disabilities of the Arm, Shoulder, and Hand; PRWHE: Patient-Rated Wrist/Hand Evaluation; NRS: Numeric Rating Scale for pain; ROM: Range of Motion; TFCC: Triangular Fibrocartilage Complex.

Patient demographics, primary concerns and symptoms, baseline DASH scores, PRWHE scores, and NRS for pain, along with key findings from the physical examination, are presented. This table illustrates the heterogeneity of the cohort and the severity of baseline impairments prior to VR integration.

CLINICAL FINDINGS

Diagnostic Assessment

Diagnostic Testing:

Each patient underwent a comprehensive diagnostic evaluation, including:

• **Physical Examination (PE):** Assessing swelling, deformity, tenderness, ROM, grip strength, and sensation.

• **Laboratory Testing:** Blood tests for inflammatory markers, especially for systemic conditions.

• **Imaging:** X-rays and MRIs to evaluate fractures, ligament injuries, and structural abnormalities.

• **Surveys:** DASH, PRWHE, and NRS for pain.

The diagnostic summary is provided in Table 2.

Diagnostic Challenges:

• **Access to Testing:** Logistical challenges for specialized imaging, particularly in rural areas.

• **Financial Constraints:** High costs of advanced imaging and repeated tests.

• **Cultural Barriers:** Varied perceptions of technology in rehabilitation affecting engagement.

TABLE 2. Diagnostic assessment and prognosis summary.

Patient	Primary Diagnosis	Differential Diagnoses Considered	Prognosis
P1	Functional deficit due to Wegener's vasculitis	Rheumatoid arthritis, systemic lupus erythematosus	Guarded
P2	Radius fracture and TFCC lesion	Carpal tunnel syndrome, De Quervain's tenosynovitis	Favorable
P3	Wrist and proximal phalanges fractures	Osteoarthritis, rheumatoid arthritis	Moderate
P4	Bilateral congenital syndactyly	Congenital hand anomalies, connective tissue disorders	Excellent
P5	Wrist fracture	Osteoporosis-related fractures, rheumatoid arthritis	Moderate
P6	Wrist fracture	Osteoarthritis, repetitive strain injury	Favorable
P7	Wrist fracture	Chronic pain syndrome, neuropathy	Favorable

Table 2 presents the summary of primary diagnoses, differential diagnoses considered, and prognosis for each patient included in the case series. This table highlights the clinical complexity and the expected outcomes associated with the various hand pathologies addressed.

Therapeutic Intervention

Types of Therapeutic Intervention

Each patient received a combination of standard physical therapy and VR therapy. Additional interventions included pharmacologic treatment, surgical procedures, and preventive self-care measures tailored to their specific conditions. Changes in therapeutic interventions are presented in Table 3.

• **Pharmacologic:** Pain management and anti-inflammatory medications.

• **Surgical:** Surgical repair for fractures and congenital anomalies.

• **Preventive:** Self-care education to prevent further injury and promote healing.

• **Rehabilitative:** Standard physical therapy and VR-based rehabilitation using the Oculus Meta Quest 2 and Hand Physics Lab software.

TABLE 3. Changes in therapeutic intervention.

Patient	Initial Intervention	Changes in Intervention (with Rationale)
P1	Conservative management, standard PT	Addition of VR therapy to enhance engagement and motivation due to limited progress with standard PT alone.
P2	Surgical repair, standard PT	Introduction of VR therapy to expedite functional recovery and improve wrist mobility post-surgery.
P3	Conservative management, standard PT	VR therapy added to address chronic pain and improve grip strength after limited improvement with standard PT.
P4	Surgical correction of syndactyly, standard PT	Integration of VR therapy to improve dexterity and reduce pain, enhancing engagement for a young patient.
P5	Surgical fixation, standard PT	Incorporation of VR therapy to aid in reducing pain and increasing ROM in the presence of rheumatoid arthritis.
P6	Surgical treatment, standard PT	Addition of VR therapy to address persistent pain and limited wrist function post-surgery.
P7	Surgical repair, standard PT	Introduction of VR therapy to improve functional recovery and maintain motivation due to chronic pain issues.

Administration of Therapeutic Intervention

• **VR Therapy** (Figures 2 and 3): Each session consisted of 60 minutes divided into:

40 minutes of standard physical therapy focusing on ROM and muscle strengthening.

20 minutes of VR-based exercises designed to enhance hand function through interactive tasks.

• **Dosage and Duration:**

20 sessions over three months, with sessions conducted 2–3 times per week.

Table 3 presents the initial interventions and subsequent modifications in therapeutic management for each patient. The rationale for introducing VR therapy is provided, highlighting its role as an adjunct to standard physiotherapy to enhance patient engagement, reduce pain, and improve functional recovery.

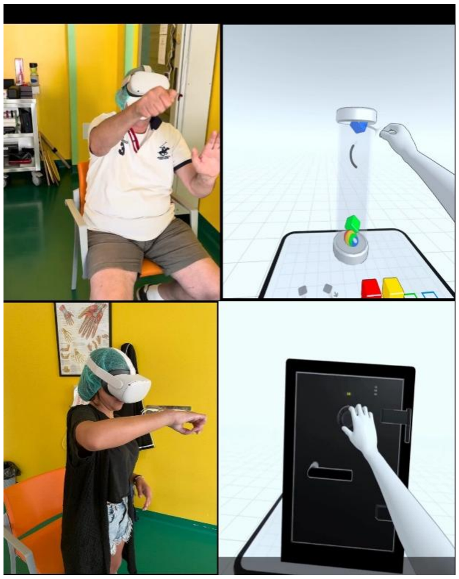

FIGURE 2. Patients engaging in VR therapy. Patients engaged in VR-based rehabilitation sessions using the Oculus Meta Quest 2 and Hand Physics Lab software. The immersive environment encouraged active participation and facilitated training of range of motion, strength, and dexterity in an engaging setting.

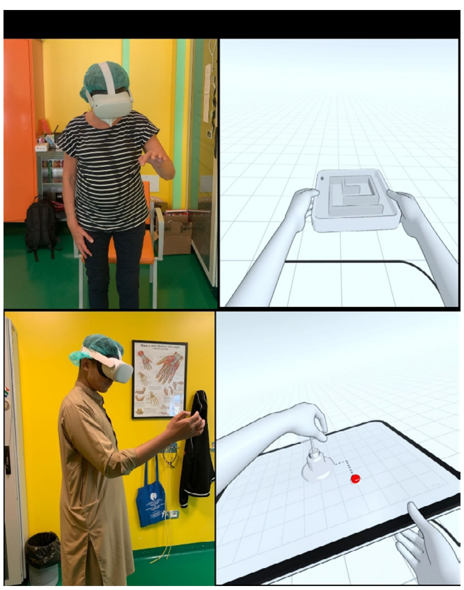

FIGURE 3. Interactive VR Rehabilitation Exercises. Examples of interactive VR rehabilitation exercises performed during therapy. Tasks included grasping, object manipulation, and precision movements, designed to enhance grip strength, functional dexterity, and motor coordination.

This case study adheres to the CARE Checklist[19] guidelines for reporting case studies.

FOLLOW-UP OUTCOME

Clinician and Patient-Assessed Outcomes

Follow-up evaluations were conducted at 1-month (T1), 2-month (T2), and 3-month (T3) intervals using the DASH, PRWHE, and NRS scales. Both clinician assessments and patient self-reports were included. Improvements in outcomes over time are summarized in Table 4.

TABLE 4. Follow-up and outcomes summary.

Patient	DASH Score (T1)	DASH Score (T2)	DASH Score (T3)	PRWHE Score (T1)	PRWHE Score (T2)	PRWHE Score (T3)	NRS Score (T1)	NRS Score (T2)	NRS Score (T3)
P1	55	48	40	62	55	48	7	6	5
P2	42	33	24	52	42	34	5	3	2
P3	50	41	33	58	48	41	6	5	4
P4	40	30	20	45	35	25	5	4	3
P5	50	42	35	55	47	40	6	5	4
P6	45	36	28	50	41	33	5	4	3
P7	44	36	29	48	40	32	5	4	3

Table 4 presents the follow-up outcomes at 1 month (T1), 2 months (T2), and 3 months (T3) for each patient, including DASH, PRWHE, and NRS scores. The table illustrates progressive improvements in functional ability and pain reduction across the cohort during the rehabilitation program.

This table summarizes the follow-up outcomes for each patient at 1-month (T1), 2-month (T2), and 3-month (T3) intervals. It includes scores from the DASH survey, the PRWHE, and the NRS for pain, highlighting improvements in functional abilities and reductions in pain over time.

Follow-up Diagnostic and Other Test Results

- **P1**: Reduced inflammatory markers; slight improvement in joint structure.
- **P2**: Proper healing of the radius fracture; reduced inflammation in TFCC.
- **P3**: Proper bone healing; improved grip strength.

• **P4**: Improved finger dexterity; reduced tightness in surgical areas.

• **P5**: Good bone healing; stable rheumatoid arthritis markers.

• **P6**: Good wrist fracture healing; improved ROM.

• **P7**: Proper healing; improved wrist function and reduced pain.

Intervention Adherence and Tolerability

• **Adherence:** Monitored through attendance records and patient self-reports. High adherence was noted.

• **Tolerability:** VR therapy was well tolerated. Feedback collected through surveys and direct interviews.

Adverse and Unanticipated Events

• **P1:** Mild dizziness during initial sessions, resolved with adjustments.

• **P2:** Temporary increase in pain after first session, managed with therapy intensity adjustments.

• **P3:** No adverse events reported.

• **P4:** No adverse events reported.

• **P5:** Mild VR-induced motion sickness, resolved with shorter sessions.

• **P6:** Mild wrist discomfort during some VR tasks, managed by modifying exercises.

• **P7:** No adverse events reported

Patient Perspective

The integration of VR into my rehabilitation program was transformative. Initially, I was skeptical about using technology for therapy, but the immersive and engaging nature of VR made the exercises enjoyable and less monotonous. The real-time feedback and interactive tasks kept me motivated, allowing me to observe my progress after each session. This contrasted sharply with traditional therapy, which often felt repetitive and frustrating. The VR sessions not only helped reduce my pain but also significantly improved my hand function. I felt more involved in my recovery process, which boosted my confidence and commitment to therapy. Additionally, performing exercises in a virtual environment provided a sense of accomplishment and distraction from the discomfort associated with physical therapy. The personalized VR tasks made each session feel tailored to my specific needs and limitations. Overall, I found VR therapy to be highly effective and a valuable addition to my rehabilitation, and I would highly recommend it to others undergoing similar treatments.

DISCUSSION

The integration of VR into hand pathology rehabilitation demonstrates substantial potential, offering an innovative approach that enhances patient engagement and therapeutic outcomes. This case series, which includes a diverse group of patients with various hand pathologies, highlights the broad applicability of VR technology across different clinical scenarios. The use of validated outcome measures, such as the DASH survey, the PRWHE, and the NRS for pain, provides a robust assessment of functional improvements and pain reduction, offering a comprehensive evaluation of the therapy's effectiveness. A key strength of this study is its innovative application of VR in rehabilitation, creating a stimulating environment that promotes active participation. These findings are consistent with those of Sveistrup[20] and Hoffman et al.[21] who demonstrated that VR can enhance patient engagement and reduce pain perception, respectively. The diverse patient population included in this study, ranging from acute injuries to chronic conditions, further underscores VR's versatility in addressing different clinical needs. However, the study has certain limitations. The small sample size restricts the generalizability of the findings, highlighting the need for larger studies to validate these preliminary results. Additionally, the short follow-up period of three months may not fully capture the long-term benefits and potential challenges associated with VR-based rehabilitation.[22] The reliance on patient self-reports for some outcomes introduces potential bias, highlighting the need for objective measures and extended follow-up periods to confirm these findings. The scientific rationale for incorporating VR into rehabilitation is based on its ability to provide immersive, multi-sensory feedback and gamified experiences that enhance patient motivation and adherence. VR environments engage patients more effectively than traditional therapy methods, promoting sustained participation and facilitating neuroplastic changes that support functional recovery. By integrating VR with standard physical therapy, this study aimed to leverage these benefits to address the limitations of conventional rehabilitation, particularly regarding patient engagement and motivation.[23] The findings from this case series are consistent with the broader evidence supporting the efficacy of VR in rehabilitation. Improvements in DASH, PRWHE, and NRS scores across all patients indicate that VR can enhance functional recovery and pain management in hand pathology rehabilitation. Nevertheless, the noted limitations highlight the need for further research to optimize VR therapy protocols and validate their effectiveness in larger, more diverse populations. In conclusion, this case series demonstrates the potential of VR as a transformative tool in the rehabilitation of hand pathologies. Integrating VR technology into standard therapy protocols led to significant improvements in functional outcomes and pain reduction across a diverse patient population. Despite the constraints of a small sample size and short follow-up period, the findings suggest that VR can enhance patient engagement and therapeutic efficacy. Further research with larger cohorts and extended follow-up is required to confirm these results and refine VR-based rehabilitation protocols. The primary takeaway is that VR holds promise as an innovative adjunct to traditional rehabilitation, providing a compelling approach to improve patient outcomes in the treatment of hand pathologies.

AUTHOR CONTRIBUTIONS

All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

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DATA AVAILABILITY STATEMENT

Not applicable.

CONFLICTS OF INTEREST

The authors declare they have no competing interests.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Informed consent has been obtained from all individuals included in this study. Requests for further information regarding ethical approval can be directed to the corresponding author.

CONSENT FOR PUBLICATION

Not applicable.

FURTHER DISCLOSURE

Not applicable.

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ORIGINAL RESEARCH ARTICLE

Restoring Global Offset Enhances Gluteus Medius Muscle Activity Following Total Hip Arthroplasty

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ABSTRACT

Background: There is limited evidence investigating how the summed measure of femoral offset (FO) and acetabular offset (AO), known as global offset (GO), correlates with clinical outcomes, especially for postoperative abductor muscle strength. The aim was to assess (1) how changes in GO impact hip joint abductor muscle activity of the treated hip following total hip arthroplasty (THA) using surface electromyography (sEMG) and (2) to determine if such variations affect clinical and functional outcomes. **Methods:** 123 consecutive hips undergoing primary unilateral THA between October 2015 and October 2016 were prospectively assessed. The anterolateral approach in a supine position was used for each patient. Patients were divided into three groups according to postoperative GO measurements on the operated side and the contralateral side as follows: Group 1, GO < 4.5 mm (reduced); Group 2, GO = 5 ± 0.5 mm (restored); and Group 3, GO > 5.5 mm (increased). Based on their inclusion as the initial members of that group, 20 patients were selected consecutively for each cohort. The Kruskal–Wallis test was used to compare differences of mean sEMG improvements across the cohorts and to examine the influence of GO measurements on improvement in patient-reported outcome measures. **Results:** Significant improvement in postoperative muscle activity was observed across all groups ($p < 0.05$), with the restored GO group showing the greatest enhancements in gluteus medius and tensor fascia latae EMG activity ($p > 0.05$). The Kruskal–Wallis test revealed statistically significant differences in improvement in gluteus medius activity, particularly between the reduced and restored GO groups ($p < 0.05$), indicating that restoring the GO is associated with higher postoperative muscle activation. Significant improvement in the Harris Hip Score and EuroQol 5 Dimension scoring was observed within each cohort. **Conclusion:** Surgical restoration of GO for optimizing postoperative muscle activity should be respected. However, the direct impact of these biomechanical adjustments on patient-reported outcomes in the short term appears minimal..

Keywords—*Anterior-based muscle sparing approach, Electromiography, Anterolateral approach, Gluteus medius, Offset.*

INTRODUCTION

Optimal placement of prosthetic components and the restoration of hip geometry are paramount for achieving high satisfaction and good functionality following total hip arthroplasty (THA) surgery.[1] The joint reaction forces (JRFs) across the hip joint depend on two components: femoral offset (FO) and acetabular offset (AO).[2,3] Therefore, it is essential to restore the lever arm of the abductor mechanism for the biomechanics and long-term success of hip replacement. It is also imperative to understand the maximum offset increase that can be tolerated to enhance joint stability without sacrificing the abductor muscle strength and the patient's discomfort.

Recreating physiological/pre-pathological femoral offset during THA plays a pivotal role in enhancing joint stability, thereby lowering the likelihood of dislocation and minimizing polyethylene wear.

Many studies have explored the effects of femoral offset modifications on the overall outcomes of THA.[4–6] However, femoral offset does not account for the alterations resulting from diverse placements of the acetabular cup.

There is limited evidence investigating how the summed measure of FO and AO, known as global offset (GO), correlates with clinical outcomes, especially for postoperative abductor muscle strength. Dastane et al. found that computer-navigated THAs with a mini-posterior approach achieved a 95% restoration ratio of GO, also qualitatively assessing muscle strength through clinical examination.[6]

Mahmood et al. evaluated the recovery proportions of GO in standard THA surgeries, demonstrating decreased values, compared to Dastane's restoration ratio, reporting 33% of restored GO.[6,7] They found that the group with reduced GO was associated with poorer abductor muscle strength assessed through an electronic dynamometer.[7] However, both methods used to assess muscle strength provided only an estimation, rather than directly showing the actual activity of the abductor muscles. Moreover, no solid evidence reporting how different acetabular and femoral reconstruction parameters affect the response of the abductor muscles has been proposed, especially for anterior-based muscle sparing (ABMS) approach in THA surgery.[8]

This study aimed to investigate the impact of postoperative GO changes on activities of the gluteus medius (GM) and tensor fascia latae (TFL) and patient-reported outcome measures (PROMs) in individuals undergoing THA using surface electromyography (sEMG).

MATERIALS AND METHODS

Study Design and Settings

In all, 123 patients and 123 consecutive hips undergoing primary unilateral THA between October 2015 and October 2016 at a single Institution were enrolled and prospectively assessed. The final follow-up was conducted at 12 months postoperatively. Data collection was performed by two independent residents. After surgery, patients were divided into three groups based on the postoperative GO measurements of the operated hip, compared to the unaffected contralateral hip (Figure 1):

• Reduced (Group 1): GO of the operated hip was < 4.5 mm, compared to the contralateral hip

• Restored (Group 2): GO of the operated hip was equal to 5 ± 0.5 mm, compared to the contralateral hip.

• Increased (Group 3): GO of the operated hip was > 5.5 mm, compared to the contralateral hip.

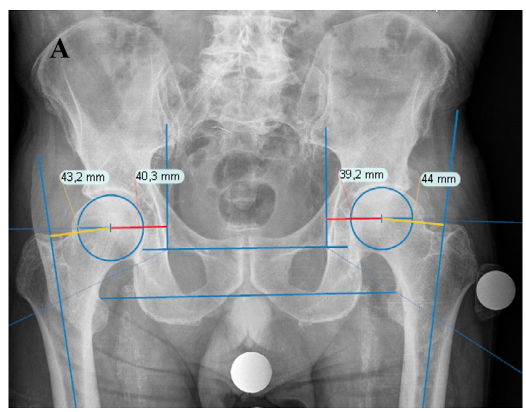

FIGURE 1. The FO (yellow line) was measured as the perpendicular distance between the COR of the femoral head and the proximal femoral shaft axis. The AO (red line) was the perpendicular distance between the COR and a vertical line through the ipsilateral teardrop figure. GO was the sum of FO and AO. Radiographic assessment included 28-mm calipered antero-posterior (AP) radiographs of the hip and pelvis and latero-lateral (LL) with 15° of limb intra-rotation. FO, AO, and GO were measured pre- and post-operatively for each patient, in both affected and contralateral hip.

In all, 20 patients were selected per group. The parameters for group classification were chosen based on current literature and clinical relevance.[9–15]

The study was conducted according to the Helsinki Declaration and its later amendments.

The inclusion criteria were as follows: Tonnis grade III unilateral primary osteoarthritis (OA) of the hip, FICAT Stage 3 and higher avascular necrosis (AVN) of the femoral head, Crowe type I developmental dysplasia of the hip (DDH), and surgery performed with press-fit implants. Exclusion criteria included patients with contralateral hip with evidence of DDH Crowe Type II and higher, post-traumatic hip disease, Perthes disease, bilateral Tonnis grade III OA, previous surgery around the hip, primary bilateral THA, and without consent or unwilling to participate in the study. The exclusion criteria were set to ensure that the sample population consisted of individuals with a native contralateral hip.

All procedures were performed by three specialized hip replacement orthopedic surgeons using cementless acetabular component (Regenerex®; Zimmer Biomet, Indiana, USA) coupled with a cementless flat tapered wedge stem (Taperloc Microplasty®; Zimmer Biomet), a ceramic BIOLOX® head, and a vitamin E-stabilized highly cross-linked polyethylene.

The ABMS approach in a supine position with both legs draped sterile into the operative field was used for each patient.[8] The dissection of the hip was performed through the intermuscular plane between the TFL and GM, without any detachment of the abductor muscles. Surgeons aimed for neutral stem alignment for varus/valgus position and leg length restoration.

All patients underwent clinical and radiological preoperative assessment and out-patient follow-up assessment at 1 month, and 6 and 12 months at the same institution. Radiographic analysis was performed with the Traumacad software (CarestreamHelth, Rochester, NY), which was used to measure GO and leg length discrepancy (LLD).

The study was conducted following the ethical standards proposed by the Declaration of Helsinki and its subsequent amendments. All patients had provided informed consent for the treatment protocol, the operation protocol, and the rehabilitation and follow-up plan. All patients gave their written informed consent for participation and data collection and their anonymous use for scientific purposes; there was no financial interest involved. This study was conducted and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies.[16] The STROBE checklist was used to ensure comprehensive and transparent reporting of the study's methodology, data analysis, and results.

Primary Outcome

The primary outcome was to evaluate the influence of GO variation on hip joint abductor muscle strength of the treated hip. To perform a comparative analysis, an sEMG was performed to record the abductor muscle activity for all patients from each group. The examination was conducted preoperatively, and at 6 and 12 months. The muscle's activity was recorded with the Freeemg® sEMG system (BTS Bioengineering, Italy). Bipolar Ag/AgCl surface electrodes (Kendall, Germany) were placed on the skin over the GM and TFL muscles of the affected hip according to the European recommendations for sEMG.[17]

The subjects performed maximal voluntary isometric contractions (MVICs) to normalize the raw EMG data. For this purpose, subjects performed three 5-second MVICs keeping the leg involved at 30° of abduction and rested for 1 minute between each effort and during this test, participants did not receive manual resistance. To standardize each position and maintain balance, subjects were instructed to keep their pelvis level and their trunk in a vertical alignment while gently placing their fingertips on a table ledge. A computer algorithm determined the maximum root-mean-square amplitude recorded over a moving 500-millisecond average window across the three MVICs. The window of activity having the greatest amplitude was identified and the TFL and GM activities were expressed as a percentage of these maximal values. Mean sEMG amplitudes (mV) were recorded while patients performed a dynamic abduction moving the leg from 0° to 30° for three sets of 15 repetitions with rest for 1 minute between sets. The data acquired during dynamic exercise were normalized by calculating the amplitude of the electrical signal detected during the repetitions as a percentage amplitude detected during SVICs. Normalization provided a standard reference of electrical activity for the abductor activity, and all EMG data were expressed as a percentage of SVIC for statistical analysis.

Secondary Outcome

Harris Hip Score (HHS) and EuroQo 5 Dimension (EQ-5D) questionnaire were administered during every outpatient control.[18,19] Differences from pre- to postoperative in HHS and EQ-5D across cohorts were evaluated to assess for any clinical improvement differences across cohorts.

Risk of Bias

To limit any potential font of bias, all the above-mentioned procedures were standardized for each patient. During outpatient visits, the radiographic, EMGs, and functional data collection were performed by two independent residents and doubled-checked at the end of each session to assess for any discrepancies or data entry error. Any discrepancy was settled by a senior orthopedic surgeon.

Data Analysis

Statistical analyses were performed using the SPSS® software (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0; IBM Corp., Armonk, NY, USA). For descriptive statistics, data are expressed as mean ± standard deviation (SD). For inferential statistics, particularly when comparing mean values across different samples, we used standard error (SE) to better estimate the precision of sample's mean as it relates to the population mean. The main effect size was calculated as the mean difference of GO among cohorts. No missing data were recorded. The InterClass Coefficient (ICC) was calculated as absolute agreement between the observers about the GO and LLD measurements with 95% confidence intervals (95% CI). All statistical analyses were conducted using non-parametric methods. The Kruskal–Wallis test was used to compare the differences of the mean sEMG improvements and to examine the influence of GO measurements on PROMs improvement across all cohorts. Post hoc analysis was conducted with Mann–Witney test. Friedman test was used to test postoperative improvement in muscle activity. The level of statistical significance was set at $p < 0.05$. A Bonferroni correction was implemented for post hoc analysis ($\alpha/3 = 0.05/3 = \alpha1 = 0.0167$). A priori power analysis was conducted using the *statistical software* G*Power to determine appropriate sample size with equal allocation requiring the Kruskall–Wallis test to detect a medium effect size ($f = 0.5$) with a power of 0.9 ($1 - \beta$) at an alpha level of 0.05. A nonparametric alternative to ANOVA was chosen because the sample size was limited and the data could not have met the assumptions of normality. The analysis indicated that a total sample size of 54 participants was needed. The actual power achieved with this sample size was 0.90.

RESULTS

From the initial 123 patients, 63 patients were excluded for the following reasons: three did not give consent for participation, nine were implanted with cemented stems, 18 were diagnosed with bilateral Tonnis grade III OA, four underwent bilateral THA, three had radiographical signs of Paprosky ≥ 2 bone loss, 12 had a severe hemophilic arthropathy, 10 did not attend the preoperative radiographic protocol at the time of surgery, two have had previous surgery on the affected hip, one had a history of a contralateral fracture, and one suffered a Crowe ≥ 2 DDH. No patient was lost during the follow-up. Figure 2 presents a flow diagram illustrating the inclusion process for the final study population.

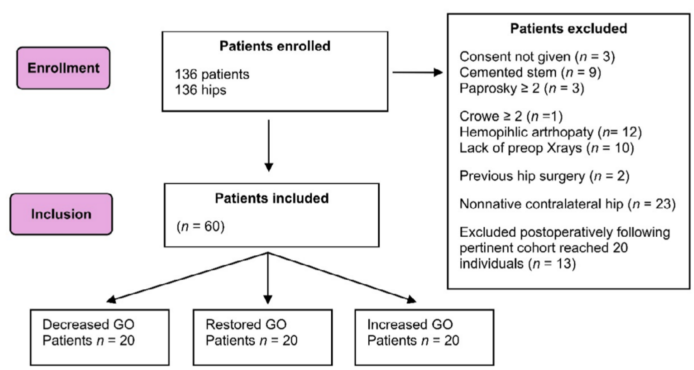

FIGURE 2. Flow diagram illustrating the inclusion process for the final study population.

Baseline characteristics of the final population across cohorts are shown in Table 1. The overall ICC for measurements between two observers was 0.942 (95% CI 0.889–0.972, $p < 0.001$) for GO and 0.966 (95% CI

0.901–0.992, $p < 0.001$) for LLD. The Kruskal–Wallis test showed a statistically significant difference in age and body mass index (BMI) distribution across all cohorts ($H = 2.01$, $p = 0.03$ and $H = 1.53$, $p = 0.025$, respectively), but not for preoperative LLD ($H = 2.54$, $p = 0.91$) and preoperative affected side and contralateral side GO ($H = 4.17$, $P = 0.78$ and $H = 3.66$, $p = 0.11$, respectively).

TABLE 1. Patient demographics across cohorts.

	Reduced	Restored	Increased	*p* value
Number of Hips	20	20	20	-
Gender (Female : Male)	11 : 9	12 : 8	13 : 7	-
Age at Surgery (yr)	66.8 ± 4.3	65.1 ± 5.8	67.9 ± 8.9	0.134
Height (m)	1.70 ± 0.08	1.75 ± 0.07	1.68 ± 0.09	0.311
Weight (kg)	77.7 ± 5.5	85.8 ± 3.5	81.5 ± 4.2	0.272
Body Mass Index (BMI; kg/m²)	26.9 ± 4.8	28.0 ± 3.1	28.9 ± 5.1	0.196
Diagnosis (Frequency)				-
Primary Osteoarthritis (OA) of The Hip	16	17	17	-
Avascular Necrosis of The Femoral Head (AVN)	2	1	1	-
Rheumatoid Arthritis (RA)	0	1	1	-
Mild Hemophilic arthropathy	1	0	1	-
Crowe Grade I Developmental Dysplasia of The Hip (DDH)	1	0	0	-

Note: Data are presented as mean ± SD.

Contralateral GO measures and pre- and post-operative affected side GO and LLD values across cohorts are shown in Table 2. The mean difference in GO changes from preoperative to postoperative were −7.8 mm in the reduced GO group (range −8.2 – −5.4), −0.3 mm (Range −3.2–3.5) in restored GO group, and +6.4 mm (Range 5.4–7.8) in the increased GO group.

TABLE 2. Patients hip metrics across the cohorts.

	Affected GO			Contralateral GO	LLD		
	Pre-operative	Post-operatove	p value		Pre-operative	Post-operative	p value
Reduced	45.88 ± 5.2	38.08 ± 6.2	< 0.001	46.36 ± 4.5	7.11 ± 1.6	0.91 ± 1.1	< 0.001
Restored	43.93 ± 3.4	43.63 ± 5.3	0.089	43.11 ± 3.9	6.97 ± 1.2	1.09 ± 0.9	< 0.001
Increased	41.12 ± 4.2	47.52 ± 5.7	< 0.001	41.43 ± 3.1	7.39 ± 1.7	1.5 ± 1.4	< 0.001

Note: Data are presented as mean ± SD. GO: global offset; LLD: leg length discrepancy.

Preoperative and postoperative PROMs are shown in Table 3. The Kruskal–Wallis results showed no significant differences in score improvements across the groups for HHS and EQ-5D ($H = 2.89$, $p = 0.19$, and $H = 1.12$, $p = 0.65$, respectively).

TABLE 3. Pre- and post-operative Harris Hip Score (HHS) and EQ-5D for each group at the final follow-up.

	Harris Hip Score			EQ-5D		
	Pre-operative	Post-operative	*p value*	Pre- operative	Post- operative	*p value*
Reduced	46.7 ± 14.4	85.2 ± 8.3	< 0.001	0.42 ± 0.24	0.81 ± 0.18	< 0.001
Restored	45.7 ± 13.2	93.4 ± 11.2	< 0.001	0.40 ± 0.19	0.85 ± 0.16	< 0.001
Increased	47.5 ± 13.7	94.2 ± 12.4	< 0.001	0.52 ± 0.64	0.84 ± 0.17	< 0.001

Note: Data (in mm) are presented as mean ± SE. EQ-5D: EuroQo 5 dimension.

Preoperative and postoperative SVICs% are shown in Table 4. Significant postoperative improvements in muscle activity measured through sEMG were observed for reduced, restored, and increased cohorts ($\chi^2 = 3.46$, $p < 0.001$, $\chi^2 = 0.21$, $p = 0.001$, $\chi^2 = 3.09$, $p = 0.002$, respectively). Specifically, in the decreased GO group, the GM and TFL exhibited notable increase in mean ± SE in EMG activity, with respective improvement of 8.1 ± 0.92 and 8.4 ± 1.25. The restored GO group had greater enhancements, with both GM and TFL recording respective mean ± SE increase of 11.4 ± 0.74 and 9.1 ± 0.84. The Increased GO group also demonstrated improvements, with the GM and TFL showing the respective mean ± SE increase of 10.1 ± 1.08 and 8.5 ± 0.76.

TABLE 4. sEMG amplitudes of the affected hip in each cohort during dynamic exercise expressed as a percentage of maximal voluntary isometric contraction (% SVIC) at the last follow-up.

		Pre-operative	Post-operative	*p* value
Reduced	Gluteus medius	48.8 ± 3.2	56.9 ± 2.6	< 0.001
	TFL	24.9 ± 4.1	33.3 ± 3.8	< 0.001
Restored	Gluteus medius	47.3 ± 2.3	58.7 ± 2.4	< 0.001
	TFL	25.2 ± 2.1	34.3 ± 3.1	< 0.001

		Pre-operative	Post-operative	*p* value
Increased	Gluteus medius	49.1 ± 3.1	59.2 ± 3.7	< 0.001
	TFL	25.7 ± 2.7	34.2 ± 2.1	< 0.001

Note: Data are presented as mean ± SD. sEMG: surface electromyography.

To assess impact on GM activity, the Kruskal–Wallis test was extended to compare differences in mean improvements across all cohorts, revealing a statistically significant difference ($H = 4.92$, $p = 0.04$). Post hoc pairwise comparisons using the Mann–Whitney *U* test with Bonferroni correction highlighted a significant difference between the reduced and restored GO groups in GM activity ($p = 0.01$), suggesting that restoration of GO is associated with higher postoperative muscle EMG activity, compared to a decreased GO. However, no significant differences were observed between reduced and increased GO groups ($p = 0.045$), or between the restored and increased GO groups ($p = 0.03$).

Additionally, the analysis of TFL activity across all three groups discovered no significant differences ($H = 0.28$, $p = 0.86$).

DISCUSSION

The most significant finding of the study is that restoring GO appears to be more beneficial in improving GM muscle activity postoperatively, compared to decreasing or increasing GO. The enhanced muscle activity associated with restoration of GO could contribute to improved stability and functioning of the hip joint, potentially reducing the risk of postoperative complications and accelerating the recovery process. A significant increase in the muscle activity for GM and TFL in all groups, particularly noted in the restored GO group, suggests that appropriate restoration of GO is crucial for optimizing muscle function post-THA. This is further supported by the post hoc analyses, which identified a significant difference in GM activity between the decreased and restored GO groups as well as between decreased and increased GO groups.

Another important finding is that although GO restoration may lead to better GM muscle activity outcomes, it does not significantly impact PROMs in the early term follow-up. While significant differences in muscle activity were observed, variations in GO did not translate into statistically significant differences in HHS and EQ-5D score improvements across the cohorts.

Finally, no effect on TFL activity was discovered in the current study across different cohorts. The differing impact of GO changes on TFL activity, compared to the GM, could be attributed to several factors related to their anatomical functions, biomechanical roles, and the specific effects of THA on hip joint mechanics. Both GM and TFL muscles have distinct roles in hip stability and movement, and GM is primarily responsible for stabilizing the pelvis during gait and mediating hip abduction, whereas TFL aids in hip abduction, internal rotation, and stabilization of the knee. Different functions and mechanical leverages may result in varied sensitivities to changes in hip geometry post-THA. THA can alter the length–tension relationships and mechanical advantages of hip muscles. Given the closer proximity of GM to the surgical site and its direct role in hip stabilization, changes in GO might more significantly affect its functioning. In contrast, TFL's contribution to hip stability and its action might be less directly influenced by changes in GO, thus explaining the lack of significant change in activity postoperatively.

A meta-analysis reported that following THA, postoperative abductor muscle strength was diminished, compared to the unaffected contralateral side.[20] Moreover, abductor muscle strength was reported as enhanced compared to preoperative levels, but still it did not appear to equalize with the strength of the unaffected contralateral side in cases of unilateral THA, even during follow-up sessions extending beyond 24 months.[20] The current study, focusing on EMG activity, rather than muscle strengths, aligns with these observations, suggesting a similar pattern of muscle recovery following THA.

Wongsak et al. have discovered more recently that hip abductor muscle power experiences a slight and insignificant decrease 2 weeks after surgery, followed by gradual improvement.[21] By the 3rd month post-surgery, both hip abductor muscles' power is significantly improved compared to preoperative levels. However, despite favorable magnetic resonance imaging (MRI) evidence of healing of the GM muscle, complete recovery of hip abductor muscle strength was not achieved at 6 months postoperative.[21] It is worth to mention that Wongsak et al. performed THAs via anterolateral approach (AL) by cutting the anterior one-third of GM. These different results could be explained by the different approaches used in the study population.

Interestingly, Lalevée et al. discovered a decrease in maximal isometric muscle activity of the GM TFL after AL approach THA in a series of 16 patients at the final follow-up of 1 year. These results differ from the current outcome, and these differences may arrive from a different sample size and patient demographics.[22]

Bahl et al. found that when acetabular offset and femoral offset remain unchanged from preoperative, the abductor muscles produce a significantly larger force according to the current results.[23] Tanaka et al. also found that the proximalization of the center of rotation (COR) after ABMS approach in THA surgery may cause a delayed recovery of abductor muscle strength.[24] This finding agreed with the notion that a reduced acetabular offset and a restored GO improve implant longevity and patient outcomes by lowering stress on femoral head.[13,25–27]

Finally, our study revealed a significant improvement in GM muscle activity following THA, particularly when GO was restored. However, these improvements in muscle activity did not translate into statistically significant differences in PROMs across different GO groups. Several factors may explain this apparent contradiction. Although HHS and EQ-5D are validated tools, they may not be sensitive enough to detect subtle functional improvements resulting from enhanced muscle activity. PROMs encompass various aspects of patient experience, including relief in pain, overall mobility, and psychological factors. While improved muscle activity is important, it may be overshadowed by other factors in the patient's overall assessment of their outcome. Significant differences in preoperative PROMs across cohorts, as mentioned in our limitations, may have influenced postoperative scores and potentially masked the effects of improved muscle activity. Lastly, patients may develop compensatory mechanisms that allow them to achieve satisfactory functions despite variations in muscle activity, thus equalizing PROMs across groups.

This study comes with its limitations. The sample size, while statistically adequate for detecting differences in muscle activity, presents a limitation regarding the generalizability of our findings. A larger sample size could provide robust insights, especially in relation to variability in PROMs. Additionally, while our cohorts were formed based on clear inclusion criteria, further standardization across patient demographics and preoperative conditions would strengthen the comparability and applicability of the results. Future studies should consider larger and more diverse populations and stricter cohort standardization to confirm these findings and enhance their external validity. Moreover, significant differences were found between preoperative PROMs across the cohorts, meaning that the included population was not standardized. Another potential limitation of our research is the lack of established protocols for using EMG to assess abductor muscle activity through specific movements. In this study, we standardized our measurements by requiring maximal contraction, and we used repetitive abduction movements to evaluate muscle activity despite the absence of a universally accepted gold standard for these procedures.

CONCLUSIONS

Surgical restoration of GO plays a meaningful role in optimizing postoperative gluteus medius activity following THA and should be pursued during preoperative templating and intraoperative execution. Restoring GO within ±0.5 mm of the contralateral native hip was associated with the greatest improvement of the abductor mechanism, supporting the biomechanical rationale that proper offset reconstruction preserves the abductor lever arm and enhances muscle efficiency. Surgeons should consider both femoral and acetabular offset together when assessing reconstruction adequacy.

AUTHOR CONTRIBUTIONS

Conceptualization, A.C.L., M.I., and M.V.; Methodology, A.C.L., M.I., and M.V.; Formal Analysis, F.L., P.F., R.C.; Investigation, A.C.L. and C.C.; Data Curation, C.C.; Writing–Original Draft Preparation, F.L., P.F., R.C.; Writing–Review & Editing, F.L., P.F., M.I., and R.C.; Visualization, C.C.; Validation, A.C.L. and C.C.

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DATA AVAILABILITY STATEMENT

The data supporting the findings of this study can be obtained upon request from the corresponding author, FL. These data are not publicly accessible due to restrictions related to compromising the privacy of research participants.

CONFLICTS OF INTEREST

The authors did not receive support from any organization for the submitted work. The authors certified that they had no affiliations with or involvement in any organization or entity with any financial interest, or nonfinancial interest, in the subject matter or the material discussed in this manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Written informed consent was obtained from all participants included in the study. The study was carried out in accordance with the World Medical Association Declaration of Helsinki.

CONSENT FOR PUBLICATION

Written informed consent was obtained from all participants included in the study for publication.

FURTHER DISCLOSURE

Not applicable.

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Review

Applications of Machine Learning in Histopathology: From Diagnostic Accuracy to Prognostic Insights

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ABSTRACT

Background: Histopathological examination remains the gold standard for evaluating morphological alterations in tissues and plays a pivotal role in both disease diagnosis and therapeutic decision-making. With the exponential growth of digital pathology, the integration of artificial intelligence (AI), particularly machine learning (ML) algorithms, has emerged as a transformative approach to optimize histopathological workflows. **Objective:** This review aims to systematically evaluate recent advances in ML applications within histopathology, focusing on their roles in enhancing diagnostic precision and enabling prognostic stratification across various malignancies. **Methods:** A comprehensive literature analysis was conducted, encompassing peer-reviewed studies that investigate the implementation of ML models in histopathological image interpretation, classification, segmentation, and outcome prediction. Emphasis was placed on convolutional neural networks, and ensemble learning techniques. **Findings:** Machine learning-based approaches demonstrate high sensitivity and specificity in the detection and classification of neoplastic lesions, particularly in breast, colorectal, thyroid, gastric, and head and neck cancers. These tools facilitate intraoperative consultation, mitotic figure quantification, and tumor grading, thereby improving diagnostic accuracy and reproducibility. Moreover, emerging prognostic models incorporating histopathological features show potential in predicting disease recurrence, overall survival, and treatment response, supporting the paradigm shift toward personalized medicine. **Conclusions:** The incorporation of ML into histopathological practice holds substantial potential to revolutionize diagnostic and prognostic processes. As algorithmic models continue to evolve and validate in clinical settings, their integration may redefine standard-of-care practices and bridge the gap between pathology and computational medicine.

Keywords—*Artificial intelligence, Histopathology, Cancer diagnosis, Digital pathology, Personalized treatment.*

INTRODUCTION

Histopathology, as a diagnostic method, constitutes a fundamental aspect of modern medicine by analyzing structural and cellular changes at the tissue level, playing a crucial role in the diagnosis and treatment of various conditions, including cancer.[1] The integration of artificial intelligence (AI) into healthcare holds significant potential to enhance both volume of histomorphological assessments and precision of histopathological diagnoses.[2]

The application of AI technologies in histopathology could revolutionize the diagnosis and treatment of diseases, such as cancer, by improving accuracy and introducing a new dimension to personalized medicine. Recent studies have demonstrated that advances in AI have significantly transformed the processes of disease diagnosis and classification.[3] AI methodologies, utilized in tasks such as object recognition, detection, and segmentation play a significant role in driving advancements within histopathological practice.[4,5] Current literature clearly highlights the efficacy of AI-based methods in enhancing diagnostic accuracy and expediting workflows in histopathology.[6] It is stated that the future research will further expand the applications of AI in this field.

THE WORKING PRINCIPLE OF ARTIFICIAL INTELLIGENCE

Artificial intelligence is associated with significant advancements in various fields, particularly pathology, by enabling advanced data analysis.[7] AI equips machines with cognitive abilities through computational networks (neural networks) that mimic biological nervous systems.[8] In a traditional algorithm, the computer executes predefined, explicitly programmed instructions each time it encounters a trigger. In contrast, AI can modify algorithms in response to learned inputs without human intervention. Machine learning (ML), a subset of AI, focuses on developing algorithms that use statistical analysis to make inferences by processing input data without explicit programming. Deep learning (DL), an evolution of ML algorithms, employs artificial neural networks in a hierarchical manner to extract higher-level features gradually from raw input.[9] In this context, the use of AI in healthcare holds significant potential in histopathology, offering high accuracy in the diagnosis and prognosis of diseases, such as cancer.

Machine learning algorithms form the core of AI by transforming input data into actionable outputs through coded instructions. As a subset of AI, ML applies statistical and mathematical modeling techniques to analyze large datasets rapidly and generate predictions or decisions with varying levels of autonomy.[10]

Machine learning can be categorized into supervised, unsupervised, and reinforcement learning, based on how models interpret data. In supervised learning, algorithms learn from labeled datasets to predict outcomes, whereas unsupervised learning involves identifying hidden structures in unlabeled data. Reinforcement learning, on the other hand, enables models to learn optimal actions through a feedback system of rewards and penalties.[11]

Deep learning, a subset of ML, utilizes multi-layered neural networks to extract hierarchical features from data and can operate in supervised, unsupervised, or semi-supervised settings. Deep learning approaches typically require extensive, high-quality datasets for effective training and are tightly linked to big data methodologies, leading to substantial demands on storage and computational resources.[12] These advancements collectively enable AI to efficiently process complex medical data, making it a powerful tool for clinical decision support and precision diagnostics in cancer.

APPLICATIONS OF ARTIFICIAL INTELLIGENCE IN HISTOPATHOLOGY

Artificial Intelligence in Diagnosis and Classification in Oncopathology

Artificial Intelligence is utilized to predict prognosis and treatment responses based on histological features.[13] In this regard, directly correlating various tumor characteristics, the surrounding microenvironment, and genetic profiles with survival outcomes and treatment responses to adjuvant/neoadjuvant therapy can provide valuable insights. Additionally, the use of AI in histopathological diagnosis and classification processes can enhance accuracy and precision in clinical applications.

In a 2024 study, ML was used to predict malignancy in thyroid nodules. The logistic regression model based on backward stepwise regression demonstrated high discrimination, with Area Under the Curve (AUC) values of 0.83 and 0.80 during the training and validation phases, respectively. AUC is a performance metric that measures the ability of a model to distinguish between classes, with higher values indicating better discrimination.[14] The nomogram developed with this model aims to reduce unnecessary surgeries and improve clinical decision-making by providing personalized risk assessments. In another study, AI-assisted Raman histology was used for intraoperative tissue diagnosis. High accuracy was achieved for meningiomas and gliomas, with an AUC value of 0.93 reported for predicting isocitrate dehydrogenase (IDH) mutations.[15] In this context, AI can enhance accurate intraoperative diagnoses, thereby improving surgical decision-making.

Artificial Intelligence-based research in histopathology has conducted analyses focusing on the differentiation of atypical and typical mitoses in breast and colon cancers. In the breast cancer study, AI models achieved an F1 score of 94.49% for detecting invasive carcinoma (the F1 score is a performance metric that combines precision and recall, offering a single measure of a model's accuracy in datasets where class distribution may be imbalanced). In the mitosis project, F1 scores were reported as 80.18% for mitosis, 97.40% for atypical mitosis, and 97.68% for typical mitosis layers. For the colon cancer study, the models achieved the overall F1 scores of 90.02% for invasive carcinoma, 94.81% for the submucosal layer, and 98.02% for vessels and lymph nodes.[16]

Additionally, Yoshida et al. developed the "e-Pathologist" software for classifying carcinoma, adenoma, and malignant lesions in gastric biopsies, achieving 90% sensitivity and 50% specificity.[17] In 2023, Wibawa et al. introduced an AI-based model for whole-slide analysis of head and neck cancers, particularly nasopharyngeal carcinoma.[18] This system accurately evaluated the spatial distribution and density of tumor-infiltrating lymphocytes (TILs: immune cells that migrate into the tumor microenvironment and play a critical role in the immune response against tumors). By assessing TIL distribution with high precision, the model provided significant prognostic information to guide personalized treatment strategies.[17,18] The literature also highlights that ML models can serve as valuable tools for assessing malignancy risk in oral lesions and for detecting and grading malignant lesions.[19,20] Collectively, these studies demonstrate the substantial potential of AI-based analyses in advancing cancer diagnosis and treatment planning.

The deep learning-based system developed by Lan et al. significantly reduced error rates of pathologists and diagnosis period for the analysis of 2020 gastric slide images.[21] Similarly, another study trained a neural model based on the Inception-v3 framework to classify whole-slide images of gastric biopsies into three categories: adenocarcinoma, adenoma, and non-neoplastic. The model was validated using a test cohort of 45 whole-slide images, achieving an accuracy of 95.6% and an AUC of 0.924.[22] These studies highlight the potential of AI to enhance both accuracy and efficiency of pathological diagnosis.

In 2019, Jeyaraj et al. achieved an accuracy of 91.4% (sensitivity: 0.94; specificity: 0.91) in the early diagnosis of oral cancer and in classifying malignant tumors and normal tissues using a dataset of 100 images.[23] These results demonstrated that AI-based models performed with high accuracy in histopathological analyses and were particularly effective in detecting invasive carcinoma, mitotic types, submucosal layer, and vascular and lymph node structures in breast and colon cancers.[24]

Artificial Intelligence holds significant potential for accelerating diagnostic processes and improving accuracy in these areas. By expediting diagnoses and enhancing clinical accuracy in cancers, such as breast, colon, and thyroid cancers, AI can contribute to improved surgical decision-making and personalized risk assessments.

Artificial Intelligence in Cancer Metastasis and Recurrence Prediction

Artificial Intelligence significantly contributes to survival analysis and clinical decision-making by predicting the risk of metastasis and recurrence in cancer patients. In 2024, AI-based models provided personalized survival predictions for patients with advanced non-small cell lung cancer (NSCLC) based on clinical and radiological features. The Random Survival Forest (RSF) model successfully distinguished poor survivors treated with pembrolizumab because of high programmed death-ligand 1 (PD-L1) expression and patients receiving targeted therapy for driver oncogenes.[25] In another study, a deep learning model was developed to predict lymph node metastasis in lung squamous cell carcinoma. The model demonstrated high performance using the ExtraTrees algorithm, achieving AUC values of 0.941 in the training set and 0.788 in the test set.[26]

Wang and colleagues trained a ML model using nuclear orientation, nuclear shape, tissue, and tumor architecture from hematoxylin and eosin (H&E)-stained tissue microarray (TMA) slides to predict recurrence in early-stage NSCLC.[27] Their model achieved accuracy rates of 82% and 75% in two independent early-stage NSCLC cohorts. These findings suggest that deep learning-based approaches have clinical value in predicting metastasis and survival outcomes in lung cancer. Studies indicate that AI-based approaches can guide survival analyses and clinical decision-making by predicting metastasis and recurrence risks in cancer treatment.

Prediction of Mutations Using Artificial Intelligence in Histopathology

Histopathology plays a crucial role in elucidating the molecular mechanisms of diseases by providing insights into the effects of mutations at cellular level. In this context, the potential of AI to detect subtle or hidden features that pathologists might overlook is highly compelling. Studies have reported that driver gene mutations or microsatellite instability can be predicted from H&E-stained images of certain cancer types.[28]

In a 2018 study, a deep convolutional neural network (DCNN, Inception-V3) was developed to classify lung cancer into adenocarcinoma, squamous cell carcinoma, and normal lung tissue. Additionally, the platform was trained to predict the most common mutations in 10 genes from histopathological images of lung adenocarcinoma. The predicted genes (STK11, EGFR, FAT1, SETBP1, KRAS, and TP53) exhibited AUC values ranging from 0.733 to 0.856.[29]

Although the sensitivity and specificity of this approach have not yet reached clinically significant levels, future advancements could significantly contribute to areas such as pre-sequencing sample selection, clonality assessment, and evaluation of tumor heterogeneity. Further studies utilizing advanced techniques such as laser capture microdissection to analyze genetic signatures in heterogeneous tumor foci may help to validate these findings.

Integration of Histopathology with Artificial Intelligence in Non-Cancer Fields

Histopathology plays a crucial role in diagnosing and understanding the pathogenesis of various inflammatory, infectious, and degenerative diseases, in addition to cancer, by enabling detailed examination of cellular changes. This capability guides both clinical practice and research. In this context, AI-assisted analyses significantly enhance the accuracy and efficiency of clinical decision support systems by facilitating an in-depth evaluation of cellular morphology in non-cancerous diseases.

In 2018, a convolutional neural network (CNN) model was developed to detect clinical heart failure using H&E-stained endomyocardial biopsies. The study utilized biopsy samples from 104 patients for model training and from an independent cohort of 105 patients for testing. The model achieved an AUC of 0.97 in detecting heart failure from H&E-stained whole tissue sections, surpassing the evaluations of two expert pathologists (AUC: 0.75).[30]

Similarly, a 2019 study developed a neural network model to distinguish between celiac disease, nonspecific duodenitis, and normal tissues. The model was trained and optimized on a dataset of 1018 duodenal biopsy images and later validated on an independent cohort comprising biopsies from 212 different patients. The performance of model was benchmarked against the evaluations of three gastrointestinal pathologists. The deep learning model achieved a high performance with an AUC > 0.95 for slide-level classification across all categories.[31]

Artificial Intelligence-assisted histopathological analyses have demonstrated significant advancements in diagnosing and prognosticating non-cancerous diseases. By enabling comprehensive evaluation of cellular morphology, these technologies contribute to the improvement of clinical diagnostic systems.

DISCUSSION

This review indicates the potential applications of AI in histopathology and highlights innovative developments in the field. AI holds significant promise, particularly in identifying and analyzing subtle or complex pathological features that may be challenging for pathologists to distinguish.[32] ML can be applied to various tasks in histopathological interpretation, including cancer classification, tumor grading, genetic mutation prediction, cell classification, treatment planning, and survival prediction.[33]

The integration of AI into healthcare has a significant potential to accelerate early diagnosis, provide more accurate diagnoses, uncover novel insights into human biology, and advance personalized patient care. In the field of histopathology, AI-based tools promise groundbreaking innovations in both clinical practice and research. High-quality histopathological analysis is a cornerstone of clinical studies and medical research, offering deeper insights into tumor biology and disease mechanisms. However, the limitations of AI must also be considered. Traditional ML algorithms heavily depend on the quality of training data and may experience performance degradation when faced with new datasets. Additionally, the lack of transparency in the decision-making processes of these systems presents a major challenge to their clinical integrainte.[34]

In order for AI-based models to be safely implemented in healthcare, it is essential to improve data quality, enhance the generalizability of models, and increase the explainability of decision-making processes. Addressing issues of transparency and interpretability in deep learning approaches could facilitate the broader adoption of these technologies. It is important to consider AI not only as a diagnostic tool but also as a platform that can be used to understand disease mechanisms and support innovative therapeutic approaches. Additionally, data derived from H&E-stained slides provide a rich resource for deep learning models to identify nuanced patterns in tumor morphology and develop precise risk stratification criteria.[35] Furthermore, integrating histopathology with "omics" sciences, such as transcriptomics, proteomics, and metabolomics, could support a better understanding of diseases and the development of personalized treatment strategies.[36,37] The ability of AI to combine such datasets can not only improve diagnostic accuracy but also contribute to the development of prognostic and predictive models.

One of the most impressive capabilities of AI is its ability to detect rare or ambiguous histopathological patterns. AI has been shown to out perform traditional methods, particularly in areas such as the detection of micrometastases.[38] However, AI techniques based on traditional ML algorithms have limitations, including dependence on the quality of training data and a lack of transparency. To overcome these challenges, new approaches are needed.[39,40]

In addition, pathologists should adopt AI-integrated workflows in diagnostic environments while paying attention to ethical considerations and quality assurance. The increasing use of AI methods requires a better understanding of their roles in cancer cytopathology.[41,42] In addition to diagnosis, providing supplementary information, such as prognostic indications and predictions of treatment effects, is more suitable for clinical needs. Such integrated pathological diagnoses may become feasible in the future. The development of integrated AI methods has been reported in the literature.[43,44] In this context, the adoption of AI-integrated workflows by pathologists will enhance the accuracy of diagnostic processes and improve the quality of healthcare services by providing valuable prognostic and treatment guidance.

In line with the growing demand for personalized cancer approaches, AI must provide more accurate biomarker evaluations and quantitative histopathological analyses. In this context, pathologists require new methodologies and tools to enhance diagnostic sensitivity and specificity. It is clear that AI is the next step toward precision pathology. However, for these technologies to be applied effectively and safely in healthcare, addressing technical, ethical, and clinical limitations, as well as increasing healthcare professionals' trust in these systems, is of critical importance.

RESEARCH GAPS AND FUTURE OPPORTUNITIES

The successful implementation of AI in healthcare relies heavily on the engagement of clinicians, patients, and investors. A major obstacle remains the skills gap among healthcare professionals and their hesitation in adopting unfamiliar technologies, highlighting the need for tailored training programs and user-friendly AI interfaces.[45] Patient acceptance is often hindered by limited exposure to AI tools and concerns about reliability and deviation from traditional care norms. For investors, the rapid pace of technological evolution poses uncertainty, leading to cautious or inconsistent funding in AI-driven healthcare solutions.[46] Hence, despite notable progress in AI-based cancer diagnostics, challenges remain in the generalizability of models because of limited dataset diversity and lack of multi-center validation studies. The future research should focus on developing explainable and ethically transparent algorithms that can be seamlessly integrated into clinical workflows. Moreover, expanding AI applications to rare cancers and addressing regulatory and infrastructural barriers is critical for widespread clinical adoption.

Data Privacy and Ethical Considerations

The implementation of AI in cancer diagnostics raises significant concerns regarding patient data privacy and ethical governance. Histopathological images and associated clinical metadata often contain sensitive and identifiable information, making secure data handling a critical requirement. Traditional anonymization techniques may be insufficient in safeguarding complex biomedical datasets, particularly when combined with external data sources.[47] Therefore, the future research should prioritize the development of privacy-preserving ML frameworks, such as federated learning and differential privacy, to facilitate collaborative model training without compromising patient confidentiality. Establishing clear ethical guidelines and robust institutional policies are also essential to ensure responsible AI integration in clinical practice.

Clinical Validation and Regulatory Challenges

Despite the growing body of research highlighting the diagnostic accuracy of AI-based systems in histopathological image analysis, their translation into routine clinical practice remains limited. Securing regulatory approval demands comprehensive assessment of algorithmic safety, generalizability, and seamless integration into existing clinical infrastructures.[48] Overcoming these hurdles necessitates sustained interdisciplinary collaboration among computational scientists, pathologists, healthcare providers, and regulatory authorities to ensure both clinical relevance and compliance with ethical and legal standards. Also, the majority of AI research in histopathology is focused on common cancers, such as breast and colorectal carcinoma. Rare tumors and histological subtypes remain largely underrepresented in datasets and in model development. Expanding research to encompass these less frequent but clinically significant conditions could improve diagnostic equity and enable earlier detection strategies.

AUTHOR CONTRIBUTIONS

Conceptualization, Methodology, Formal Analysis, Investigation, Resources, Writing–Original Draft Preparation, Writing–Review & Editing, Project Administration: D.Z. The sole author, Doğanyiğit Züleyha, contributed to all aspects of the work, and have read and agreed to the published version of the manuscript.

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Review

AI in Medical Devices: Application, Regulatory Landscape in US and EU, Ethical Challenges, and Future Outlook

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ABSTRACT

Background: By increasing patient management, enabling individualized treatment, and boosting diagnostic accuracy, artificial intelligence (AI) is revolutionizing the medical device market. However, issues with bias, transparency, data privacy, and regulatory compliance are brought up by its incorporation. **Objective:** While addressing important ethical and societal issues, this review will look at how AI is used in medical devices and contrast the legal systems in the US and the EU. **Material and Methods:** Scientific publications, policy documents, and regulatory guidelines pertaining to AI-based medical devices were used in a review of the literature. We gathered and compared data on applications, regulatory strategies, and ethical issues. **Results:** Through applications like wearable technology, personalized medicine, and diagnostic imaging, AI-based medical devices enhance clinical outcomes. While the EU implements a risk-based framework under the AI Act and MDR, emphasizing openness and human oversight, the US FDA uses a Total Product Life Cycle (TPLC)-based strategy that focuses on continuous monitoring and Good Machine Learning Practices (GMLP). Notwithstanding these developments, issues including algorithmic bias, interpretability issues, and regulatory inequalities continue to exist, particularly in low- and middle-income nations. Conclusion: Medical equipment could be greatly advanced by AI, but in order to guarantee safety and efficacy, robust legal frameworks, and moral standards are crucial. For AI to be used responsibly in healthcare, global regulatory harmonization, and ongoing oversight are essential.

Keywords—*Medical device, AI regulation, FDA, EU's AI Act, Software as medical device, Ethical challenge, USA, EU, Artificial intelligence (AI).*

INTRODUCTION

Artificial intelligence (AI) employs algorithms and computational models to perform activities and demonstrate behaviors such as learning, decision-making, and prediction.[1] AI is significantly changing medical device industry by contributing to the development of regulatory framework that is more streamlined, data-driven, and adaptable to technological innovation.[2] It is also creating new opportunities to enhance healthcare delivery, improve clinical practices, support human health initiatives, and promote the well-being of both patients and healthy individuals.[3]

However, primary algorithmic biases cause a significant risk of harm when these systems are implemented.[4,5] Inaccurate predictions for certain patient groups contribute to health inequalities and support racial and gender biases.[6] For example, an algorithm developed to detect melanoma from mole images may yield less accurate results for individuals with darker skin tones if the training data primarily consist of images from lighter-skin individuals.[7]

Hence, regulatory frameworks are essential for minimizing the risk of system errors that could harm patients. These regulations also help to create moral principles for the adoption of AI in the medical sector, while addressing critical concerns such as patient privacy, informed consent, and securely managing sensitive medical data. In the lack of strong regulatory safeguards, there is an increased risk of abuse or unauthorized access to personal health data.[8]

In 2024, the European Union (EU) introduced EU AI Act, a comprehensive risk-oriented regulations for machine intelligence.[9] It is designed to guide the development and implementation of AI in alignment with European values and offer supervision over multiple AI applications.[10–12] However, the US Food and Drug Administration (FDA) plays a leading role in creating guidelines to assess the safety and performance of AI-powered medical devices on a global scale.[2] The US FDA has also published several guidance documents on AI–machine learning (ML)-based medical technologies and Software as Medical Device (SaMD).[13]

This article gives an outline of how AI is applied in medical devices, and reviews the regulatory frameworks regulating its use in the United States and EU. It also explores ethical concerns, identifies challenges related to AI integration in medical technologies, and includes a gap analysis with recommendations for future improvements.

ROLE OF AI IN MEDICAL DEVICES' UPGRADING TECHNOLOGY

Intelligence technologies are playing a crucial role in evolving medical devices, offering advanced features in diagnosis, treatment personalization, and patient management through different and innovative applications. Here are some examples of advancement in healthcare through AI.

Diagnostic Imaging

A prominent use of AI in medical devices is in diagnostic imaging, where algorithms can analyze images such as X-rays, magnetic resonance imaging (MRI), and computed tomography (CT) scans with remarkable accuracy. These systems have the ability to identify abnormalities, such as tumours and fractures, and often overtake human radiologists in detection precision.[14]

AI for Personalized Medicine

By analyzing genetic information, medical history, and lifestyle factors, AI tools can suggest the most suitable treatments and provide more precise and effective therapeutic interventions.[2]

AI-Enabled Wearable Devices

Health monitoring applications are increasing due to evolution in AI hardware and software, which promote the analysis of physical health data collected from sensors, thereby accelerating the expansion of wearable devices, such as smart watches.[15]

Continuous Development by Learning and Improvement

Intelligent systems possess the ability to evolve through practical deployment, enabling them to enhance functionality progressively and improve their performance over time, and also from emerging clinical studies, these systems improve detection accuracy, ultimately contributing to better patient outcomes.[2]

AI-Powered Blood Glucose Management System

In order to maintain optimal glucose levels, AI-based systems are used, which through ML algorithms assist in glucose management by continuous glucose monitors (CGMs) and use real-time data to generate personalized insulin dosage recommendations.[16]

AI in Oral and Maxillofacial Surgery

Advancement in robotic-assisted procedures through AI in oral surgery has resulted in the creation of various robotic systems, which have proven increasingly efficient and are capable of performing semi-automated surgical tasks under the guidance of experienced surgeons.[17]

AI for Diagnostics

The automated interpretation of medical test results, including electrocardiograms (ECGs) and blood analyses, is carried out with the help of ML models integrated into diagnostic devices.[2]

Automated Clinical Documentation Using Natural Language Processing (NPL)

Intelligence language interpretation technology can automate and simplify clinical documentation process, supporting regulatory compliance and improving the accuracy of patient medical records.[2]

AI in Early Diagnosis of Cancer through Biomarker Analysis

For cancer detection, intelligence technologies, particularly algorithmic learning and deep learning (DL) techniques, are used to analyze complex, large-scale datasets from liquid biopsies and whole-genome sequencing.[17]

Governance and Oversight of Clinical Trials

Artificial intelligence has a potential to expedite regulatory submission by automating information, verification, and metadata evaluation. Additionally, it enhances clinical studies by forecasting results, improving participant-enrolment strategies, and supporting adherence to international regulatory requirements.[2]

LEGAL FRAMEWORK FOR AI TECHNOLOGIES IN MEDICAL DEVICES

Across global regulations, the application of AI in health services is primarily monitored under the existing medical device frameworks, specifically categorized under SaMD.[18] This regulatory framework plays a vital role in safeguarding patient well-being, effectiveness, and promoting responsible deployment of intelligent technologies. FDA has played a leading role in establishing regulations for AI technologies in medical devices and is progressively evolving to serve as a global benchmark.[19] In parallel, during April 2021, the EU introduced AI Act, working toward the establishment of a unified legal framework for AI products and services, covering their entire lifecycle from development to deployment.[20] Building on these foundational frameworks, the regulation of AI in medical devices is evolving.

Overview of FDA's AI Medical Device Regulations

The US regulatory approach to AI, especially in the healthcare industry, is distinguished by a sectoral model that makes use of the current federal rules and regulations with the goal of eventually introducing separate AI legislation and a dedicated federal regulatory authority.[21]

In April 2019, the FDA introduced the "Proposed Regulatory Framework for Modifications to AI/ML based SaMD," which placed responsibility on programmers to ensure practical functionality of their AI systems. The framework stated that developers must notify the FDA about any updates related to system performance or changes in input data.[22] It also emphasized that any changes to the intended function of an AI system would require a new authorization process.[23]

In January 2021, the US regulatory agency released the "AI/ML based SaMD Action Plan," presenting a structured approach to overseeing AI/ML technologies used in SaMD.[24–26] This plan is based on the Total

Product Life Cycle (TPLC) framework and includes the following five key actions:

1. Predetermined change control plan (PCCP).
2. Promoting best practices in ML development and application.
3. Adopting a patient-centered approach with a focus on transparency.
4. Implementing strategies to reduce bias and improve algorithm performance.
5. Launching pilot programs to monitor real-world performance.

The TPLC framework allows manufacturer to submit control plans that are developed and incorporated prior to the initial premarket review.[25] This guidance serves as a framework for handling modification in smart medical devices using AI. It defines expected future changes in the software intended for medical device purposes pre-specifications (SPSs) and outlines the processes for safe implementing of these updates, known as the algorithm change protocol (ACP).[24]

The FDA hosted an event titled "Good Machine Learning Practice for Medical Device Development: Guiding Principles" in October 2021.[2] The objective was to guide developers of AI-enabled SaMD to incorporate good machine learning practices (GMLPs) into TPLC. These practices emphasize sound software engineering and quality system principles, characterized by the following elements:

1. Use of clinically relevant data aligned with current medical practice.
2. Data collection should be consistent and aligned with the device's intended use.
3. Future modification plans should be clearly outlined.
4. Well-established boundaries for datasets used in training, tuning, and testing.
5. There should be transparency in how algorithms function and how results are communicated to users.[23]

Key Recommendations For AI- and ML-based Software as Medical Device Regulations

Comprehensive-Validation

Both AI and ML algorithms must be strictly verified to demonstrate that their performance aligns with intended use and produces accurate results. This typically includes clinical evaluations and benchmarking against established diagnostic methods.[2]

Risk-Management

Risks associated with AI/ML models, such as biases in training data, algorithmic errors, and cyber security vulnerabilities must be identified and mitigated by developers.[27]

Real-World Performance Monitoring

Continuous monitoring using real-world clinical data is crucial to assess the accuracy and performance of AI/ML systems, which are capable of learning and improving over time.[2]

Adherence to GMLPs

The FDA defines GMLPs as adherence to developing best practices across the full AI lifecycle. This involves using high-quality data, maintaining reliable validation procedures, and enduring strong version control of the software.[2]

Predetermined Change Control Plans (PCCP)

Owing to the evolving nature of AI/ML, manufacturer should outline how changes are managed. PCCPs must include methods to identify, assess, and reduce risks related to algorithm updates.[28]

Clear User Manuals

SaMD products should be accompanied by detailed manuals that clearly explain the device's functions, limitations, and how its AI/ML components operate.

Transparency of Data

Developers should be informed about the categories of information used during training the models and be made aware of any potential biases that could affect the performance.

Algorithmic Transparency

The transparency of AI/ML algorithms depends on the device's complexity.[29] The US FDA not only recognizes the potential of AI and ML to transform health technologies but also discerns traditional regulatory models that may not be suitable for managing rapidly evolving technologies. Therefore, it launched a new TPLC-based method that integrates the established premarket review pathways with risk mitigation strategies and insights from its pre-certification (Pre-Cert) program.[30]

This program aims to improve regulatory process and support advancement. It allows pre-approved companies to introduce updates and launch new products more swiftly, promoting quicker integration of advanced technologies. This initiative also offers adaptability to accommodate emerging advancements such as AI/ML while ensuring safety through ongoing post-market surveillance and regular evaluations of organizational excellence.[31]

Overview of EU's AI Medical Device Regulations

The EU initially introduced non-binding frameworks, such as the ethical guidelines for reliable AI[32], and the policy and investment insights and recommendations, released in 2019.[33] Following that, in May 2017, the EU implemented a legislative framework by introducing the European Medical Device Regulation (EMDR), which classified the risk of SaMD based on their diagnostic and treatment-focused functions.

The EU AI Act established a unified legal structure for AI systems and applications that covers all stages from development to deployment.[20] Articles 1–15 of the frameworks outline the requirements for AI technologies concerning risk management, data governance, human oversight, transparency, accuracy, robustness, and cyber security. This shift clearly indicates the EU's transition from a soft-law approach to a more binding and enforceable legislative framework for AI regulation.[34]

To govern AI system, the AI Act adopts a risk-oriented framework. Within the healthcare sector, AI systems classified as significant risk include those used for biometric identification, patient categorization based on their pre-existing conditions, and software-based management of public healthcare services and electronic health records.[35] Under this act, manufacturers of critical risk base systems must prioritize data compliance and risk control as key requirements. For minimal and limited risk AI technologies, such as chatbots interacting with humans in the health sector, a voluntary code of conduct is recommended to ensure reliable service accompanying safety.[36]

Moreover, the Medical Device Coordination Group (MDCG) has published a guidance document outlining comprehensive criteria for the qualification and categorization of medical device software, in adherence to the EU's Medical Device Regulation (MDR), in vitro Diagnostic Regulation (IVDR), or both.[37]

When using Conformité Européenne (CE)-certified devices in clinical trials, additional requirements must be met to ensure the protection of participant's rights, safety, and the overall welfare as well as to maintain the honesty and relevance of the assessment records. The reflection paper makes evident the integrity and relevance of the evaluation data. The reflection paper also makes it evident that the EU's European Medicines Agency (EMA) carefully assesses whether a medical device's features are appropriate for producing the evidence required in a marketing authorization application or for supporting recommendations included in the Summary of Product Characteristics (SmPC).[38]

The EMA's process for analyzing AI integration across the medicinal product lifecycle is outlined in the reflection paper (regarding the implementation of AI and ML across the entire lifecycle of medications). This includes medical devices employed during clinical studies to generate evidence for product approval applications as well as those used in conjunction with pharmaceutical products.[39] The EMA evaluates these devices to determine whether they can generate sufficient evidence to support approval within EU member states. The agency also provides guidance on conducting AI-related research, which must be updated regularly to reflect the ongoing advancement and emerging scientific insights. With the SmPC medical device, the EMA considers all aspects of that integration into account during its assessment.[40]

As outlined in the reflection paper, the general guidelines and expectations for medical devices are equally relevant in the context of human studies and market approval when using AI/ML-based approaches.[40] Overall, the EMA is implementing a risk-based approach, advising investors to evaluate whether the AI system poses any risks to patients. If such risks are identified, early regulatory consultation with the EMA is recommended. The agency is actively preparing to assess the implementation that integrates intelligent technologies throughout the lifecycle of medicinal products.[41]

EXAMPLES SHOWING ETHICAL, LEGAL, AND SOCIAL CHALLENGES

Ethical Implication and Regulatory Disparities in Low- and Middle-Income Countries (LMICs)

Till date, advancements in AI regulation have primarily emerged from high-income countries, particularly the United States and the EU. Whereas, LMICs face ethical challenges, such as data bias, because of limited access to representative and high-quality datasets which influence the adoption of AI-enabled medical technologies. However, technologically, as it is trained using health data from high-income countries, it does not work well for poorer countries because their health situations are different and not included in the training data.

In LIMCs, even if new technology is available, many people still can not benefit from the same because of limited access to the technology, especially in rural or undeserved communities. For example, fewer women use mobile internet, they are not well represented in health data, and this can cause gender inequality in healthcare because decisions are based on incomplete information.

Inflexible Regulatory Framework and Contextual Bias

As LMICs often have limited regulatory capacity to independently assess and approve AI technologies, they tend to rely on tools that have already approved by governing agencies, such as the US FDA and EMA. However, standards, datasets, and development contexts from these regions are not always directly transferable to LMICs, which often overlook local needs, epidemiology, or resource limitation. As a result, contextual bias can arise, where AI systems fail to provide treatments that are affordable, accessible, or appropriate in resource-limited settings.

Accountability for “Black Box” and Algorithm

The medical community faces challenges with “black box” nature of AI systems. This lack of disclosure can hinder clear communication of risks, benefits, and decision-making logic to healthcare providers and patients. Addressing this issue requires an urgent need on algorithmic accountability within AI governance frameworks. To ensure safety and fairness, regulatory bodies must implement mechanisms that assign liability to those best positioned to mitigate harm, including developers, vendors, or healthcare institutions, based on their roles in the AI lifecycle.

Limitations of Conventional Validation Methods

Traditionally, validation testing is used to confirm that a product meets specific user needs and functioning standards. However, AI technologies introduce more complexities that conventional methods are unable to address completely. For instance, lack of interpretability in AI models complicates standard evaluation processes and makes it more difficult to assess how decisions are made. Furthermore, the domain of medical AI liability remains under development, involving a complex web of responsibilities among multiple stakeholders.[25,42]

Patient-Centered Regulation and Transparency

To enhance trust and ensure ethical AI deployment, establishing regulatory frameworks that promote algorithmic transparency is a crucial step. Many regulatory bodies, such as the FDA, have emphasized a patient-centered approach as a top priority. This includes compelling manufacturers to supply clear, accessible information about how AI/ML-driven medical devices operate. Such transparency enables healthcare professionals and patients to make well-informed decisions by offering a detailed understanding of the device's benefits, risks, and limitations.[43]

Bridging the AI Chasm

Trust in AI-based healthcare tools relies on whether they can transition safely and effectively from laboratory testing or small pilot studies and actually work to real-world clinical settings. The term "AI chasm" refers to the gap between creating strong AI algorithm in research and real-world, practical, and ethical use in actual healthcare settings.[42]

Case Study: Google's Automated Retinal Disease Assessment (ARDA) Deployment

Google's ARDA, an AI-based tool designed to detect diabetic retinopathy, is a notable example that illustrates these challenges. This case highlights the difficulties of deploying advanced AI systems in real-world clinical settings, especially when local infrastructure, training, and validation are not addressed adequately.[44] It highlights the need for context-specific adaptation, thorough regulatory oversight, and ethical deployment strategies.

ESSENTIAL ELEMENTS OF HARMONIZED AI–SAMD REGULATION

TABLE 1. Harmonized AI–SaMD regulation.

Component	Considerations
Accountability and Transparency	**Explainability**: Manufacturers need to clearly explain how AI models make judgments, especially for applications that pose a significant risk. **Documentation**: Comprehensive records of performance metrics, model architecture, and training data are necessary. **Accountability**: Manufacturers and developers have distinct lines of accountability and culpability. Systems that monitor and document decision-making procedures for post hoc analysis are known as audit trails.
Risk Control	Continuous risk assessment is the process of continuously evaluating risks during the course of an AI system. **Bias detection and mitigation**: Manufacturers should recognize and deal with biases, particularly those that result in different patient outcomes. **Monitoring performance**: Keeping an eye out for new threats in the real world. Adaptive regulation ensures safety while allowing for quick developments in AI.
Security of Data	Enforce strong encryption for the transmission and storage of data. Strict access controls are in place to stop unwanted access. Resilience against attacks that alter AI outputs is known as adversarial attack mitigation. Utilizing privacy-enhancing technology such as federated learning and differential privacy are examples of privacy-preserving strategies.
Clinical Evidence and Performance	Establish performance measures that are standardized so that AI–SaMD products are compared. Guidelines for utilizing real-world data to augment conventional clinical studies are known as "real-world evidence." **Performance monitoring**: Continuous post-market observation to guarantee performance. **Reporting transparency**: Providing stakeholders with clear information about clinical performance and results.

Accountability and Transparency[45]:

Building trust in AI-SaMD requires accountability and transparency.[2,26] For efficient monitoring, regulatory frameworks must require thorough documentation of AI models and decision-making procedures. Manufacturers should keep thorough records of training data, model architecture, and performance metrics, as well as explain how their AI models make decisions, especially in high-risk applications. Decision-making processes should be monitored and documented by systems for post-hoc examination. Together, these actions improve accountability and transparency in the AI-SaMD ecosystem. Transparency and accountability go beyond documentation and include strict development, implementation, and ongoing monitoring of AI technologies. Regulations should require routine audits and inspections to confirm safety and effectiveness, especially for high-risk medical applications. To guarantee prompt issue resolution and patient safety, clear protocols for reporting adverse occurrences or unexpected results should be created. In order to help medical professionals understand and interpret AI-generated recommendations, manufacturers should also incorporate user-friendly interfaces. Instead of blindly following automated recommendations, this transparency helps clinicians make well-informed decisions. These actions foster public trust and guarantee the moral advancement and application of AI in healthcare by encouraging transparency and accountability.

Risk Management[45]:

AI's flexibility and potential biases present unique issues for risk management in AI-SaMD. Because AI is dynamic and requires continuous risk assessment throughout the product lifetime, harmonized regulatory frameworks must incorporate thorough risk assessment approaches to guarantee patient safety. Manufacturers should be required by frameworks to recognize and address biases in AI models, particularly those that impact various patient populations. Monitoring performance in the real world is crucial for identifying and mitigating new threats. Furthermore, while maintaining strict safety standards, regulatory frameworks must be adaptable to keep up with AI developments. Frequent independent third-party audits and inspections should confirm compliance and guarantee ongoing safety and effectiveness. To safeguard AI-SaMD systems from attacks and unauthorized access, manufacturers must also put strong cybersecurity safeguards in place. Lastly, in order to promptly identify and address problems, a consistent reporting system for AI-SaMD adverse events should be implemented.

Data Security [45]:

Ensuring data security for AI-SaMD is a difficult task that requires strong technical implementations and extensive regulatory regulations to handle data breaches and sophisticated threats like adversarial and cyberattacks. Strong data storage and transmission encryption are crucial security measures that safeguard private patient data even in the event that it is intercepted. Strict authentication procedures and access controls must restrict data exposure to those who are permitted. Manufacturers must demonstrate how resilient their systems are to adversarial attacks, which could alter AI model outputs and result in inaccurate diagnosis or treatment recommendations.[13,29] Thorough testing and validation are necessary for this. Federated learning and differential privacy are two examples of privacy-enhancing technologies that should be promoted or required in order to minimize the exposure of individual patient data and enable the construction of AI models. Together, these steps create a thorough security framework to guard against present dangers and upcoming difficulties in AI-SaMD.

Clinical Evidence and Performance[45]:

In order to guarantee patient safety and treatment effectiveness, clinical evaluation requirements for AI-SaMD are crucial. Comprehensive performance criteria, such as precision, recall, specificity, positive and negative predictive values, and algorithmic fairness and bias assessments, should be part of these standards in order to compare various AI-SaMD products objectively. Guidelines for gathering and applying real-world data should also supplement conventional clinical trial findings, providing a comprehensive picture of AI-SaMD performance in many contexts. By assuring consistent post-launch evaluation and identifying unanticipated problems or performance degradation over time, standardizing postmarket surveillance across regulatory bodies will improve the continuing evaluation process. It is also necessary to develop transparent and uniform reporting rules for clinical performance and results. These guidelines would guarantee that patients and healthcare professionals are informed about the possibilities and limitations of AI-SaMD, facilitating informed decision-making and the proper application of these technologies in clinical practice. By putting these policies into place, AI-SaMD would be more trusted and their responsible integration into healthcare systems would be supported.

FUTURE OUTLOOK

Aligning and standardizing legal frameworks can enable a more effective future use of AI in medical devices. As regulators address the sector, leading manufacturers are shifting from traditional production methods to smart, data-driven business models.

Enhancing Treatment Accuracy and Safety

Application of AI not only enhances treatment accuracy but also helps to prevent harm and fatalities associated with medical devices. As healthcare generates vast amounts of data, especially from medical devices, these large data sets are utilized to predict the safety and efficacy of such devices.

Application of AI in Medical Devices in the Current Era

For instance, smart infusion pump systems have become a favored approach for ensuring the safe delivery of intravenous medications. While many of these rely on AI expert systems, rather than ML, their proven reliability and durability have paved the way for more advanced ML-based solutions such as implantable insulin pumps and the development of closed-loop artificial pancreas systems.[15]

Regulatory Harmonization by Unified International Regulations

The concept of single global regulatory framework reflects the goal of establishing a standardization of regulations and confirms that AI-powered healthcare devices consistently comply with safety, ethical standard, and efficacy around different regions. This vision goes beyond standardization; it aims to create an environment that supports innovation without being constrained by varying regulatory demands across regions.

Accelerating Global Adoption through Harmonized Regulation

Artificial intelligence technologies are accelerated by regulatory harmonization, which helps to make advanced healthcare solutions more widely available across the globe. A "one world, one regulation" strategy is significant for reaching the full capabilities of AI-assisted healthcare, ensuring that it is reliable and efficient for using to improve patient outcomes globally.[2]

CONCLUSIONS

Artificial intelligence is transforming medical devices by enhancing diagnostic capabilities, personalized treatments, and improved patient management. Regulatory guidelines in the United States and the EU are evolving to manage the distinct challenges posed by these advanced techniques, emphasizing patient safety, transparency, and ongoing risk management.

The US FDA's TPLC-based strategy and the EU's risk-based AI Act represent different yet complementary strategies to assure that AI-assisted medical equipments fulfil high standards of safety, therapeutic effectiveness, and ethical compliance. However, challenges such as algorithmic bias, transparency, and regulatory disparities, especially in LMICs highlight requirements for adaptable, context-aware policies.

Harmonizing regulatory frameworks globally is crucial for advancing AI, and the vision of "One World, One Regulation" aims to streamline innovation while maintaining consistent safety and ethical standards across regions. Through collaboration, continuous oversight, and patient-centered regulation, AI- powered medical technologies can greatly enhance healthcare outcomes globally.

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Conceptualization, A.P. and Z.P.; Methodology, A.P.; Software, A.P.; Hardware, A,P.; Validation, A.P., V.M., and Z.P.; Formal Analysis, Z.P.; Investigation, A.P.; Resources, A.P.; Data Curation, A.P.; Writing–Original Draft Preparation, A.P.; Writing–Review & Editing, Z.P.; Visualization, V.M.; Supervision, Z.P.; Project Administration, V.M.

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Engineering Report

Preventive Maintenance as an Organizational Challenge: Evidence from Private Hospital Networks

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ABSTRACT

Preventive maintenance of medical-hospital equipment (MHE) is essential for patient safety and operational efficiency in healthcare organizations. This study analyzes the organizational and technical factors that interfere with the execution of preventive maintenance planning in private supplementary healthcare hospitals. A qualitative study was conducted using structured questionnaires applied to clinical engineers from a private hospital network comprising 33 units. The findings demonstrate that failures in interdepartmental communication, equipment availability, workforce training, and logistics significantly compromise the execution of preventive maintenance. The results highlight preventive maintenance as an organizational challenge rather than a purely technical activity, reinforcing the need for integrated management strategies.

Keywords—*Preventive maintenance, Clinical engineering, Hospital management, Organizational processes, Lean healthcare.*

INTRODUCTION

The increasing technological complexity of medical-hospital equipment (MHE), combined with growing demands for quality, safety, and regulatory compliance, poses significant challenges for hospital organizations. International guidance recognizes medical equipment maintenance programs as structured activities that require planning, management, implementation, inventory control, and performance monitoring.[1–3] Preventive maintenance is a key strategy to reduce operational failures, extend lifespan of equipment, and ensure patient safety. Despite the availability of computerized maintenance management systems and specialized professionals, many private hospitals struggle to execute preventive maintenance plans effectively. The literature on healthcare technology management emphasizes that medical equipment maintenance is not limited to technical repair; it also depends on institutional policies, risk classification, stakeholder coordination, documentation, and performance measurement.[4–6] Therefore, preventive maintenance must be understood as part of hospital governance and not merely as an isolated technical routine.

This study aims to identify the main organizational and technical factors that interfere with the execution of preventive maintenance planning in private hospital networks, emphasizing preventive maintenance as an organizational challenge embedded in hospital governance structures.

MATERIALS AND METHODS

This exploratory qualitative study was conducted using a structured questionnaire for clinical engineers, who work in a private supplementary healthcare network comprising 33 hospital units nationwide. The questionnaire included closed-ended questions addressing technical, operational, and organizational aspects related to execution of preventive maintenance.

Responses were analyzed using descriptive statistics and subsequently categorized into the following three analytical dimensions: (1) human resources, (2) machines and materials, and (3) processes and methods. This framework allowed the identification of systemic organizational patterns affecting preventive maintenance beyond isolated technical issues.

RESULTS

As shown in Table 1, of the 33 hospitals invited to participate, 20 completed the questionnaire, representing a response rate of 60.6%. All participating hospitals reported the presence of computerized maintenance management systems and dedicated clinical engineering professionals. However, the majority of respondents (89%) indicated difficulties in executing preventive maintenance according to the established schedule.

TABLE 1. Characterization of participating hospitals.

Characteristic	Description
Total hospitals in network	33
Questionnaires completed	20 (60.6%)
Hospital type	Private supplementary healthcare
Geographic coverage	Nationwide
Maintenance management software	100%
Clinical engineering department	100%

The most frequently reported factors affecting preventive maintenance execution are presented in Table 2.

TABLE 2. Critical factors affecting preventive maintenance execution.

Category	Critical factor	Frequency (%)
Human resources	Insufficient technical training	35%
Machines and materials	Lack of spare parts and kits	30%
Processes	Failures in interdepartmental communication	60%
Processes	Unavailability of equipment for maintenance	65%

DISCUSSION

The findings demonstrate that failure of preventive maintenance is predominantly associated with organizational factors, rather than purely technical limitations. Although hospitals possess trained professionals and management systems, ineffective communication with care units and unavailability of equipment significantly limit execution of maintenance.

These results reinforce the understanding of preventive maintenance as an organizational process dependent on institutional coordination, negotiation between clinical and technical priorities, and governance mechanisms. Clinical engineering operates at the intersection of care delivery, technology management, and administrative planning, requiring integrated strategies to achieve effective preventive maintenance outcomes.[1–3]

The frequency of failures in interdepartmental communication and equipment unavailability suggests that preventive maintenance performance depends on negotiation between clinical priorities and technical requirements. Clinical engineering operates at the intersection of care delivery, technology management, and administrative planning. For this reason, preventive maintenance should be integrated into governance routines, risk-based prioritization, and performance monitoring rather than treated only as a technical checklist.[4–7]

Lean Healthcare concepts may support this integration by strengthening process visibility, reducing operational waste, improving coordination between departments, and encouraging system-wide improvement rather than isolated corrective actions.[8] However, the application of Lean principles to preventive maintenance should be adapted to the specific realities of hospital operations, including the need for equipment availability, user training, spare parts logistics, and clinical schedule alignment.

CONCLUSION

Planning of preventive maintenance in private hospital networks faces substantial organizational challenges, even in contexts with adequate technological infrastructure and specialized personnel. Failures related to communication, training, logistics, and planning compromise effectiveness of preventive maintenance.

The study highlights the importance of adopting integrated management approaches, such as Lean Healthcare, to strengthen interdepartmental coordination, improve resource allocation, and enhance patient safety. The future research should expand the sample to include public hospitals and comparative analyses across different healthcare systems.

AUTHOR CONTRIBUTIONS

Conceptualization, Methodology, Data Curation, Writing–Original Draft Preparation, Writing–Review & Editing, F.A.S.

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DATA AVAILABILITY STATEMENT

The data analyzed in this engineering report were obtained from questionnaire responses collected for the study and are not publicly available due to institutional confidentiality.

CONFLICTS OF INTEREST

The author declares no conflicts of interest.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

FURTHER DISCLOSURE

Not applicable.

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Original Research Article

Analysis of Adverse Events in Medical Devices Used in Homecare

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ABSTRACT

This article aims to analyze adverse events and their probable causes associated with medical devices used in homecare to identify and categorize main problems. The work aims to establish strategies in health technology management in techno-surveillance processes to mitigate risks. A quantitative study of adverse events reported in Brazilian and North American databases between 2019 and 2024 was conducted. Reports regarding glucose monitors and continuous positive airway pressure were analyzed and the Ishikawa diagram quality tool was applied to categorize the causes of adverse events. The number of techno-surveillance notifications for medical devices reported by Brazilian National Health Surveillance Agency between 2019 and 2024 was 106,900, while on the Manufacturer and User Facility Device Experience/Food and Drug Administration (MAUDE/FDA) platform, there were 12,457,700 notifications for the same period. Medical devices used in homecare are among the technologies with the highest number of notifications. The probable causes of the failures were categorized into six factors: human, technological, environmental, interconnectivity and data security, metrological, and protocol. Technological development inserted in a Living Lab ecosystem and implementing accessible guidance resources are some strategies presented to mitigate the occurrence of adverse events. The occurrence of adverse events in medical devices in homecare has a direct impact on the quality of care. These technologies are operated by the users themselves to support decision-making. Therefore, strategies to mitigate the occurrence of adverse events in medical devices in homecare should be applied in the pre- and post-marketing stages.

Keywords—*Adverse events, Medical devices, Techno-surveillance, Homecare, Health technology management.*

INTRODUCTION

Owing to the increasing incorporation of technology, combined with its increased use in the prevention, diagnosis, and treatment of various diseases, the process of health technology management (HTM) consists of an approach to quality input aiming at ensuring the safety of patient and other users.[1] A medical device, according to the World Health Organization (WHO), can be "any instrument, apparatus, implementation, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination for a medical purpose." There are an estimated 2 million different types of medical devices on the world market, categorized into more than 7,000 generic device groups.[2] Medical equipment is classified as one of the types of medical devices.

A wide variety of health technologies used by healthcare professionals and users of the most diverse profiles globally makes the occurrence of errors practically inevitable.[3] To minimize these incidents, the implementation of a techno-surveillance control programs, consisting of the area of clinical engineering for monitoring post-market adverse events and technical complaints, combined with the consideration of human factors in health, can help to prevent failures and errors that often trigger harmful health accidents.[4]

Health technologies have potential to improve the efficiency of healthcare, help reduce costs, and promote greater quality and safety. However, they can also introduce errors and be involved in the occurrence of failures during their use that can harm the patient. These incidents are called adverse events.[5] Adverse events are defined as incidents that cause, or carry the potential to cause, unexpected or undesirable outcomes that compromise the safety of patients, operators, caregivers, and healthcare professionals interacting with these technologies.[6,7] These could be mild or severe events and are involved in various types of environments, from operating rooms, intensive care units, hospitalization rooms, clinical laboratories, and even homecare settings.[4]

According to the WHO, around 1 in every 10 patients is harmed during healthcare and more than 3 million deaths occur annually because of unsafe care. In low-to-middle-income countries, as many as 4 in 100 people die due to unsafe care. More than 50% harm (1 in every 20 patients) is preventable, and in primary and ambulatory settings, some estimates suggest that as many as 4 in 10 patients are harmed.[8] High occurrence of harmful incidents is a global concern, and because of the growing presence of technology in the diagnosis and treatment of patients, it triggers an increase in adverse events associated with medical devices.

Some of the main problems faced by health technologies that lead to harmful incidents are inadequate maintenance, inadequate planning to implement the technology, inefficient technology design that does not consider human factors, and user ergonomic principles.[3] User errors are a common cause of failures in the health environment and are attributed to differences in functionality between equipment of different manufacturers, lack of standardization, poor design, inefficient maintenance services, and problems often arising from hidden failures, that is, errors that are not direct and easy to identify. One such example is human factors problems. Usability testing has revealed that users generally face greater difficulties when using equipment features less frequently. Design failures related to usability are often implicated in adverse events.[9]

Techno-surveillance corresponds to the system of monitoring adverse events and technical complaints of health products available on the market, aiming at product protection and its quality for the population.[10] It represents an essential interface for articulation among key players within the medical device lifecycle, bridging early-stage development with real-world, post-market usage.[10] Post-market surveillance of medical equipment assists in quality and performance evaluation[11], in identifying new risks, in addition to improving the usability and in functionality of the device. Post-market monitoring corresponds to a systematic process that collects and analyzes the experience obtained by the technologies available on the market, and the analysis of adverse events is one of these activities incorporated into the HTM program.[6]

Countries have specific programs to monitor adverse events of medical devices. Canada has the Canada Vigilance Program, Brazil has a techno-surveillance program, and India has a material vigilance program. Many countries make some adverse event notification data available publicly, such as the Manufacturer and User Facility Device Experience (MAUDE) database in the United States, the Database of Adverse Event Notifications (DAEN) in Australia, and the techno-surveillance analytical portal in Brazil.

Many countries have platforms available to make data on alerts, recalls, and safety information related to medical devices. However, the lack of notification of adverse events data is still a global reality. Underreporting of adverse events is a serious problem in technology usability assessments, because these data are essential for identifying problems, analyzing performance and quality[11], preventing damage, and assisting in the designing of the technology-user interface.[12] Studies estimate that only 0.5% of adverse events involving medical equipment are reported, and this number may be even lower in official reports.[13,14] Research with health professionals finds that approximately 78% have never reported these incidents.[15] These data reinforce the importance of discussing the impacts of human factors in identifying problems that can lead to the occurrence of adverse events, aiming to encourage a culture of reporting, in addition to the need to analyze this information by the area of clinical engineering to contribute to the safest and most reliable use of technology.

Studies indicate a significant underreporting of adverse events.[16] There is a strong culture of non-reporting by healthcare professionals, with the main barriers being fear of guilt, lack of time, lack of perception of effectiveness in reporting, and lack of knowledge of the reporting system.[12,13,17] In countries such as India, with a diversity of the languages spoken by the population, language can lead to a significant gap between linguistic equality and accessibility in the healthcare system as well as a barrier for reporting adverse events.[18]

Research in the area of adverse events has been increasingly discussed at national and global levels, bringing new data and discussions of great relevance for developments and improvements in the area. A retrospective study based on an analysis of adverse events from a Japanese database showed that equipment failures and breakdowns are one of the causes of adverse events in the country.[19] Another study aimed to explore the perception of nurses in Intensive Care Units (ICUs) of a hospital (a complex multidisciplinary workplace that requires the use of different technologies) regarding adverse events in medical equipment. A questionnaire was developed to address issues related to medical equipment widely used in ICUs, such as ventilators, defibrillators, monitors, and infusion pumps; 66.7% of nurses reported having experienced an adverse event related to equipment failure during device use, and 78% never reported these adverse events[15], implying a deficiency in the reporting process of these incidents. Another study presented some probable strategies to solve problems related to equipment usage in hospitals, viz. involvement of clinical staff in the purchase and usability testing of medical equipment, because one of the most common root causes of adverse events includes technical failures associated with medical equipment.[20]

In order to mitigate potential health risks and harms involving health technologies, adverse event surveillance is internationally globally accepted method for safe technological management.[21] Identifying problems related to the use of technology is a useful trend that can be applied in the process of technological development in healthcare[22], including improvement to the designing of technology–user interface.[23]

Medical devices are increasingly incorporated into various environments outside hospitals, including homes. The home healthcare environment includes the home in which the patient lives as well as other places where patients are present, except for professional healthcare facilities where operators with medical training are available continuously. The safety of medical equipment in this uncontrolled environment in relation to electrical installations and related means of safety and protection are of concern.[24]

Nowadays, many patients/users use medical devices, such as pacemakers, stents, blood pressure monitors, glucometers, insulin pumps, respirators, nebulizers, thermometers, and oximeters, among others. Thus, there is a need not only to increase consumer awareness of probable adverse events and reporting mechanisms but also to increase understanding of the devices, what constitutes an adverse event, and guidance on correct and safe use to mitigate harm to the user.[25] In Brazil, there are regulations that guide minimum requirements for the operation of home environments, such as RDC 11/2016, which provides for the technical regulation for the operation of services that provide homecare[26], and normative No. 963 (of 27 May 2013), which redefines homecare within the scope of a unified health system.[27]

Usability challenges with home-use medical devices for patients and caregivers are at the top of the health technology risks highlighted by the Emergency Care Research Institute (ECRI) for the year 2024. Evidence shows that more people are receiving medical care at home and many devices used in hospitals, such as infusion pumps and ventilators, are being used at home. As a result, many times caregivers and patients using such medical devices are not sufficiently trained.[28] Health technologies used in homecare are often operated by nonprofessional users, that is, people who do not have sufficient training for their proper operation, which can lead to serious harm to patients.

Another danger highlighted by ECRI involves communication gaps in home-use medical device recalls, which can confuse patients and lead to severe harm. Accurate and understandable information about medical device recalls often does not reach patients using those devices at home; this gap in information is growing every year as healthcare moves into home settings. In many cases, device manufacturers do not have direct communication with homecare patients, making it difficult to contact patients in the event of a safety alert.[29] Without a clear understanding of the risks involved, patients could be harmed by continuous use of an unsafe device, or by discontinuing the use inappropriately.

Therefore, analyzing adverse events associated with medical devices used in homecare is essential to identify problems and establish strategies to mitigate risks and make healthcare environment safer. Owing to the high incidence of errors that may result in adverse events involving healthcare technologies, understanding human–technology interaction has become fundamental to ensuring the reliability, safety, and effectiveness of technological processes.[30] In order to implement actions aimed at reducing the occurrence of errors, it is necessary to have a descriptive analysis of the problems by obtaining real-world data and, with this, establishing solutions focused on continuous improvements. Therefore, this article aims to analyze data on the occurrence of adverse events involving medical devices used in the homecare environment in order to assist in the management of health technologies in techno-surveillance and risk mitigation.

METHODOLOGY

This is a descriptive and retrospective study with a quantitative approach. The research consists of studying reports of adverse events involving medical devices. The data on adverse events analyzed were extracted from two databases, one from the National Health Surveillance Agency in Brazil, and the other from the United States. In Brazil, adverse events must be reported to the Brazilian National Health Surveillance Agency (ANVISA) that aims to promote the protection of population health through the NOTIVISA notification system. In the United States, these incidents must be reported to the US Food & Drug Administration (FDA), a regulatory agency that can be consulted on the MAUDE platform. Initially, a quantitative study of notifications involving medical devices was conducted between January 2019 and December 2024. The analysis was accomplished between March 2025 and April 2025. Owing to terminological heterogeneity between NOTIVISA and MAUDE databases, the data were harmonized to enable comparative analysis using the technical name of the technology. The data were exported to an Excel spreadsheet, and matrix was created in Microsoft Excel®. The variables were categorized into specific columns (device type, year of notification, reported equipment problem, and effect on the patient), allowing the application of pivot tables to consolidate results. From this processed database, graphical representations were generated that summarized devices with the highest incidence of adverse events, ensuring integrity and statistical comparability between Brazilian and US scenarios. The graphical representations with the number of notifications per database were generated as well as the medical devices with the highest number of notifications for this period.

In the second stage, an analysis of adverse event reports related to medical devices used in homecare was realized. The selection of devices such as blood glucose monitor, also called a glucometer, and continuous positive airway pressure (CPAP) as the focus of this study is justified by their high usage in homecare settings and their role as critical decision-support technologies. These devices are the primary tools for managing chronic conditions outside the hospital environment. CPAP is one of the most commonly used medical devices in homecare settings[31], and glucometer is a frequent source of adverse events because of the complexity of their operation by nonprofessional users and the severity of clinical outcomes, such as severe hypoglycemia, resulting from device's inaccuracy or malfunctioning.[33] The data were extracted and exported to a spreadsheet containing the following information: date of notification, risk class, cause and effect of the occurrence, and technical name of the equipment.

In order to verify the main causes of adverse events and to seek strategies and implement actions to mitigate the occurrence of such incidents, the Ishikawa diagram quality tool was applied to assist in identifying the causes generated. The construction of Ishikawa diagram is based on some of the following steps: problem definition, identification of groups of causes, identification of causes, and classification of causes.[33] Adverse event reports were stratified and classified into six factors: human, technological, environmental, interconnectivity and data security, metrological, and protocol. The current study elucidated global causes involving medical devices in homecare environments to present problems with higher recurrence of adverse event reports involving medical devices. Actions to be implemented in the establishment were proposed to reduce failures and improve patient safety.

RESULTS

Quantitative Study of Techno-Surveillance Notifications in Medical Devices

The number of techno-surveillance notifications for medical devices by ANVISA, involving adverse events and technical complaints between 2019 and 2024, was 106,900. Of these, 12,806 involved medical equipment. Specifically, there were 6,230 notifications of adverse events related to medical equipment. Figure 1 graphically shows the total number of year-wise techno-surveillance notifications for 2019–2024. Medical devices with maximum number of notifications by ANVISA included tubing of infusion pump (with 7,928 notifications), followed by catheters (with 7,678 notifications). Specifically regarding medical devices, the highest number of notifications on the database was for infusion pumps (1,551 notifications), followed by robotic surgical systems (943 notifications) and multiple-use devices in aesthetics (515 notifications).

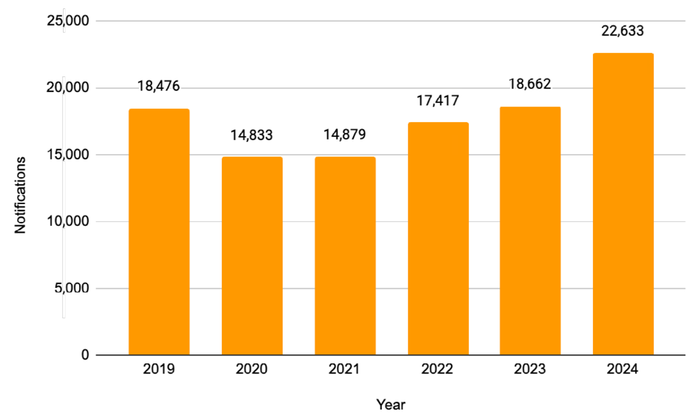

FIGURE 1. Number of techno-surveillance notifications per year by ANVISA.

As illustrated in Figure 2, the MAUDE/FDA database documented a total of 12,457,700 notifications between 2019 and 2024. Of these, 5,900,801 (47.4%) were related to adverse events, a significant number when compared to those reported by the Brazilian platform.

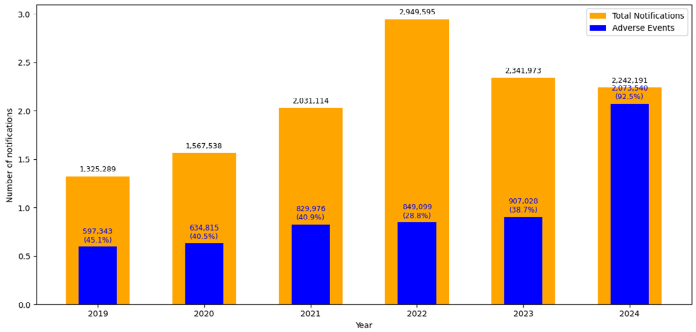

FIGURE 2. Number of notifications per year by MAUDE/FDA.

Data from the FDA/MAUDE database (2019–2024) indicated that endosseous dental implants (DZE) generated the highest volume of notifications, closely followed by infusion pumps (FRN). Notably, infusion pumps represented the leading medical device in terms of adverse event reports across both the North American and Brazilian registries. High notification frequencies were also prevalent among diabetes management technologies, including integrated continuous glucose monitoring systems (QBJ, QLG), alternate controller-enabled insulin pumps (QFG), automated insulin dosing systems (OZP, OZO), insulin infusion pumps (OYC, LZG), and invasive glucose sensors (PZE). Furthermore, substantial notification volumes were documented for noncontinuous (BZD) and continuous ventilators (CBK), spinal-cord stimulators (LGW), breast prostheses (FTR), intravascular administration sets (FPA), automated external defibrillators (MKJ), ventricular bypass devices (DSQ), as well as cardiac rhythm management components like permanent pacemaker electrodes (DTB, NVN) and implantable cardioverter defibrillators (LWS).

The rising number of adverse event notifications in homecare underscores the need for robust HTM. However, underreporting remains a challenge because of barriers, such as fear of blame, lack of time, perceived ineffectiveness of reporting, and complex notification platforms.[12,13,17] To improve the process of reporting adverse events, strategies should include the following: (i) automated reminders within monitoring apps; (ii) adoption of Unique Device Identifiers (UDI) integrated into interoperable platforms[18]; (iii) simplified reporting interfaces; and (iv) targeted training for both health professionals and end users. Furthermore, incorporating technovigilance into health sciences curricula is essential for long-term safety culture.

Study of Techno-Surveillance Notifications for Glucometer

Glucometer is used to measure blood glucose levels and is essential for monitoring diabetes. On ANVISA platform, records relating to the nomenclatures of self-test instrument for glucose, self-test instrument for glucose and ketone bodies, and self-test for glucose were analyzed. A total of 1,581 notifications notified between 2019 and 2024 were analyzed, of which 566 were related to adverse events and 1,015 were technical complaints about product defects without impact to the patient. On MAUDE/FDA platform, the device with code NBW (regarding Glucose test system) was analyzed and had a total of 55,958 notifications for the same period.

Main problems reported with glucometer, as well as effects on patients associated with notifications on MAUDE/FDA and ANVISA platforms, are shown in Table 1. According to the data observed on MAUDE/FDA, failure to turn on, incorrect or inaccurate results, high values in the results, and display that is difficult to read are among the main problems associated with glucometer. The data converge with the problems in the output and incorrect or inadequate results, which were the most reported causes of problems on ANVISA regarding the glucose self-test instrument. Regarding the effects on patients, no consequences or impacts on patients were discovered in the main results. However, hypoglycemia and hyperglycemia were among the two effects on patients that converged with the main effects reported by ANVISA.

TABLE 1. Main problems with glucometer, and the effects reported on ANVISA and MAUDE/FDA platforms.

Main Problems with Device, Adverse Events		Main Effects on Patients	
ANVISA	**MAUDE/FDA**	**ANVISA**	**MAUDE/FDA**
Output problem; incorrect or inadequate result (40.11%)	Failure to power up (58.7%)	Hypoglycemia (34.63%)	No clinical signs, symptoms, or conditions
Output problem; no output or result (23.67%)	Incorrect, inadequate, or imprecise results or readings (21.6%)	Hyperglycemia (32.33%)	No known impact or consequences on patients
Ignored (16.08%)	High test results (4.6%)	Localized skin reaction (9.72%)	No consequences or impact on patients
Other (12.37%)	Display difficult to read (3.1%)	Diabetic ketoacidosis (1.94%)	Hypoglycemia
Unintended function; incorrect message (4.24%)	High readings (2%)	Skin allergy (1.59%)	Hyperglycemia
Electric electronic; power supply problem (< 2%)	Low test results (< 2%)	Loss of consciousness (1.41%)	Dizziness
Unintended function; failure to adhere or fix (< 2%)	Missing test Results (< 2%)	Allergic reaction (1.06%)	Shaking/tremors
Usage error; inoperative medical device (< 2%)	Image display error/ artifact (< 2%)	Aggravated hypoglycemia (0.71%)	Loss of consciousness
Mechanical/ calibration (< 2%)	Device displays incorrect message (< 2%)	Skin infection (0.53%)	Fatigue
Mechanical/ ignored (< 2%)	Unable to obtain readings (< 2%)	Cerebral seizure (0.35%)	Insufficient information

Study of Techno-Surveillance Notifications in Case of CPAP

Continuous positive airway pressure is used to assist patients with sleep apnea. In the ANVISA database, records related to CPAP, CPAP circuit, and CPAP nomenclatures were analyzed. Between 2019 and 2024, a total of 76 notifications were analyzed, of which 15 were related to adverse events and 61 were technical complaints resulting from product defects without impact to the patient. Material degradation was the most reported cause of the problem, with 76.32% of complaints.

In the MAUDE/FDA database, noncontinuous ventilator (code BZD) was analyzed, with 193,430 notifications for 2019–2024. A large increase in notifications over the years was notable. In 2019, 188 notifications were reported; in 2022, 90,783 and in 2024, 69,277 notifications were reported, as shown in Figure 3.

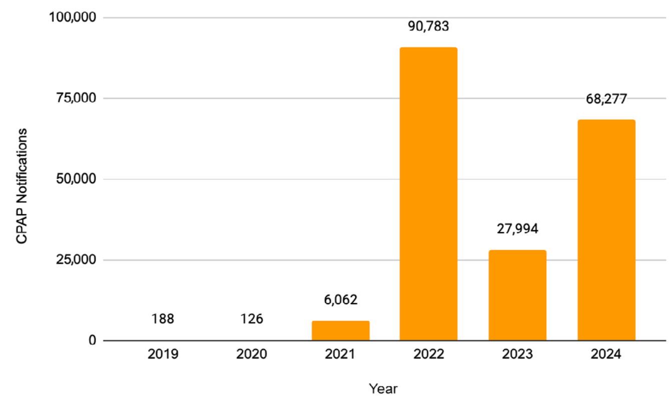

FIGURE 3. Number of CPAP notifications on MAUDE/FDA platform.

Data in the MAUDE/FDA database identified critical failure for CPAP devices, including degradation, contamination, corrosion, material integrity issues, and overheating. Reported clinical consequences of these failures included respiratory and systemic distress, such as "eye and nasal irritation, dizziness, headaches, and acute asthma exacerbation." Furthermore, mechanical failures, such as total loss of airflow or contamination within the air passage, rendered the device unusable, directly interrupting patient treatment.

In all, 14 recalls involving CPAP devices were recorded between 2019 and 2024, reflecting systemic safety concerns. Primary causes for these recalls included detachment of breathing circuit connections leading to loss of ventilation; communication errors with cloud-based care management applications; and magnetic interference between CPAP masks and active medical implants (e.g., pacemakers) that posed a high risk to patients with ferromagnetic materials. One of the recalls referred to no contraindication/warning regarding magnetic components in CPAP masks for patients with implantable devices or metallic splinters in the eyes, characterizing a labeling error.

Technological traceability is a challenge in domestic environments because of the lack of historical records of the device. An effective communication program must be implemented so that in the event of a recall, all patients using this equipment are notified to prevent possible damage.

Application of the Ishikawa Diagram Quality Tool to Identify Causes of Adverse Events in Medical Devices

Ishikawa diagram was applied to identify the probable causes of adverse events occurring in medical devices in homecare environments as shown in Figure 4.

The occurrence of adverse events must be analyzed from a holistic perspective, aimed at problem-solving, considering the entire context of use. Analysis of the cause of adverse events is an essential tool to elucidate and assist in the development and implementation of strategies aimed at reducing these occurrences. By applying the Ishikawa diagram tool, the main causes of adverse events are categorized and presented as the following six factors: (1) human, such as improper use and lack of training and accessible usage guidelines; (2) technological, such as battery problems and non-intuitive and inaccessible interfaces; (3) environmental, which refers to both internal infrastructure and improper storage in home environments, as well as external environment, such as improper waste disposal; (4) interconnectivity, such as connection and data integration problems as well as data security aspects, such as cyber vulnerability; (5) metrological, such as the lack of reliability in measurement results, presenting discrepancies and lack of confidence for decision-making; and (6) protocol, such as lack of procedures for proper use and reporting of adverse events.

The occurrence of adverse events in use of medical devices in homecare has a direct impact on the quality of care in the home environment. The fact that patients independently operate these devices to manage their treatments amplifies the risk; technical or usability issues can result in sub-optimal management and

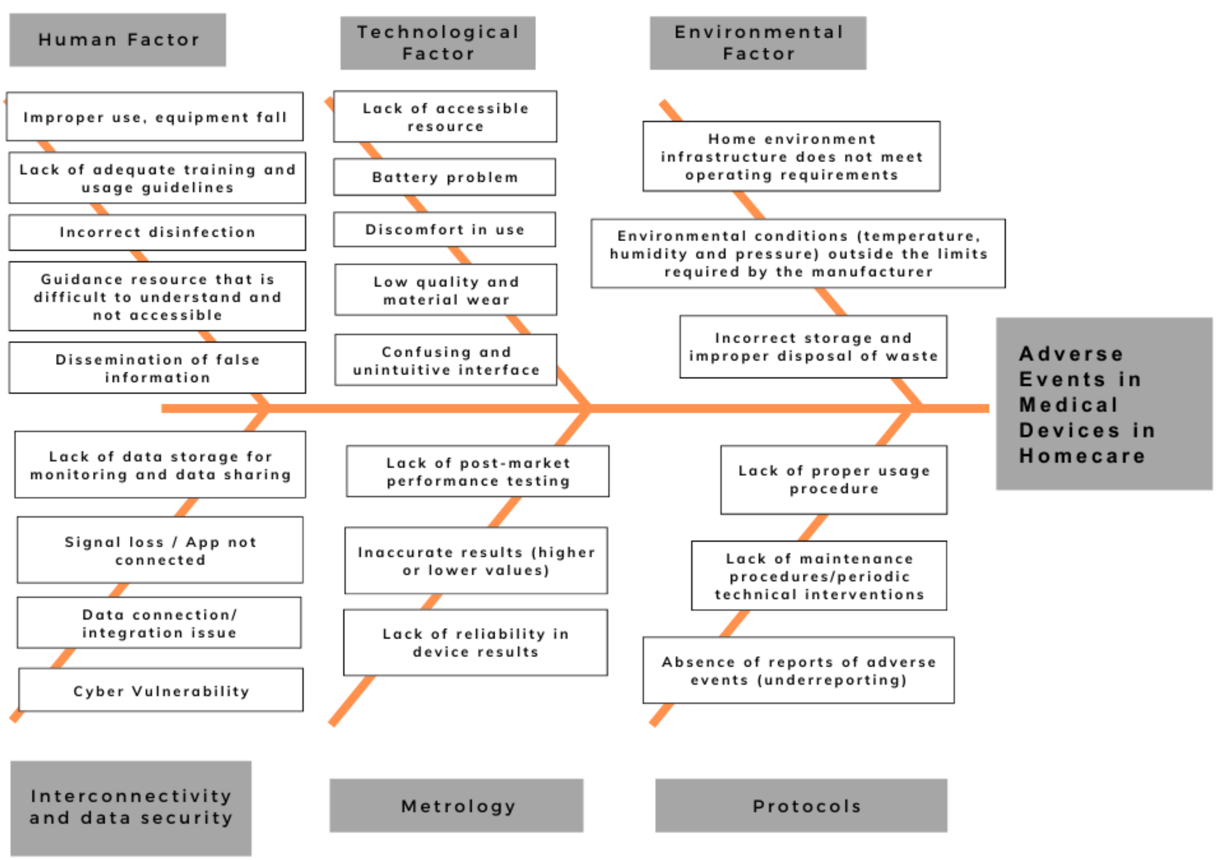

FIGURE 4. Ishikawa diagram with the probable causes of adverse events.

dangerous delays in care, leading to clinical decline. To prevent adverse events, comprehensive mitigation strategies must be applied throughout the entire lifecycle of these devices, integrating both pre-market evaluation and post-market surveillance.

DISCUSSION

The analysis of reporting of adverse events should be conducted throughout the life cycle of health technologies, from pre-marketing to post-marketing stages. In line with the results of the study conducted by Giuliano[32], the application of usability techniques through analysis of adverse events allows identifying sources of hazards and investigating the causes of these incidents associated with the use of medical devices, and thus assisting both pre-marketing and post-marketing of technologies, and creating a feedback information system. To this end, through the evaluation and analysis of adverse events in databases, it is possible to optimize risk control solutions in the usage of medical devices and achieve satisfactory usability results to contribute to the development of public health and better user experiences.[21]

Improper use, inefficient product design, interoperability issues, cyber vulnerability, and metrological aspects are among the main causes of adverse events associated with medical devices in homecare. Owing to the increase in connected devices, cybersecurity must be considered for the development of products to prevent harm to patients and ensure data privacy. To develop medical devices with fewer risks to users, it is recommended to implement a Living Lab ecosystem in a collaborative and interdisciplinary environment that involves different actors, such as manufacturers, users, health professionals, and government agencies.

Through interaction between different perspectives, it is possible to develop technologies with better usability and accessibility for all people. Another approach, as discussed by Fung et al.[31] and Brandao and Garcia[34] and less explored by other studies, is the use of technology by individuals with physical/sensory disabilities, demonstrating that medical devices are often not designed to meet the needs of some specific users. It is recommended to consider accessibility from the product development stage to develop adjustable and customizable technology, taking into account universal design, to design more accessible products for people with different limitations and characteristics.

Post-market surveillance of medical devices helps with quality and performance assessment, identifying new risks, verifying safety aspects for continued use of technology, and improving the usability, accessibility, and functionality of the device. The results of analyzing techno-surveillance alerts showed that several factors could cause adverse events: problems in usage, inefficient design with usability failure, and metrological aspects were the corroborating aspects. Many adverse events were due to lack of accurate diagnosis and appropriate treatment by patients who use certain medical devices for decision-making. These results discovered in the study converge with the data reported by ECRI report, which discussed the dangers associated with medical devices in the home environment.[28]

Apart from glucometers and CPAP devices, other homecare equipment, such as automatic blood pressure monitors, thermometers, and oximeters, frequently present accuracy issues. For instance, reports indicated significant discrepancies (e.g., 20 mm Hg) between home monitor and clinical readings, potentially leading to incorrect self-management. High-risk implantable devices, including pacemakers and defibrillators, also figure prominently in the MAUDE/FDA database, with prevalent issues such as over-sensing, premature battery discharge, and inappropriate stimulation. Notably, among 20 devices with the highest notification volume between 2019 and 2024, eight were related to diabetes management (infusion pumps and continuous monitors). These figures reinforce the urgency of investigating root causes of adverse events in home settings to establish effective risk mitigation strategies.

The data in the current study reinforced the importance of analyzing the causes of adverse events in order to mitigate their occurrences. Lack of training, inadequate use, lack of preventive maintenance, and technologies developed with confusing interfaces without user involvement in the development process are among some of the causes that trigger the occurrence of adverse events. It is recommended to implement a continuing education program for users who use medical devices in their homes. Developing more interactive, personalized, and accessible guidance resources with objective and clear language is essential to improve adherence.

CONCLUSION

Healthcare environments have extended to homecare, and therefore it is necessary to develop strategies to identify, analyze, and implement improvements to reduce adverse events and increase patient safety in technological processes within the new healthcare system models. Techno-surveillance requires multidisciplinary interaction to investigate recurring failure of medical devices that compromise patient safety. Analyzing these incidents and their root causes is fundamental to developing solutions that improve technological performance and clinical outcomes.

Medical devices used in home environments are also subjected to adverse events that can harm users, with improper usage, inefficient product design, interconnectivity problems and cyber vulnerability, and metrological aspects being the main causes of adverse events associated with medical devices in homecare. This work reinforces the importance of interdisciplinary integration to mitigate risks, requiring the involvement of clinical engineering, healthcare professionals, end users, caregivers, government agencies as well as device developers and manufacturers regarding usability issues of medical technology. It is recommended that healthcare technologies must be developed within an interdisciplinary Living Lab ecosystem centered on the user to improve usability and accessibility. In addition, investment in ongoing training programs and a more detailed analysis of the cause of failures must be conducted to implement more assertive strategies to address the root cause of problems.

A primary limitation of this study is the prevalence of incomplete or poor-quality reporting in national databases. Many records lack detailed descriptions of causes and clinical effects, resulting in data that do not fully reflect the reality of device failures. Furthermore, lack of standardized nomenclature, where multiple names or codes refer to the same device, hampers data consolidation. Promoting a robust reporting culture and implementing training programs to ensure the standardized completion of notification forms are crucial steps toward improving data integrity and preventing future healthcare errors.

Systematic analysis of the causes of adverse events is a core component of efficient HTM. By retrospectively assessing errors to prospectively mitigate failures, HTM ensures the safety and quality of medical devices, ultimately fostering a more secure healthcare environment for end users.

AUTHOR CONTRIBUTIONS

Author Contributions: Conceptualization, M.R.B; Methodology, M.R.B; Validation, M.R.B. and V.F.F.; Formal Analysis, M.R.B. and V.F.F.; Investigation, M.R.B.; Data Curation, M.R.B.; Writing–Original Draft Preparation, M.R.B. and V.F.F.; Writing–Review & Editing, M.R.B., V.F.F, R.G.O. and J.B.M.; Supervision, R.G.O. and J.B.M.

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CONFLICTS OF INTEREST

The authors declare they have no competing interests.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

FURTHER DISCLOSURE

Not applicable.

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Review

Mapping the Knowledge Landscape of Mental Health Stigma and Digital Interventions: A Bibliometric Study

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ABSTRACT

Mental health stigma remains one of the most pervasive barriers to achieving psychological well-being and treatment access across societies. As the digital technologies rapidly integrated into healthcare, novel interventions, such as mobile health (mHealth), telepsychiatry, and artificial intelligence-driven platforms have emerged to challenge traditional stigmatizing attitudes and improve mental health outreach. This study aims to systematically map the intellectual structure, collaboration patterns, and thematic evolution of research on mental health stigma and digital interventions through a comprehensive bibliometric analysis. The dataset comprises 487 documents published between 2000 and 2024 retrieved from the Scopus database. Using advanced bibliometric tools—Biblioshiny (R-based) for performance analysis and VOSviewer for science mapping—the study identifies publication trends, influential authors, prolific institutions, top contributing countries, and thematic clusters. The annual publication trend reveals a notable surge post-2018, reflecting the global emphasis on digital mental health during and after the COVID-19 pandemic. The United States, United Kingdom, and Australia emerge as the most productive countries, while keywords, such as mental health stigma, digital intervention, telehealth, mHealth, and online therapy, dominate the research network. The findings provide a consolidated understanding of the field's evolution, offering valuable insights for policymakers, clinicians, and researchers in designing inclusive, technology-enabled anti-stigma strategies.

Keywords—*Bibliometric analysis ,Mental health stigma, Digital interventions, mHealth, Teletherapy, AI chatbots.*

INTRODUCTION

The concept of mental health stigma—the social disapproval, stereotyping, and discrimination directed toward individuals with mental disorders—has been a longstanding public health challenge. Early research in the 1990s and 2000s focused primarily on understanding attitudes toward mental illness and their sociocultural determinants.[1] However, despite advances in awareness campaigns and policy frameworks, stigma continues to impede help-seeking, adherence to treatment, and psychological recovery.[2] The evolution of digital era has offered new opportunities to address this barrier through the development of technology-based mental health interventions that combine accessibility, anonymity, and personalization.

In recent years, digital platforms, such as teletherapy, mHealth apps, artificial intelligence (AI) chatbots, and virtual peer support groups, have gained traction as stigma-reducing tools. These interventions not only democratize mental health services but also provide discreet and immediate support for individuals reluctant to engage in face-to-face therapy.[3] The COVID-19 pandemic further accelerated this trend, pushing telepsychiatry and app-based counselling into the mainstream of healthcare.[4] The resulting surge in research on digital mental health underscores an interdisciplinary convergence among psychology, informatics, and public health.

Given this growth, it becomes essential to map how digital interventions have shaped scholarly attention to mental health stigma. A bibliometric approach provides a systematic means of understanding this evolution—quantifying publications, authorship patterns, geographical distribution, and thematic shifts.[5] Such analysis allows for identifying not only the most influential contributors but also emerging domains, such as AI-powered therapy, gamified mental health tools, and digital empathy design.

Hence, this bibliometric review explores the development and research trends in mental health stigma and digital interventions over the last two decades. The study is guided by the following research questions (RQ):

RQ1. What is the publication productivity and growth pattern of research on mental health stigma and digital interventions?

RQ2. Who are the most influential authors and what collaborative patterns characterize this field?

RQ3. Which countries, institutions, and journals contribute most significantly to this domain?

RQ4. What are the dominant keywords, clusters, and emerging research themes shaping the intellectual structure of this literature?

The subsequent sections provide a background overview, methodological framework, results, implications, and future directions to deepen understanding of this evolving interdisciplinary landscape.

BACKGROUND

Mental Health Stigma

Mental health stigma refers to negative beliefs, prejudices, and discriminatory behaviors directed toward people experiencing psychological disorders. Goffman's classical theory of stigma conceptualized it as a form of social labelling that reduces an individual's identity to a "tainted" status.[6] Later scholars expanded this notion to include public stigma, self-stigma, and structural stigma.[7] Empirical research has consistently shown that stigma undermines help-seeking intentions, delays early intervention, and exacerbates the treatment gap, particularly in low- and middle-income countries.[8]

Over the past two decades, stigma research has diversified into cognitive, affective, and behavioral dimensions. While early studies examined public perceptions and media portrayals of mental illness, later works have shifted toward anti-stigma campaigns and contact-based interventions. Despite these advancements, traditional stigma reduction approaches often suffer from limited scalability and sustainability. This shortfall has catalysed a growing interest in leveraging digital technologies to design, test, and disseminate innovative anti-stigma solutions.

Digital Interventions

Digital interventions refer to technology-mediated strategies that employ online platforms, mobile devices, or AI to promote mental health literacy, provide therapy, or reduce stigma. The evolution began with web-based psychoeducation modules in the early 2000s and has since expanded to include mobile health (mHealth) applications, virtual reality exposure therapy, and AI-based conversational agents.[9,10] These digital tools enhance accessibility, anonymity, and user engagement—factors crucial for individuals deterred by fear of judgment or labelling.

Moreover, studies have demonstrated that digital platforms can significantly reduce stigma by normalizing mental health discourse in online spaces.[11] For example, social media campaigns and peer-support communities create inclusive environments where mental health challenges are discussed openly, counteracting stereotypes. Likewise, AI-driven chatbots, such as Woebot or Wysa, have shown promise in facilitating early therapeutic interactions, thereby lowering psychological barriers to care.[12]

Given these technological and psychosocial shifts, the integration of digital tools into mental health frameworks has become a global priority. Consequently, understanding the trajectory and thematic evolution of scholarship on this convergence—between stigma and digital mental health—is vital for shaping future research, policy, and practice.

METHODOLOGY

Bibliometric Search

The term "bibliometric" refers to a systematic and quantitative technique that evaluates scholarly publications to uncover trends, structures, and intellectual linkages within a field. By adopting this approach, researchers examine the evolution, influence, and collaborative dynamics that define an emerging research domain. The present study employs this technique to map the intersection of mental health stigma and digital interventions, thereby capturing how psychological and technological research streams have converged over the last two decades. The Scopus database was chosen as the primary data source because of its extensive coverage of peer-reviewed scientific literature, reliable citation indexing, and compatibility with bibliometric software.[13] Scopus has also been widely acknowledged as a high-quality data repository for mapping research fronts.[5] The selected timeframe spans from 2000 to 2024, corresponding to the earliest emergence of online therapy and mental health informatics studies, while ensuring inclusion of post-pandemic technological acceleration in mental healthcare. The bibliometric process was implemented through four sequential stages—Database Search, Scholarly Filtration, Language Filtration, and Bibliometric Review—as illustrated in Figure 1. Each stage ensured refinement, consistency, and replicability of data across subsequent analyses.

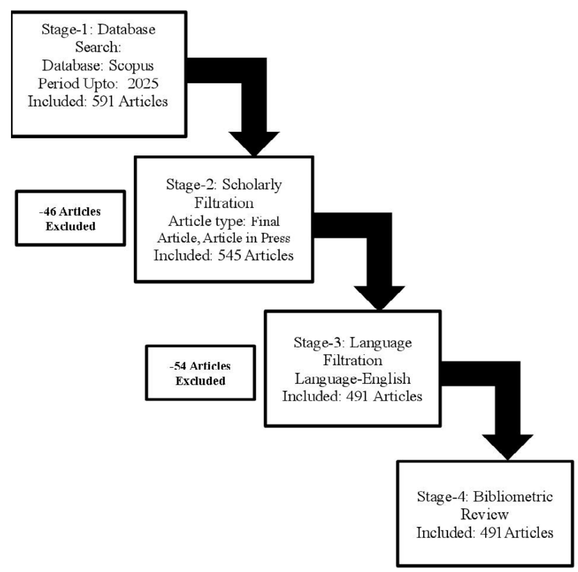

FIGURE1. Bibliometric review strategy.

Database Search

The first stage involved executing an advanced Boolean query in Scopus, designed to capture both conceptual dimensions: mental health stigma and digital interventions. Searches were restricted to the fields of title, abstract, and keyword to ensure thematic precision. The query was constructed as follows:

(TITLE-ABS-KEY ("mental health stigma" OR "stigma toward mental illness" OR "mental illness stigma" OR "psychological stigma" OR "social stigma" OR "public stigma" OR "self-stigma" OR "perceived stigma" OR "attitudes toward mental illness" OR "discrimination in mental health" OR "mental health literacy" OR "mental illness perception")) and (TITLE-ABS-KEY("digital intervention" OR "online intervention*" OR "e-health" OR "mHealth" OR "telehealth" OR "teletherapy" OR "telepsychiatry" OR "mobile health" OR "digital mental health" OR "digital therapy" OR "internet-based intervention*" OR "app-based intervention*" OR "virtual therapy" OR "AI chatbot*" OR "mental health app*" OR "digital platform*" OR "digital counselling" OR "digital cognitive behavioral therapy" OR "online support group*" OR "technology-based intervention*" OR "digital wellbeing")) and (LIMIT-TO (LANGUAGE, "English")) AND (LIMIT-TO (DOCTYPE, "ar") OR LIMIT-TO (DOCTYPE, "re") OR LIMIT-TO (DOCTYPE, "cp") OR LIMIT-TO (DOCTYPE, "ch")) AND (PUBYEAR > 1999 AND PUBYEAR < 2025).

The search yielded 491 documents. This corpus covered seminal studies on early e-therapy pilots, telepsychiatry evaluations, and AI-driven stigma reduction campaigns. The retrieval period was intentionally broad to capture the initial conceptualization of digital mental health interventions and the subsequent maturity of the field in the post-2018 digital health boom.

Scholarly and Language Filtration

The second stage, scholarly filtration, ensured that only credible, peer-reviewed sources were retained. Conference reviews, editorials, and non-academic materials were excluded to maintain analytical rigour. This refinement reduced the dataset to 591 documents.

The third stage, language filtration, further limited the corpus to English-language publications for consistency in bibliometric processing. This step excluded 100 documents published in other languages, such as Spanish, Chinese, and Portuguese, leaving a consolidated dataset of 491 documents ready for performance and network analysis.

Bibliometric Review and Analytical Tools

The fourth stage consisted of bibliometric evaluation through performance and science mapping as indicated in Table 1. Two software tools were used:

- Biblioshiny (R version 4.3.2): Applied for performance analysis, encompassing descriptive statistics (publication growth, annual citation rate, and collaboration index) and productivity metrics (*h*-index, *g*-index, and *m*-index).
- VOSviewer (version 1.6.20): Utilized for science mapping, including visualization of co-authorship networks, country collaborations, keyword co-occurrence, and thematic clusters.

TABLE 1. Strengths and weaknesses of the techniques applied.

Techniques	Description	Strength	Weakness
Co-authorship analysis	Examines collaborations between two or more authors, institutions, or countries who have jointly published research on mental health stigma and digital interventions. It identifies influential authorship networks.	Collaboration patterns among authors, countries, and affiliations can be identified—an effective tool for assessing global knowledge integration in mental health informatics.	Limited visibility into author-level contribution strength and occasional bias toward multi-authored papers.
Keyword co-occurrence analysis	Measures how frequently keywords appear together within documents, thereby identifying research hotspots and emerging themes.	Reveals conceptual linkages between "mental health", "stigma", and "digital therapy", aiding in detecting evolving sub-fields and thematic density.	Rapid keyword evolution and inconsistent author terminology may cause unstable cluster interpretation.
Citation analysis	Evaluates the scholarly impact of documents and authors through global and local citation counts within the corpus.	High citation frequency signifies influential studies that define intellectual foundations of the field, assisting in pinpointing landmark works.	May undervalue recently published but conceptually significant papers because of citation-time lag.
Thematic analysis	Groups keywords and documents into clusters that represent major thematic areas and conceptual structures.	Helps to detect conceptual patterns, research fronts, and intellectual trajectories shaping digital mental-health stigma scholarship.	Theme grouping may lack uniformity when clusters overlap or dataset size is limited.

RESULTS AND INTERPRETATIONS

Descriptive Analysis (RQ1)

The descriptive summary of the dataset presented in Table 2 highlights the structural and performance characteristics of research on mental health stigma and digital interventions published between 2007 and 2024. A total of 491 documents drawn from 261 sources demonstrate the rapid expansion of scholarly attention to this field, supported by a strong annual growth rate of 30.64%. The average document age of 4.44 years indicates that this research domain is relatively young, yet dynamic, reflecting the post-2018 acceleration in digital mental health studies.

Each document received an average of 28.29 citations, revealing substantial intellectual influence and growing global visibility. The dataset includes 4,198 references, 2,919 keywords plus, and 1,361 author-provided keywords, representing diverse themes spanning telehealth, mHealth, AI-based therapy, stigma reduction, and digital empathy. A total of 2,649 authors contributed to this corpus, with only 27 single-authored papers, emphasizing the highly collaborative and interdisciplinary nature of the field. The average of 6.18 co-authors per document and 32.24% international co-authorship rate further reinforce the globalized and cross-disciplinary character of digital mental-health research. Overall, these metrics portray a rapidly expanding and intellectually cohesive research landscape marked by strong collaboration, conceptual diversity, and increasing scientific maturity.

The overall analytical workflow and dataset characterization supporting this descriptive analysis are illustrated in Figure 2.

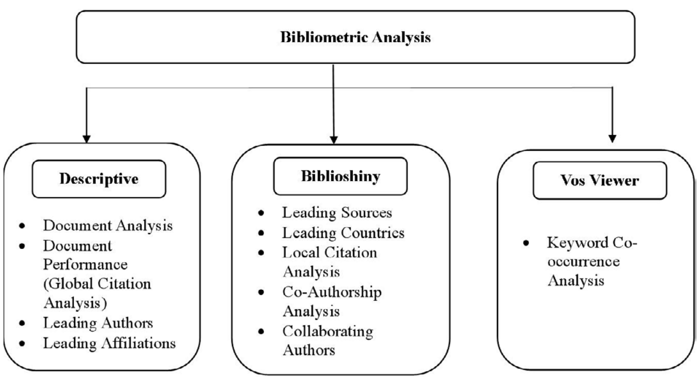

FIGURE 2. Bibliometric review strategy for analysis.

TABLE 2. Summary statistics of documents under corpus.

Main Information	Results
Timespan	2007–2024
Sources (journals, books, etc)	261
Documents	491
Annual growth rate (%)	30.640
Document's average age (years)	4.440
Average citations per document	28.290
References	4,198
Keywords Plus	2,919
Author's keywords	1,361
Authors	2,649
Authors of single-authored documents	27
Single-authored documents	27
Co-authors per document	6.180
International co-authorships (%)	32.240

Document Analysis (Annual Publication Trends)

The annual publication trend from 2007 to 2024 (Figure 3) shows a steady and accelerating growth in research on mental health stigma and digital interventions. Early output was minimal, with only one to four articles per year until 2012, reflecting the field's formative stage. A gradual rise began after 2014, coinciding with the expansion of telehealth and mHealth initiatives, reaching 27 publications in 2018. The period from 2019 to 2021 witnessed strong momentum, with outputs increasing to 61, largely influenced by the pandemic-driven adoption of digital mental health tools. The most significant growth occurred between 2022 and 2024, peaking at 94 publications, signaling the field's maturation and global integration. Overall, the trend highlights a consistent upward trajectory, demonstrating the growing academic and practical significance of technology-enabled strategies for addressing mental health stigma.

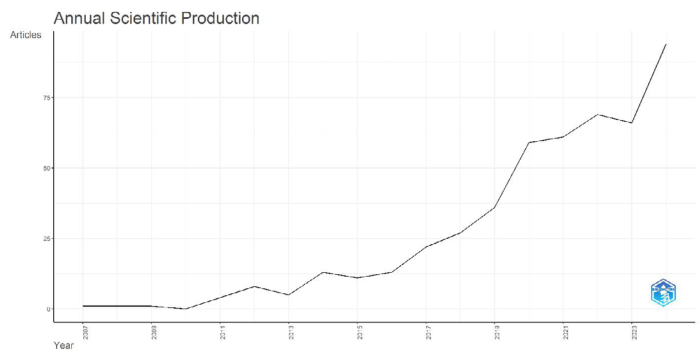

FIGURE 3. Distribution of annual publications (2020–2024).

Document Performance

Global Citations

Table 3 highlights the most influential studies shaping research on mental health stigma and digital interventions. Rajkumar in *Asian Journal of Psychiatry* leads with 2,505 citations, emphasizing pandemic-linked digital mental health insights. This is followed by Naslund et al. and Inkster et al., focusing on technology-driven stigma reduction and mHealth applications. Works by Bhugra and WPA–Lancet Psychiatry

Commission and Gulliver et al. explore global psychiatry and online help-seeking, while Bakker et al., Rice et al., and Sullivan et al., expand into digital approaches for adolescent and affective disorders. Doraiswamy and Blease, and Gupta and Grover underscore AI integration in mental healthcare. Overall, these highly cited studies form the core intellectual base driving the shift from traditional stigma perspectives to digital data-informed mental health solutions.The comparative impact of these studies is visually illustrated in Figure 4.

TABLE 3. Top-cited documents on mental health stigma and digital interventions based on global citations.

Rank	Document Title	Author(s)	Year	Citations
1	COVID-19 and mental health: a review of the existing literature	Rajkumar	2020	2,505
2	The future of mental health care: peer-to-peer support and social media	Naslund et al.	2016	783
3	An empathy-driven conversational artificial intelligence agent (Wysa) for digital mental well-being: real-world data evaluation mixed-methods study	Inkster et al.	2018	583
4	The WPA–Lancet Psychiatry Commission on the Future of Psychiatry	Bhugra and and WPA–Lancet Psychiatry Commission	2017	286
5	Internet-based interventions to promote mental health help-seeking in elite athletes: an exploratory randomized controlled trial	Gulliver et al.	2012	189
6	Implementation strategies to increase PrEP uptake in the United States	Sullivan et al.	2019	170
7	Adolescent and young adult male mental health: transforming system failures into proactive models of engagement	Rice et al.	2018	168
8	Engagement in mobile phone app for self-monitoring of emotional well-being predicts changes in mental health: MoodPrism	Bakker et al.	2018	166
9	Artificial intelligence and the future of psychiatry: insights from a global physician survey	Doraiswamy and Blease	2020	141
10	Pandemic and mental health of the front-line healthcare workers: a review and implications in the Indian context amidst COVID-19	Gupta and Grover	2020	134

Note: Top 10 most globally cited articles are based on Scopus. PrEP: pre-exposure prophylaxis.

Local Citations

The analysis of locally cited documents presented in Table 4 highlights the core studies that have significantly influenced the internal intellectual structure of research on mental health stigma and digital interventions. The most locally cited works—such as Aggarwal and Altaf Dar —reflect the field's progression from cultural examinations of stigma to contemporary digital health perspectives. Studies done by Atanasova, Bennett and Reynolds, and Blackburn and Armstrong, emphasize the growing integration of digital health literacy, behavioral science, and translational psychiatry. Similarly, Bakker et al. and Bauermeister underscore the role of digital behavior and self-monitoring tools in improving psychological well-being, while Krishnanand Taftexpand the discourse toward psychosomatic and media-based mental health contexts. Brian provides one of the earliest theoretical linkages between psychiatric well-being and digital engagement. Collectively, these locally influential studies represent the conceptual backbone of the domain, mapping its evolution from stigma-centered frameworks to digitally mediated, behaviourally adaptive mental health models. The internal citation structure is further visualized in Figure 5.

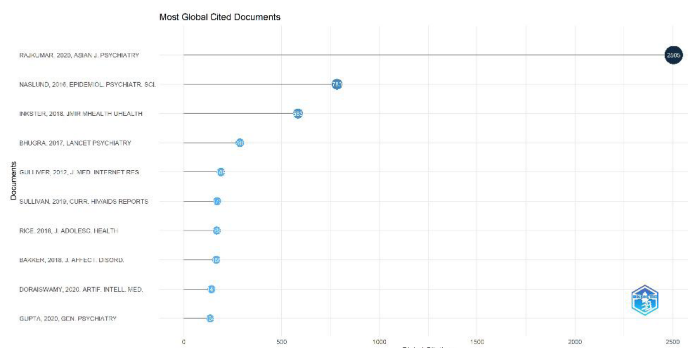

FIGURE 4. Top cited documents (global citations).

TABLE 4. Top-cited documents on mental health stigma and digital interventions based on local citations.

Rank	Document Title	Author(s)	Year	Citations
1	Exploring adolescent mental health in the digital era: a cross-sectional study	Altaf Dar	2023	2
2	Understanding stigma in Asian psychiatry: cultural dimensions and treatment barriers	Aggarwal	2012	2
3	Digital health literacy and mental health communication: a Slovenian perspective	Atanasova	2022	1
4	Health education and behavior change in digital mental health interventions	Blackburn and Armstrong	2021	1
5	Translational research approaches to digital psychiatry	Bennett and Reynolds	2021	1
6	Digital behavior and HIV stigma reduction: an intervention-based study	Bauermeister	2019	1

Rank	Document Title	Author(s)	Year	Citations
7	Engagement in mobile apps for emotional self-monitoring predicts mental health change: MoodPrism	Bakkeret al	2018	1
8	Gastrointestinal conditions and psychological comorbidities: a clinical perspective	Taft	2017	1
9	Mobile media and youth mental health: the role of digital narratives	Krishnan	2017	1
10	Social determinants of psychiatric well-being in the digital age	Brian	2014	1

Note: Top 10 most locally cited documents are derived using Biblioshiny.

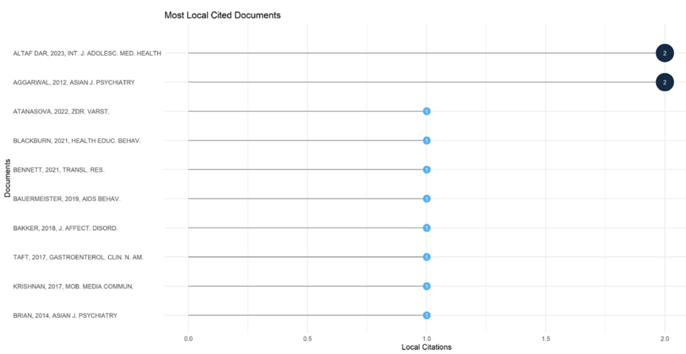

FIGURE 5. Top cited documents (local citations).

Top Contributing Authors (RQ2)

The author performance analysis presented in Table 5 reveals the leading contributors shaping the intellectual landscape of mental health stigma and digital interventions. Christensen stands out as the most influential researcher with the highest *h*-index (6) and total citations (610), indicating sustained scholarly impact since 2012. Wang, with a comparatively higher *m*-index (0.714), represents a rapidly emerging author whose recent works (post-2019) demonstrate accelerating citation growth. Authors such as Brumby et al., Kennedy, and Li X exhibit balanced productivity and citation influence, suggesting consistent engagement with digital mental-health themes. Similarly, Muessig and Hightow-Weidman have contributed significantly to interdisciplinary studies linking technology with behavioral health and stigma mitigation. Batterham and Bauer et al. also display strong citation performance relative to publication volume, reflecting their early contributions to e-mental health innovation. Overall, this author network indicates a well-connected and maturing field where both established and emerging scholars collaboratively drive theoretical and applied advancements in digital mental-health stigma research. The distribution of publications among the most productive authors is visually illustrated in Figure 6.

TABLE 5. Top influential authors.

Sources	H-index	G-index	M-index	TC	NP	PY-start
Christensen	6	7	0.429	610	7	2012
Wang	5	7	0.714	67	7	2019
Brumby et al.	4	4	0.400	102	4	2016
Hightow-Weidman	4	7	0.444	108	7	2017
Kennedy	4	4	0.400	102	4	2016
Li X	4	5	0.500	134	5	2018
Li Y	4	4	0.500	96	4	2018
Muessig	4	8	0.444	152	8	2017
Batterham	3	3	0.214	225	3	2012
Bauer et al.	3	3	0.429	60	3	2019

Note: TC: total citations; NP: number of publications.

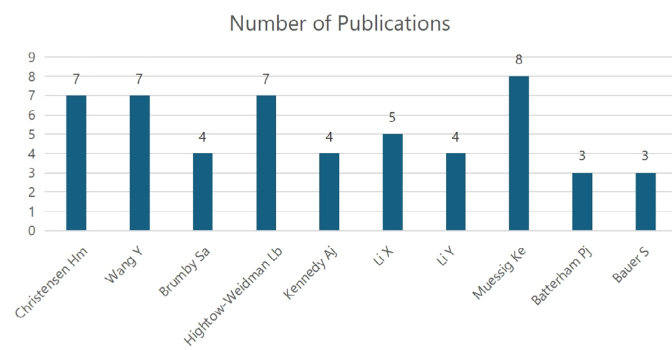

FIGURE 6. Publications according to authors.
Note: Top contributing authors with three or more publications.

Most Influential Authors

Authors play a pivotal role in defining the intellectual evolution of research on mental health stigma and digital interventions. As presented in Table 5, the most influential authors were identified based on their *h*-index, *g*-index, *m*-index, total citations, and number of publications, revealing the intellectual dominance and research consistency in this field. Christensen emerged as the leading contributor, having the highest productivity and citation strength, reflecting his longstanding influence since 2012. Following closely, Wang and Li X have demonstrated strong growth momentum with high m-index values, suggesting impactful recent contributions. Similarly, Brumby et al., Hightow-Weidman, and Muessig have consistently published collaborative and highly cited works that integrate digital technology with psychological health outcomes. The inclusion of scholars, such as Batterham and Bauer et al. underlines the blend of early and emerging academic leadership. Overall, the author-level analysis underscores that a small yet cohesive group of researchers has driven both theoretical enrichment and applied advancements in digital mental-health research.

Network of Co-Authorship Analysis

Co-authorship analysis provides insights into collaboration patterns and intellectual connectivity among researchers within the domain. The co-authorship network illustrated in Figure 7 visualizes the interlinkages between authors contributing to digital mental health and stigma studies. Each circular node represents an author, with node size corresponding to publication volume and connecting lines denoting collaborative frequency. Thicker lines illustrate stronger collaborative ties. The analysis reveals that Christensen, Wang Y., and Hightow-Weidman form the central hub of the collaboration network, often partnering with Muessig, Li X, and Brumby et al. to produce interdisciplinary outputs that combine digital innovation, behavioral psychology, and public health perspectives. This pattern highlights the interdisciplinary and globally distributed nature of the research community, with frequent cross-country collaborations. Strong clustering within the network indicates a high level of scientific cohesion, suggesting that collaboration has been instrumental in advancing empirical understanding and methodological rigor in digital mental-health scholarship.

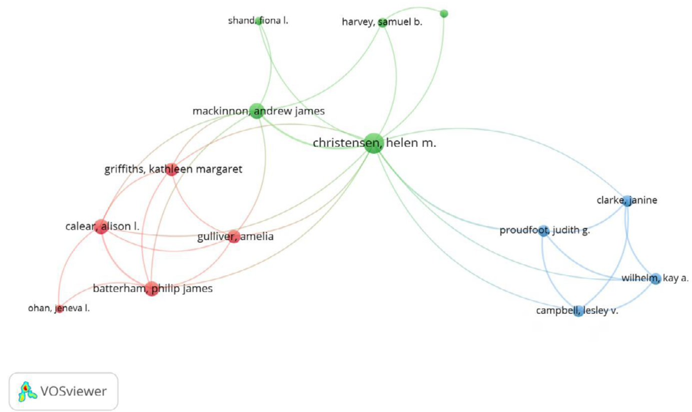

FIGURE 7. Network map of co-authorship.

Top Contributing Sources (RQ3)

The source analysis identifies the most productive journals contributing to the research domain of mental health stigma and digital interventions. The *Journal of Medical Internet Research emerges* as the leading source with 21 publications, reaffirming its role as a premier outlet for digital health and telemedicine scholarship. It is followed by the *International Journal of Environmental Research and Public Health* with 12 articles, reflecting the interdisciplinary expansion of mental health studies into public health and environmental well-being contexts. *BMJ Open, Internet Interventions, and PLOS ONE* contribute 10 papers each, signifying growing recognition of open-access platforms in disseminating digital mental health research. Specialized outlets such as *JMIR Mental Health, JMIR Research Protocols*, and *Telemedicine and e-Health* (each with 9 articles) further emphasize the strong methodological and applied focus of this field. Additionally, *Frontiers in Psychiatry and AIDS Care* represent niche yet influential sources addressing psychosocial aspects of stigma within digital care frameworks. Overall, the distribution of publications demonstrates the multidisciplinary nature of this research domain, where medical informatics, psychology, and public health converge to advance digital pathways for stigma reduction and mental well-being. The comparative influence and productivity of these sources are summarized in Table 6, while their relative publication contribution is visually illustrated in Figure 8.

TABLE 6. Top influential authors.

Sources	H-index	G-index	M-index	TC	NP	PY-start
Christensen	6	7	0.429	610	7	2012
Wang	5	7	0.714	67	7	2019
Brumby et al.	4	4	0.400	102	4	2016
Hightow-Weidman	4	7	0.444	108	7	2017
Kennedy	4	4	0.400	102	4	2016
Li X	4	5	0.500	134	5	2018
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Muessig	4	8	0.444	152	8	2017
Batterham	3	3	0.214	225	3	2012
Bauer et al.	3	3	0.429	60	3	2019

Note: TC: total citations; NP: number of publications; PY: publication year.

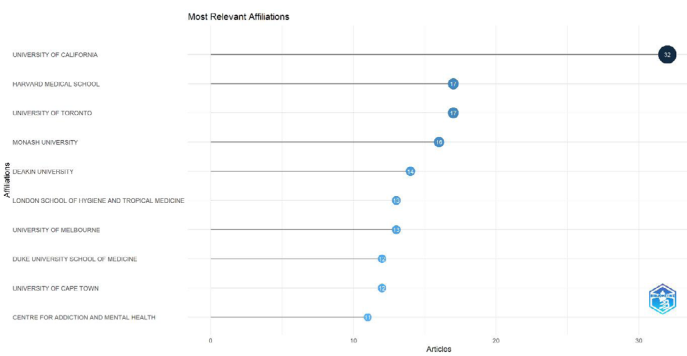

FIGURE 8. Top contributing sources.

Top-Cited Countries

The country-wise citation analysis reveals the global distribution of scholarly influence in the domain of mental health stigma and digital interventions. India ranks as the most productive and impactful contributor with a total of 3,475 citations and an impressive average of 182.9 citations per article, highlighting its growing leadership in digital mental health research, particularly during the post-pandemic years. The United States and Australia follow with 3,144 and 1,829 citations, respectively, reflecting their sustained engagement in technology-driven mental health solutions and cross-cultural stigma studies. Lebanon demonstrates remarkable citation efficiency, averaging 211.8 citations per article, indicating high-impact publications despite a smaller research volume. Other major contributors include Canada, China, and Germany, representing diversified global participation in digital psychiatry and mental well-being initiatives. Notably, smaller yet influential regions, such as Hong Kong, Ireland, and Austria, exhibit strong average citation proportions, signifying high-quality contributions within limited publication outputs. Overall, the pattern illustrates an increasingly internationalized research landscape where both developed and emerging economies contribute to the collective advancement of digital mental health scholarship. The comparative citation performance across countries is illustrated in Figure 9.

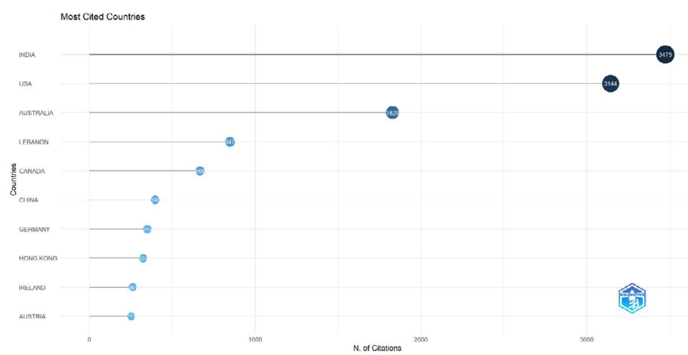

FIGURE 9. Top-cited countries.

Top Collaborating Countries

The country collaboration analysis highlights the global partnership patterns in mental health stigma and digital intervention research. The United States leads with 137 publications, accounting for 28% of total output, although its multiple country publications (MCP) rate is modest at 2.2%, indicating primarily domestic collaborations. In contrast, Australia exhibits a high intensity of collaborations, contributing 76 papers with an MCP proportion of 42.1%, showcasing its strong engagement in international research networks. Similarly, China demonstrates the highest proportion of multi-country collaborations (52%), reflecting its expanding participation in cross-border mental health and digital health studies. Other active contributors, such as Canada (37.5%), the United Kingdom (38.1%), and India (42.1%), also show a balanced mix of single-country and international co-authorship, emphasizing the global nature of digital mental health research. Smaller yet collaborative nations such as Portugal (33.3%), Ireland (28.6%), and Israel (28.6%) further reinforce diverse participation across regions. Overall, these results illustrate a vibrant international collaboration landscape, where both developed and emerging countries jointly advance innovation and inclusivity in mental health stigma research through digital technologies. The international collaboration network among countries is visualized in Figure 10.

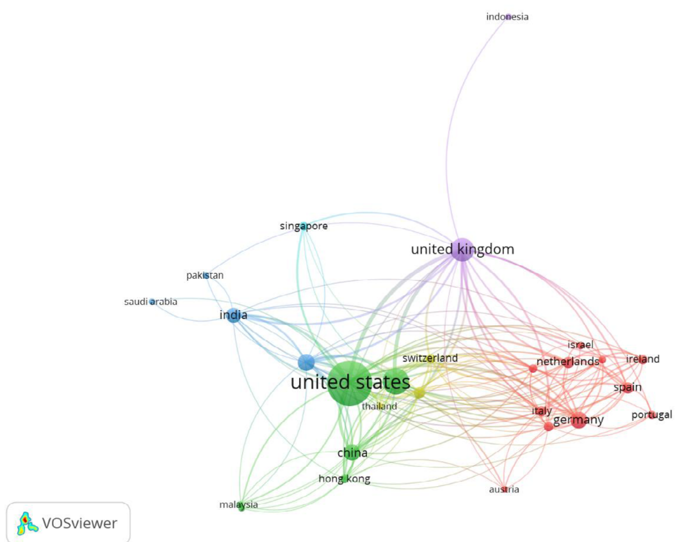

FIGURE 10. Network map of collaborating countries.

Top Contributing Affiliations

The institutional productivity analysis presented in Figure 10 identifies the leading academic affiliations contributing to the research landscape of mental health stigma and digital interventions. The University of California emerges as the most prolific institution with 32 publications, underscoring its extensive interdisciplinary work in digital mental health innovation and stigma reduction. Both Harvard Medical School and the University of Toronto follow with 17 articles each, reflecting their strong clinical and behavioral health research traditions. Monash University and Deakin University, with 16 and 14 papers respectively, demonstrate Australia's growing leadership in mental health informatics and telehealth-based intervention research. Prominent public health institutions, such as the London School of Hygiene and Tropical Medicine and the University of Melbourne, contribute 13 papers each, reinforcing the global nature of collaborative digital health research. Similarly, Duke University School of Medicine and the University of Cape Town (12 each) signify cross-continental academic engagement, while the Centre for Addiction and Mental Health adds 11 papers, highlighting its pivotal role in applied mental health research. Overall, the institutional distribution indicates a robust international collaboration anchored by globally recognized universities, reflecting an evolving academic ecosystem that bridges psychiatry, technology, and social well-being. The comparative contribution of leading affiliations is illustrated in Figure 11.

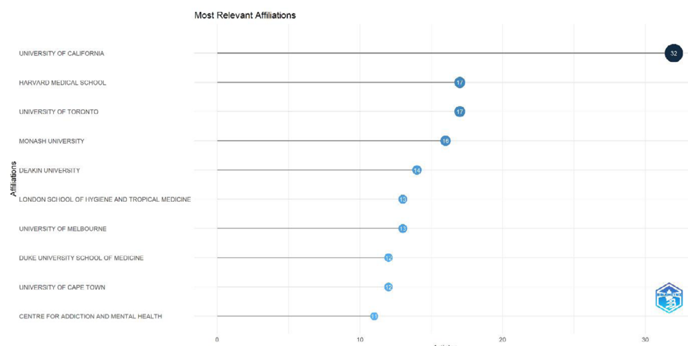

FIGURE 11. Top-cited contributing affiliations.

Keywords Analysis (RQ4)

The keyword co-occurrence and density visualizations (Figures 12 and 13) highlight the conceptual and thematic landscape of research on mental health stigma and digital interventions. The network visualization shows several interconnected clusters representing dominant themes. The central cluster revolves around keywords such as human, mental health, psychology, and social stigma, reflecting the core focus on psychological dimensions, behavioral patterns, and social perceptions of mental illness in digital contexts. Another prominent cluster includes terms such as telehealth, web-based intervention, and Internet-based intervention, emphasizing the growing role of digital tools and e-therapy platforms in reducing stigma and improving accessibility. A third thematic group features keywords such as help-seeking behavior, treatment outcome, and psychoeducation, underscoring the significance of user engagement, behavioral support, and digital literacy in mental health outcomes. Peripheral clusters highlight contextual themes such as pandemic, telepsychiatry, and suicidal behavior, pointing to contemporary research trends shaped by global health challenges. The density visualization further illustrates the intensity of research concentration around key concepts, where warmer regions signify frequently co-occurring keywords and strong intellectual linkages across multidisciplinary domains. Overall, the keyword mapping reveals an integrative and evolving research structure that connects psychological constructs, digital innovations, and public health perspectives in addressing mental health stigma. The frequency and relational strength of dominant keywords identified in the co-occurrence network are summarized in Table 7.

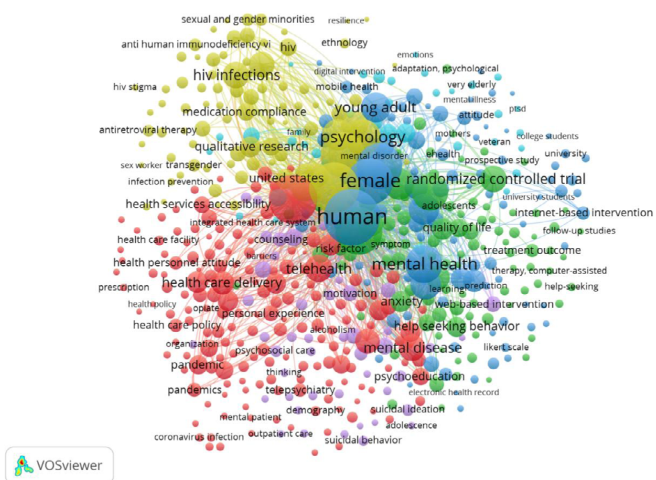

FIGURE 12. Network visualization of keywords.

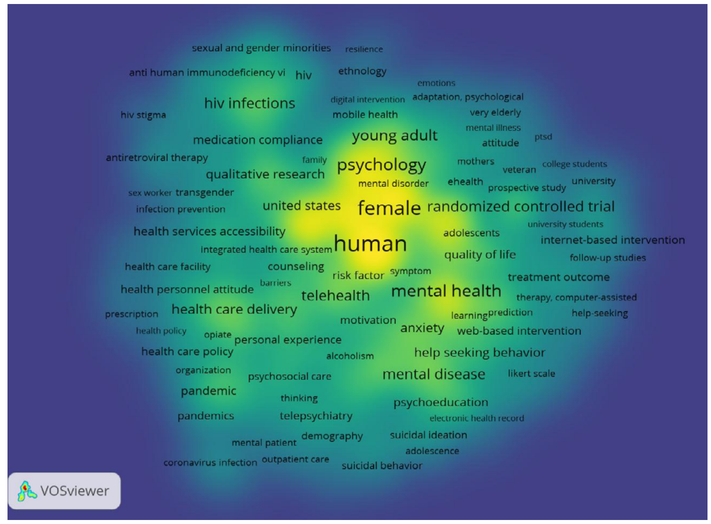

FIGURE 13. Keyword density visualization.

TABLE 7. Occurrence of keywords in the network.

Words	Occurrences	Total Link Strength
Human	383	9,634
Humans	306	7,918
Social stigma	280	7,299
Article	250	6,843
Female	243	6,640
Male	236	6,403
Adult	227	6,157
Mental health	198	4,364
Psychology	150	4,075
Controlled study	146	4,106

Major Themes

Thematic analysis revealed four dominant clusters shaping the intellectual landscape:

Cluster 1—Technology-enabled therapy: This represents the largest and most influential stream, encompassing research focused on online cognitive behavioral therapy (CBT), mobile therapy applications, telepsychiatry, and AI-driven chatbots. This cluster highlights how technology serves as a bridge between accessibility and anonymity, thereby mitigating social stigma and encouraging help-seeking behaviors among diverse populations. Studies in this domain emphasize how digital therapy platforms enable real-time emotional monitoring, algorithmic personalization, and continuous support, which reduce perceived judgment and lower the psychological barriers to treatment. The integration of AI-powered interventions has particularly transformed the therapeutic landscape by offering cost-effective, scalable, and stigma-free mental health assistance.

Cluster 2—Public perception and stigma narratives: This captures the sociocultural and communicative dimensions of digital mental health research. Scholars in this stream focus on how social media, digital storytelling, and online advocacy shape collective attitudes and public discourse around mental illness. Through platforms such as Twitter, YouTube, and online forums, individuals share lived experiences, counter stereotypes, and build communities that normalize conversations around mental well-being. The findings suggest that digital spaces not only challenge stigma but also function as participatory arenas for awareness campaigns, empathy-building, and social change.

Cluster 3—Digital inclusion and access barriers: This underscores structural inequities and digital divides that limit the reach of mental health technologies, especially in resource-constrained settings. Herin, the research discusses the challenges posed by socioeconomic disparities, limited digital literacy, and infrastructural constraints that hinder equitable access to e-health interventions. The literature calls for inclusive policies, culturally sensitive content, and context-specific implementation strategies that ensure technological interventions reach vulnerable and marginalized populations. This cluster positions digital inclusion as a moral and ethical imperative within the global health agenda.

Cluster 4—AI and gamified mental health tools: This reflects the frontier of innovation where AI, gamification, and immersive technologies such as virtual and augmented reality are leveraged to enhance mental health engagement, personalization, and empathy-driven design. These approaches integrate behavioral reinforcement techniques, biofeedback, and adaptive learning algorithms to sustain motivation and reduce stigma through experiential learning. Scholars argue that such immersive interventions humanize digital therapy by simulating supportive environments, promoting emotional resilience, and fostering long-term adherence.

IMPLICATIONS

The bibliometric and thematic analyses of research on mental health stigma and digital interventions provide valuable insights for both academia and practice, underscoring the interdisciplinary evolution of this domain. From an academic perspective, the findings enrich the existing body of knowledge by mapping how digital technologies—ranging from telepsychiatry and mobile health to AI-driven chatbots—are reshaping the understanding, treatment, and communication of mental health issues. The observed thematic clusters emphasize the field's multidimensional character, merging psychology, public health, behavioral science, and digital innovation into an integrative scholarly framework.[11] These insights create a foundation for advancing theoretical models that account for digital behavior, stigma perception, and technology acceptance in mental health contexts. Furthermore, the bibliometric mapping highlights key research gaps, such as the need for longitudinal analyses, culturally adaptive frameworks, and cross-national comparative studies, which can drive future empirical inquiries.

From a practical standpoint, the results highlight actionable pathways for mental health practitioners, policymakers, and digital health designers. The prominence of technology-enabled therapy and AI-supported interventions underscores the transformative role of digital platforms in overcoming accessibility barriers and reducing the stigma associated with traditional therapy. Practitioners can leverage mobile health tools and online communities to provide confidential, stigma-free environments that foster early diagnosis, peer support, and continuous engagement. Policymakers, on the other hand, are encouraged to develop inclusive digital health policies that address infrastructural disparities and ensure equitable access to technological mental health solutions. Integrating evidence-based AI models and gamified approaches into national mental health programs also enhances public awareness, motivation, and resilience across diverse demographic groups.

From a societal and policy perspective, this study reiterates the urgency of adopting a holistic approach to mental health advocacy, where digital platforms function not only as therapeutic tools but also as catalysts for cultural change. The widespread use of social media, narrative campaigns, and virtual communities has amplified voices that were historically marginalized, thereby reframing public perception of mental illness. These collective digital narratives contribute to a gradual normalization of mental health discourse, reducing prejudice, and fostering empathy-driven interactions in online ecosystems.

In essence, the implications of this bibliometric review extend beyond academic theory to real-world transformation. They call for a synergy between technological innovation, psychological insight, and policy reform—ensuring that digital mental health ecosystems remain inclusive, ethical, and effective in addressing stigma globally. By integrating digital inclusivity, emotional intelligence, and human-centered design, the research community and mental health stakeholders can collaboratively advance a new era of equitable, stigma-free mental well-being.

LIMITATIONS AND FUTURE SCOPE OF RESEARCH

While this bibliometric study offers valuable insights into the intellectual and thematic evolution of mental health stigma and digital interventions, several limitations must be acknowledged. First, the analysis was exclusively based on the Scopus database, which, although comprehensive, may not encompass all relevant publications indexed in other databases, such as Web of Science, PubMed, or Dimensions. Consequently, certain region-specific or emerging research contributions might have been overlooked. Second, the language filtration restricted the dataset to English-language publications, potentially excluding significant findings published in non-English journals, particularly from regions with high digital health innovation but lower global visibility. Third, the study employed quantitative bibliometric tools such as Biblioshiny and VOSviewer, which focus primarily on citation patterns and keyword co-occurrence; therefore, the interpretive depth of qualitative nuances, contextual analysis, or theoretical argumentation remains limited.

Despite these limitations, the current research opens multiple avenues for future investigation. Expanding the dataset across multiple databases and including non-English literature could enhance the comprehensiveness of global insights. Future studies could also integrate meta-analytic or systematic review approaches to triangulate bibliometric trends with empirical outcomes, thereby providing a more holistic understanding of how digital technologies impact stigma reduction and mental health outcomes. Moreover, incorporating altmetric indicators—such as social media engagement, online discussions, and public policy citations—may reveal the societal reach and real-world influence of scholarly work in this domain. Researchers are also encouraged to explore longitudinal analyses to trace evolving collaborations, emerging technologies such as AI-driven therapeutic bots, and the ethical considerations surrounding digital mental health interventions.

Overall, this study lays a foundational framework for continued scholarly exploration into the fusion of technology and mental health advocacy. By extending future research through multidisciplinary lenses and culturally inclusive methodologies, the field can progress toward designing scalable, equitable, and stigma-free digital ecosystems that effectively bridge the gaps in mental health accessibility and social perception.

CONCLUSIONS

This bibliometric study provides a comprehensive overview of the global research landscape on mental health stigma and digital interventions, capturing its intellectual evolution, thematic diversity, and collaborative trends. The analysis, conducted using Biblioshiny and VOSviewer, revealed a steady growth in scholarly output from 2007 to 2024, reflecting the increasing academic and societal recognition of digital technology's transformative role in mental health care. The most influential contributions originated from interdisciplinary and geographically diverse authors, institutions, and countries, demonstrating that the intersection of psychology, information technology, and public health has become a vibrant field of inquiry. Leading journals such as the *Journal of Medical Internet Research and Internet Interventions* emerged as key publication sources, confirming the integration of mental health research into the broader digital health ecosystem.

The keyword co-occurrence and thematic mapping uncovered four dominant clusters—technology-enabled therapy, public perception and stigma narratives, digital inclusion and access barriers, and AI and gamified mental health tools—each representing a unique yet interconnected strand of research. These clusters highlight the expanding scope of digital mental health scholarship, transitioning from early explorations of telepsychiatry and e-therapy toward data-driven, AI-enhanced, and empathy-oriented intervention models. The co-authorship and collaboration networks further emphasize the global, multidisciplinary, and cooperative nature of this domain, with strong linkages across North America, Europe, and the Asia-Pacific region.

Finally, this study not only consolidates the existing scholarly insights but also charts new directions for future research, emphasizing inclusivity, technological equity, and cross-cultural adaptation in digital mental health solutions. The findings underscore the urgent need for sustained collaboration among researchers, clinicians, technologists, and policymakers to address persistent stigma and bridge digital divides. As digital transformation continues to reshape health communication and therapeutic practice, the fusion of technology and empathy remains the cornerstone of an inclusive and stigma-free global mental health landscape.

AUTHOR CONTRIBUTIONS

Conceptualization, R.B. and Y.S.M.; Methodology, P.C.; Software, N.P.; Hardware, N.P.; Validation, R.B., P.C.; Formal Analysis, Y.S.M.; Investigation, R.B.; Resources, P.C.; Data Curation, N.P.; Writing–Original Draft Preparation, Y.S.M., P.C.; Writing–Review & Editing, R.B., N.P.; Visualization, R.B.; Supervision, P.C.; Project Administration, R.B.; Funding Acquisition, Y.S.M.

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CONFLICTS OF INTEREST

The authors declare they have no competing interests.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

FURTHER DISCLOSURE

Not applicable.

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Original Research Article

Valuation of Sustainable Practices for Solid Waste Management through Time-Series Forecasting Model Using ARIMA

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ABSTRACT

The present research investigates the integration and assessment of sustainable practices in the field of solid waste management (SWM) in Chandigarh, India, by focusing on enhancing the efficiency and sustainability of municipal waste operations through time-series forecasting. Chandigarh, an urban center, faces increasing challenges because of population burden and ever-increasing waste generation. Data-driven approaches to predict and manage municipal solid waste have become essential. In the present work, historical daily data collected from the Material Recovery Facility (a waste processing plant), Sector-25, Chandigarh, India, are utilized to develop forecasting models using the Autoregressive Integrated Moving Average (ARIMA) methodology. The present work focuses not only on forecasting the total waste received of a particular waste stream, viz. cardboard and thermocol, but also on some other specific waste categories, such as recyclable plastics, metals, glass, and coconut shells. The results revealed key trends, including a steady rise in waste quantities across most categories, seasonal fluctuations, and temporary anomalies potentially influenced by public events or climatic changes. The results revealed that integrating ARIMA-based forecasting into the Chandigarh Smart City dashboard fundamentally changes municipal waste management from a reactive struggle into a proactive strategy, which emphasizes the importance of predictive planning in SWM. Optimizing collection processes, upgrading sorting technologies at material recovery facilities, strengthening community participation in source segregation, and integrating real-time digital dashboards for municipal oversight are few recommendations. By bridging gap between academic modeling and municipal needs, this study offers a scalable framework for predictive and sustainable waste management practices in Chandigarh, India. This study contributes to the broader discourse on Chandigarh smart city infrastructure by offering useful insights for planners and urban policy makers striving to build resilient and environmentally sustainable waste systems.

Keywords—*Solid waste management (SWM), Municipal solid waste (MSW), ARIMA forecasting model, Material recovery facility (MRF), Urban sustainability.*

INTRODUCTION

Management of municipal solid waste (MSW) is a decisive aspect of urban sustainability, involving the collection, transportation, processing, and disposal of waste generated by residential, commercial, institutional, and public sources. As cities continue to expand, the optimized and sustainable solid waste management (SWM) practices have become increasingly essential, requiring effective strategies to manage rising waste volumes.[1,2] This broader challenge is clearly reflected in Chandigarh, India, where a population of 1.2 million produces nearly 500 metric tons per day (TPD) of dry and wet waste each day. The waste stream is dominated by organic materials (52%), followed by inerts (21%), plastics (7%), and paper (6%). However, despite achieving 100% waste collection efficiency, the city still faces persistent issues such as improper segregation at the source, an overburdened landfill, and limited decentralized processing facilities. These challenges highlight the gap between collection efficiency and truly sustainable waste management.

Comprehensive studies analyzing current MSW management practices are essential for identifying the existing gaps and improving system performance.[3] Efficient planning and management of solid waste rely on the ability to anticipate future waste quantities. Accurate knowledge of MSW generation rates and composition is foundational for planning infrastructure and resource allocation.[4] The development of reliable forecasting models is a key area of research to aid in proactive urban planning and waste management decisions.[5] A detailed sustainability assessment of the existing SWM practices has been performed specifically for Chandigarh, India, providing crucial context for local system improvements.

Accurate forecasting of MSW helps to optimize collection schedules and reduce operational costs to ensure long-term sustainability. In the present study, a forecasting-based approach was used with historical daily MSW data collected at one such material recovery facility (MRF) in Chandigarh, India. By identifying trends and projecting future waste generation, this study aims to support decision-makers in formulating proactive waste-management strategies.

Existing SWM Infrastructure at Chandigarh, India

Chandigarh has established a combination of centralized and decentralized waste processing facilities to manage its growing MSW. The key facilities, including one solid waste treatment plant located at Dadumajra, and three MRFs located in Sector 25, Industrial Area Phase-1 and Phase-2 in Chandigarh, respectively, play a distinct role in the systematic handling of MSW—from initial collection, sorting, resource recovery to final disposal.

The plant set up in 2008 and upgraded to 200 tons capacity recently, effectively serves as the central facility for processing the dry waste component of MSW. The city has specialized units for processing wet, horticulture, and construction and demolition (C&D) waste at different locations along with a 20-acre sanitary landfill site at Dadumajra. Recently, a Memorandum of Understanding (MoU) is signed for setting up of a 230-ton capacity compressed biogas (CBG) plant to convert organic waste into bio-energy, aiming to reduce significantly dependency on landfill, through resource recovery and clean energy generation.

Material Recovery Facility

To improve waste segregation and optimize the transfer of waste, MRFs are established at strategic locations covering 114 km^2 area comprising Sectors 01–56, 61, and 63, and 22 villages. (i) The MRF at Sector 25 (West), serves a wide area covering 31 northern and western sectors; and several villages, including Maloya, Dhanas, and Sarangpur. (ii) The second facility at the PH Store in Industrial Area Phase-1, Chandigarh, India, primarily functions for waste from eastern sectors and Mani Majra. (iii) The third facility, situated at 3-Base Repair Depot (3-BRD), Industrial Area Phase 2, manages waste from southern sectors of Chandigarh, India.

The Sector 25 (West) MRF, inaugurated in March 2022 as a "Pink" MRF (because its staff are all women), was set up under smart city initiative and is equipped with a shed, conveyor belt, weighing bridge, and boom barrier to sort out dry (cardboard/paper, plastic, metals, and glass) and wet waste, which is then compacted into transport capsules and sent to dry and wet treatment plants, respectively, for further processing (Figure 1). The present research aimed to develop an accurate time-series forecasting model using Autoregressive Integrated Moving Average (ARIMA) to predict the weekly generation of MSW in Chandigarh, India, and to analyze the implications of solid waste forecasting on improving the waste collection efficiency, resource allocation, and infrastructure planning. This research formulated and addressed the following key research questions:

RQ 1: How accurately forecasting of high value streams at a localized MRF can be done using the ARIMA (Seasonal Autoregressive Integrated Moving Average with exogenous factors) framework model?

RQ 2: What are the seasonal trends and generation patterns predicted for these waste categories in Chandigarh, India?

RQ 3: In what ways these predictive insights are utilized for economic valuation and optimization of municipal resource allocation in Chandigarh, India?

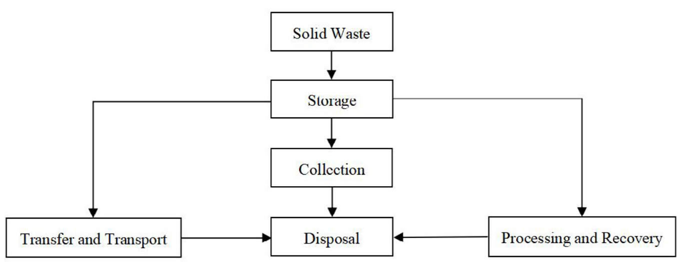


FIGURE 1. Process of MSW management in Chandigarh, India.

LITERATURE REVIEW

Forecasting MSW generation has rapidly become an indispensable tool for urban planning, especially in cities with high population growth and escalating waste volumes. By accurately predicting future waste streams, municipalities proactively streamline logistics, optimize resource allocation, and plan essential infrastructure, thereby preventing strain and eventual failure of the existing waste processing systems. Early foundational research established the viability of both linear and nonlinear models for MSW prediction.[6,7] These initial models have since been significantly enhanced by incorporating diverse influencing factors, such as meteorological data and demographic shifts.[8,9] Importantly, the sheer volume of generated waste is frequently tied to underlying socioeconomic and demographic variables.[10–12] Multi-model approaches often leverage the analysis of these parameters, notably in studies conducted in China.[13] The region-specific forecasting is tailored to unique urban environments, such as those in India and Southeast Asia.[14] The crucial local benchmarks are offered for SWM planning.[15] International studies, such as the use of time-series models for landfill management in Brazil, underscore the global relevance of this predictive approach[16], while a systematic national review provides context for the diverse methodologies applied across India. A sustainable waste management can be achieved by scientifically measuring the environment impact of every decision we take. By using life cycle assessment (LCA), we can quantify the real-world benefits of moving away from landfills toward integrated systems, such as anaerobic digestion and specialized recovery facilities. Recent studies have proved that reduced Green House emission and prevention of contamination of water and soil can be achieved simply by treating municipal and biomass waste as a resource.[17,18] Moreover, they emphasized that localizing these recovery systems is essential for minimizing the carbon intensity of urban logistics.[19] For a city like Chandigarh, adopting these LCA insights opens new doors to sustainability and circular economy.

Recently, research has strongly migrated toward data-driven techniques, including advanced time-series models, sophisticated machine learning algorithms, and hybrid stochastic methods, to achieve greater precision in waste quantification. Traditional statistical methods such as ARIMA models have shown consistent and reliable performance across various global contexts and time scales and their simplicity and interpretability keep them highly relevant even amidst the rise of complex tools.[20–22] The findings of studies for advanced ARIMA applications[23–25]; and for hybrid models, such as the Grey Rolling Model, optimized by Particle Swarm Optimization, have demonstrated this evolution. Concurrently, new machine learning approaches, including stochastic programming for routing, fuzzy-based frameworks for supply chains, and the application of long short-term memory (LSTM) artificial neural networks (ANN) for daily prediction, have shown promise by achieving higher accuracy than conventional linear methods.[26–28] Conventional techniques are no longer effective because of heterogeneity in solid waste generation process. These forecasting models are not useful for operational efficiency, particularly in optimizing systems, such as waste-to-energy (WTE) facilities, as concluded by studies.[29] Despite these significant methodological advancements, including efforts to integrate external factors such as weather and festival data in Indian metropolitan studies, the specific application of weekly time-series forecasting using actual municipal collection data has remained relatively unexplored.[30]

DATA ANALYSIS

Data analysis in solid waste involves transformation of raw data into actionable insights by analyzing quantity, composition, and movement patterns, by using suitable techniques to understand, predict, and optimize waste generation, collection, sorting, and treatment, leading to smarter systems, reduced costs, better recycling, and improved sustainability (Figure 2).

Data Collection

The dataset used in this research is a time-series dataset of solid waste collected daily category-wise (in TPD) at the MRF plant, Sector 25, Chandigarh, India. As shown in Figure 3, the total solid waste received at plant (weekly) ranges from 390 to 590 TPD and comprises dry waste, wet waste, C&D waste, household sanitary waste, and domestic hazardous waste, and includes cardboard/thermocol, recyclable plastic, metal, shoes, glass, coconut shells, etc. The data help to identify trends and patterns in waste collection and are critical for making accurate forecasts. Table 1 provides the one sight view of total solid waste collected on weekly basis.

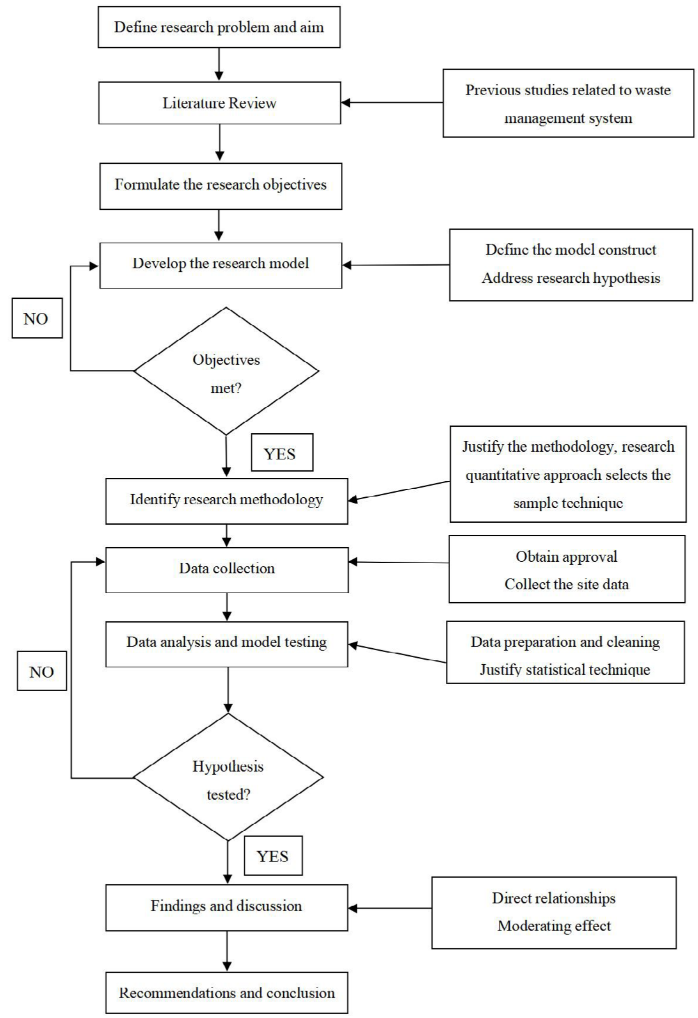


FIGURE 2. Process flow chart for present research work.

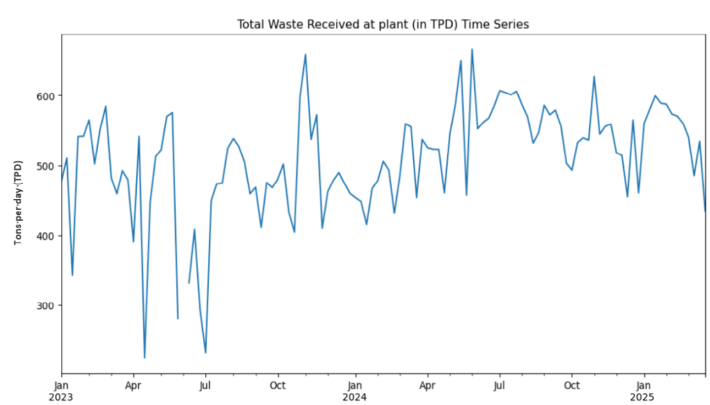


FIGURE 3. Total solid waste received in Chandigarh, India.

TABLE 1. Total solid waste collected (weekly data).

Weeks (year 2023)	Total Waste Received at Plant (in TPD)	Cardboard/ Thermacol (in TPD)	Packaging/ Recyclable Plastic (in TPD)	Metal (in TPD)	Glass (in TPD)	Coconut Shells (in TPD)	Total Dry Waste Received (in TPD)	Total Sanitary Waste Received (in TPD)	Total Hazardous Waste Received (in TPD)	Dry Waste Sent to Processing Plants (in TPD)
1st	476.690	0.255	0.135	0.011	0.069	5.380	207.97	0.6323	0.009	206.81
2nd	510.030	0.350	0.195	0.009	0.097	5.215	231.38	0.6560	0.010	230.01
3rd	342.400	0.285	0.163	0.010	0.089	3.770	160.95	0.3653	0.006	159.97
4th	540.985	0.340	0.181	0.016	0.106	6.430	214.50	0.5825	0.011	213.18
5th	541.395	0.295	0.192	0.010	0.094	6.320	209.95	0.4554	0.007	208.83
6th	564.860	0.460	0.264	0.008	0.101	7.765	203.11	0.6101	0.004	201.90
7th	501.900	0.405	0.219	0.008	0.076	10.46	187.91	0.4200	0.002	186.72
8th	551.560	0.340	0.194	0.012	0.054	9.570	165.19	0.5724	0.005	163.93

Note: TPD: tons per day.

Linear interpolation was used to fill minor gaps and maintain the continuity of the time series, ensuring that the ARIMA model did not interpret "zero-entry" errors as actual declines in waste generation data.

Training Dataset

It contains historical collected waste data with the following features:

(a) Total waste received in plant (target variable).

(b) Types of waste (forecasting is done on each type of waste).

Testing Dataset

It is used to evaluate the model on unseen data. The same features were used as an input, except for the total waste received, which was predicted.

Figure 3 showcases the total solid waste received (in TPD), on weekly basis, at the MRF plant, Sector 25, Chandigarh. This is the training dataset for analysis, as it contains historical collected waste data, received at plant, with allied features as target variables.

Application of Model

The ARIMA technique model is a statistical method used widely for forecasting of time series because of its simple algorithm and ability to identify influential parameters, wherein three key terms of model data (p, d, and q) are indicated as follows: p: the order of autoregression (AR); d: the order of differencing; and q: the order of moving average (MA). Differencing involves transforming a non-stationary time series into a stationary one by differencing consecutive observations until stationarity is achieved.

The ARIMA model requires that the statistical properties of the time series, viz. mean and variance, remain constant over time, to estimate parameters p, d, and q for further analysis of the autocorrelation function (ACF) and partial autocorrelation function (PACF) plots of the time-series data, as the ACF helps in determining the moving average order (q), and PACF helps in determining the autoregressive order (p). The model involves obtaining the most suitable coefficients for autoregressive and moving average terms by minimizing the error using maximum likelihood estimation. After fitting the model, future values are forecasted by iterating over the time.

Auto-regression (AR): it relates present value to its previous values through a regression equation,

$$Y_t = c + \emptyset_1 Y_{t-1} + \emptyset_2 Y_{t-2} + \ldots + \emptyset_p Y_{t-p} + \epsilon_t, \qquad (1)$$

where Y_t is the current observation, c is a constant, ϕ_t to ϕ_p are autoregressive parameters, and ϵ_t represents the error term at time t.

Differencing (I for integrated): A nonstationary time series is transformed into a stationary one by differencing the consecutive observations. The differencing operation can be applied for multiple times until stationarity is achieved,

$$Y_t` = Y_t - Y_{t-1}, \tag{2}$$

where $Y_t`$ is the differenced series at time t, Y_t is the original series at time t, and Y_{t-1} is the value of the series at the previous time step.

The process of differencing is typically applied for multiple times until stationarity is achieved. The notation I(d) indicates the order in which differencing is required to achieve stationarity.

Moving average (MA): this part of the ARIMA model is represented by the parameter q. This indicates that the current observation depends upon previous forecast errors,

$$Y_t = c + \in_t + \theta_1\epsilon_{t-1} + \theta_2\epsilon_{t-2} + \ldots + \theta_p\epsilon_{t-q}, \tag{3}$$

where Y_t is the current observation, c is a constant, ϵ_t is the error at time t, and θ_1 to θ_q are moving average parameters.

A general formula for a nonseasonal ARIMA model is represented as ARIMA (p, d, and q):

$$Y_t` = c + \emptyset_1 Y_{t-1}` + \emptyset_2 Y_{t-2}` + \ldots + \emptyset_p Y_{t-p}` + \epsilon_t + \theta_1\epsilon_{t-1} + \theta_2\epsilon_{t-2} + \ldots + \theta_q\epsilon_{t-q}, \tag{4}$$

where $Y_t`$ is the differenced and stationary time series at time t, c is the mean of the differenced series or a constant, ϕ_1, ϕ_2, ..., ϕ_p are autoregressive parameters that represent dependence on past values, ϵ_t is the white noise error term at time t, and θ_1, θ_2, ..., θ_q are moving average parameters that represent dependence on past forecast errors.

To check stationarity, the Augmented Dickey–Fuller test (ADF) is used to observe a significant trend—a unit root, or other patterns that change over time, which is a crucial step when building a model.

Model Assumptions

(i) The data are stationary (achieved through differencing or using seasonal components).

(ii) There is a linear relationship between the target variable and exogenous variables.

(iii) The residuals of the model or errors are normally distributed and have constant variance.

Hypothesis Testing

(i) Null hypothesis (H0): the time series is nonstationary (i.e., it has a unit root).

(ii) Alternative hypothesis (H1): the time series is stationary.

Rationale for Model Selection and Comparison

Earlier, waste forecasting was done with machine learning models, such as LSTM and ANN, but for research work, the seasonal ARIMA (SARIMAX) framework was strategically chosen because complex models, such as LSTM and ANN, require large datasets to avoid overfitting, whereas ARIMA offers forecasts for smaller datasets, as in our case for recent MRF at Sector 25 (established 2022), Chandigarh, India. Furthermore, using ARIMA model forecasting of short-to-medium term can be achieved through differencing where data are made stationary.

METHODOLOGY

The time-series data of solid waste received was subjected to a comparative study using the SARIMA technique model in various operational environments. It highlights practical effectiveness in achieving accurate predictions for MSW generation.

Using all three parameters of the ARIMA technique model, solid waste was evaluated and the models were constructed for each material. The results were established for all such types of wastes at MRF, Sector 25, Chandigarh, viz. cardboard/thermocol, plastic, metal, glass, and coconut shells.

Model Evaluation for Cardboard/thermocol Waste

The ARIMA technique model was first applied to combined solid waste data of cardboard and thermocol. Referring to Figure 4, the test is applied to the historical data for the period of January 2023–April 2025.

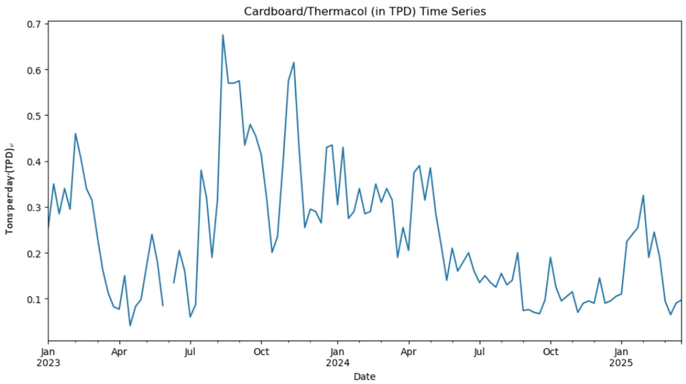
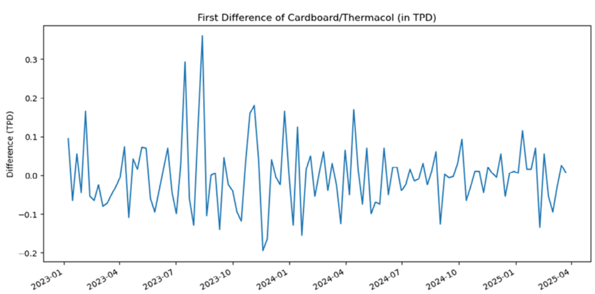


FIGURE 4. Cardboard/thermocol waste at MRF, Sector 25, Chandigarh, India.

Stationarity Test for Cardboard/Thermocol Waste

Statistical stationarity testing is done to analyze the time-series data of cardboard/thermocol waste for statistical stability. To develop accurate predictive model, ADF test, a "unit root" test, where a significant result confirms that the data are stationary, is applied (Figure 5). Since *p* value (0.099) for the ADF statistics > 0.05, further differencing is required.

```
ADF Statistic: -2.5697200239551594
p-value: 0.09941839495771476
Critical Values: {'1%': -3.489589552580676, '5%': -2.887477210140433, '10%': -2.580604145195395}
Series is not stationary - differencing required
```



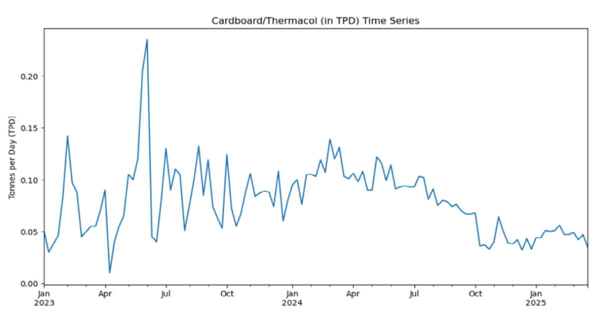


FIGURE 5. ADF test for cardboard/thermocol waste.

ACF and PACF Analysis for Cardboard and Thermocol Waste

In ARIMA model, the ACF and PACF analyses are used to understand the trends (slow decay in ACF/PACF) or seasonal patterns (significant spikes at regular intervals, e.g., monthly or weekly) to determine the order of autoregressive and moving average components. A sharp cut-off in the PACF plot indicates the presence of an autoregressive relationship, while a sharp cut-off in ACF helps to identify moving average terms by measuring correlations across all lags. Figure 6 shows the correlation between a time series and its lagged values in ACF plot.

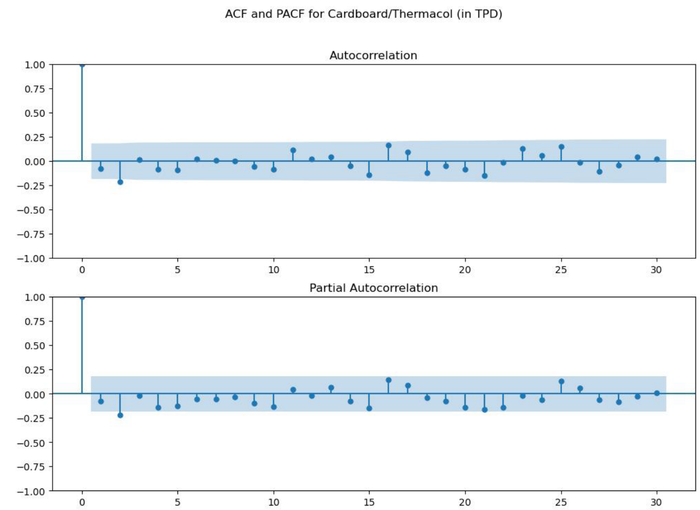


FIGURE 6. Autocorrelation and partial autocorrelation results for cardboard/thermocol.

SARIMAX Results for Cardboard and Thermocol Waste

Depending on specific x-exogenous variables and localized time-series data, the SARIMAX model results for cardboard and thermocol waste at MRF, Sector 25, Chandigarh, confirms that the model (with reductions in errors such as symmetric mean absolute percentage error [sMAPE] and root mean square error [RMSE]) shows promising results in both short-term (e.g., 2 weeks with < 10% error) and medium-long-term forecasting (e.g., 2–3 years with < 5% error).

Table 2 represents the result of the SARIMAX model for cardboard and thermocol waste with 92 observations, 01 lagged event with a confidence level of 0.975. To make sure that the forecasts were not just guessing, the SARIMAX model was put through a tough validation process to prove its reliability. First, checking of waste data stationarity was done, basically making sure that it did not have wild, unpredictable swings in its average or variance over time using the ADF test. For categories with $p > 0.05$, such as cardboard ($p = 0.099$), differencing was applied to stabilize the data and achieve a stable mean and variance.

TABLE 2. SARIMAX results for cardboard and thermocol waste.

SARIMAX Results						
Dependent Variable:	Cardboard/ Thermacol (TPD)		No. of Observations		92	
Model:	ARIMA (1, 0, 4)		Log Liklihood		94.469	
Date:	Fri, 09 May 2025		AIC		−174.93	
Time:	22:56:25		BIC		−157.28	
Sample:	0		HQIC		−167.81	
Covariance type:	opg					
	coef	std err	z	$p >$ mode of z	0.025	0.975
Const	0.2601	0.062	4.176	0.000	0.138	0.382
ar.L1	0.8646	0.129	6.712	0.000	0.612	1.117
ma.L1	−0.0229	0.192	−0.119	0.905	−0.398	0.353
ma.L2	−0.2279	0.160	−1.421	0.155	−0.542	0.086
ma.L3	0.0079	0.139	0.057	0.955	−0.265	0.281
ma.L4	−0.0278	0.103	−0.271	0.786	−0.229	0.173
Sigma2	0.0074	0.001	6.169	0.000	0.005	0.010
Ljung-Box (L1) (Q):			0.00	Jarque-Bera (JB):		52.83
Prob (Q):			0.95	Prob (JB):		0.00
Heteroskedasticity (H):			0.58	Skew:		1.29
Prob (H) (two-sided:)			0.13	Kurtosis:		5.67

Note: AIC: Akaike Information Criterion, BIC: Bayesian Information Criterion, HQIC: Hannan-Quinn Information Criterion, Cons: Constant, coef: Coefficient, std err: Standard Error, prob: Probability, Skew: Skewness.

As shown in Table 2, high probability values of the Ljung–Box test (Prob(Q) = 0.95) for both cardboard and thermocol waste stream confirm that the model is statistically sound and unbiased.

Forecasting

The next and final step of analysis is to achieve forecasting for the data variables of cardboard/thermocol waste at MRF, Sector 25, Chandigarh. Based on historical training data and generational trends, the model depicts that the RMSE for cardboard/thermocol waste at MRF, Sector 25, Chandigarh, comes out to be 0.02, that is, low and highly accurate for an individual forecast such as cardboard/thermocol waste (Figure 7).

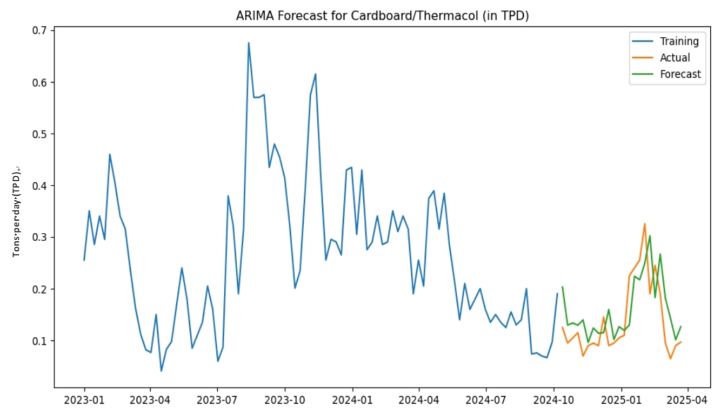


FIGURE 7. Forecast results for cardboard/thermocol waste in MRF, Sector 25, Chandigarh.

Model Evaluation of Packaging/Recycling Plastic, Metal, Glass, and Coconut Shell Waste

Based upon the similar pattern, the ARIMA models are applied and evaluated for the other categories, viz. packaging/recycling plastic, metal, glass waste, and coconut shells.

The forecasting results are obtained after required stationarity test, ADF test, and the SARIMAX model evaluations. Figure 8(a) represents the outcome of the ARIMA model applied for the packaging/recyclable plastic, depicting the results in the form of training, actual and forecasted terms, while Figure 8(b) refers to the results acquired by a similar methodology for metal waste. The glass waste evaluation is presented in Figure 8(c). Coconut shells waste (in TPD) is analyzed and shown separately in Figure 8(d).

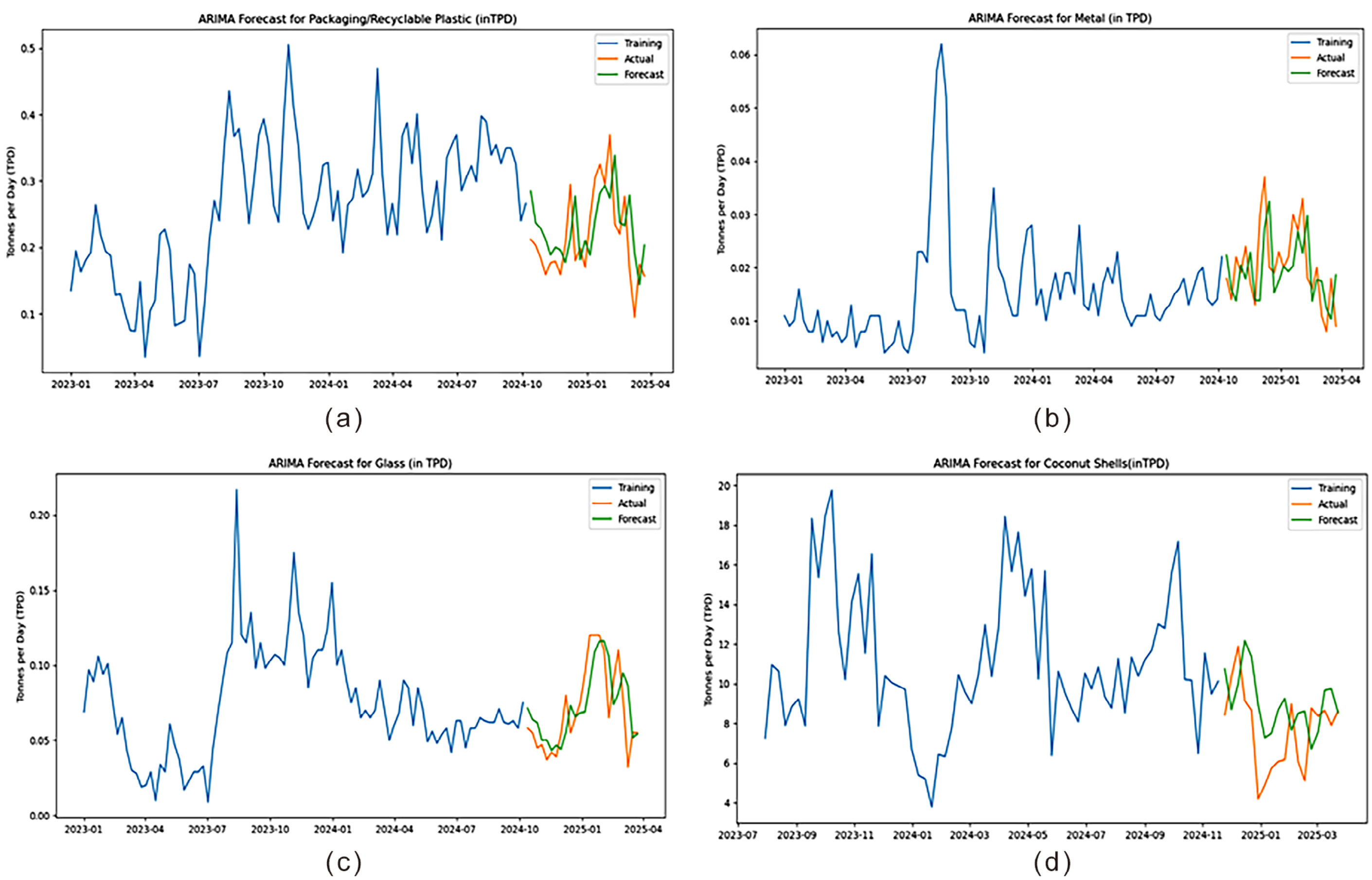


FIGURE 8. Forecasting for packaging/recycling plastic, metal, glass, and coconut shell waste.

The RMSE for ARIMA waste forecasting model measures the average magnitude of errors prediction in similar units as the waste data (e.g., tons, kg/person/day). A lower RMSE indicates a more accurate and reliable model, with zero (0) being a perfect forecast. Table 3 shows the category-wise forecasting results in terms of total RMSE for solid waste.

TABLE 3. Total RMSE of forecasting results.

Sr. No.	Category of Waste	Total RMSE (in Forecasting)
1.	Cardboard and thermocol	0.02
2.	Packaging and recyclable plastic	0.04
3.	Metal	0.00
4.	Glass	0.01
5.	Coconut shell	1.89

Note: RMSE: root mean square error.

For high-value materials, such as metals and glass, remarkably low RMSE values of 0.00 and 0.01, respectively, were calculated, which represent perfect or near-to-perfect results. This accuracy was also observed for high-volume recyclables, such as cardboard and plastics, with respective error rates as low as 0.02 and 0.04. Owing to the natural volatility of organic waste, coconut shell stream showed a higher RMSE of 1.89; however, even here the model successfully captured the significant seasonal fluctuations that define this category. These metrics prove that the model is a robust in nature and can be used to analyze various waste trends.

To make sense of the patterns in our forecasts, a closer look at how local urban life drives these numbers was done and a clear link (Pearson $r = 0.72$) between spikes in cardboard and plastic waste was determined because of major festivals, such as Depawali, where waste levels jumped by about 18.4%—mostly, thanks to massive surge in holiday shopping and e-commerce deliveries. Coconut shell waste connected entirely to the weather (Pearson r = 0.88). During colder months of November–February, for every 5°C drop in temperature, we observed waste drop by about 2.1 tons per day. This confirms that consumption is purely seasonal and driven by the climate, rather than changes in how people handle their trash.

DISCUSSION

The ARIMA-based forecasting analysis provides valuable insights into short-to-medium-term trends of waste generation across particular zone, that is, MRF, Sector 25, Chandigarh, India, by showing a consistent pattern of steady to moderate increase in waste quantities. Figure 8 shows an upward growth in cardboard and thermocol waste after monsoon season, mainly around December and January in forecasted years. Identical pattern is exhibited in the case of packaging and recyclable plastic, as shown in Figure 8(a). Patterns in metal and glass wastes followed a different trajectory of an increase in year-wise waste along with gradual season-wise decline as shown in Figures 8(b) and 8(c), respectively. This growth trend correlates with ongoing urban expansion, rising population density, increased commercial activity, and possibly improved waste collection coverage in the considered zone. A dip in metal and glass waste at municipal level is due to the fact that these materials are more valuable per kilogram, and households and businesses in Chandigarh, India, often prefer selling them directly to kabadiwalas (traditional Indian scrap dealers and informal recyclers who buy household waste) for quick cash, especially during big pre-festival cleaning or at the start of the fiscal year. At the same time, metal and glass waste is heavily tied to small-scale renovations and construction, which tend to decline during the city's extreme monsoon rains or peak winter season. This creates a visible decline in these categories at the MRF, although the volume of cardboard and plastic waste is high due to increase in e-commerce and home deliveries.

The forecasting results as shown in Tables 3 and 4 support policy makers to take decisions and plan for sustainable SWM in Chandigarh, India. During January–March 2025, collection frequency of cardboards and recyclable plastics must be increased as sharp rise in these categories is projected. This helps the Municipal Corporation of Chandigarh (MCC) to prevent overflow and sorting at MRFs. Seasonal drops in coconut shell waste—from 11 TPD to 4 TPD in winter—also help planners to manage operations at the upcoming 230-ton CBG plant by arranging alternative organic feedstock during lean periods to ensure steady bio-energy production. Additionally, highly accurate forecasts for valuable recyclables, such as metal and glass (RMSE 0.00–0.01), support precise revenue projections, enabling better budgeting and allowing proceeds from material recovery to be reinvested into welfare of workforce and upkeep of infrastructure.

TABLE 4. Trends analyzed through forecasting at MRF, Sector 25, Chandigarh, India.

Sr. No	Waste Material	Peak Tons	Notable Period	Trend
1.	Cardboard and thermocol	About 0.3 TPD	January–March 2025	Sharp rise
2.	Recyclable plastic	About 0.35 TPD	February–March 2025	Sharp spike
3.	Metal	About 0.03 TPD	December 2024–April 2025	Gradual decline
4.	Glass	About 0.12 TPD	December 2024–April 2025	Gradual decline
5.	Coconut shell	About 11 TPD	December 2024–April 2025	Seasonal variation

RECOMMENDATIONS

Integrating ARIMA-based forecasting into the Chandigarh Smart City dashboard fundamentally changes municipal waste management from a reactive struggle into a proactive strategy. MRF expansions can be initiated early by predicting rise in categories' generation. This predictive power also allows for much smarter community engagement; instead of broad, expensive awareness campaigns, the city can launch targeted "surgical" programs—such as offering QR-coded segregation incentives in specific western sectors—exactly when plastic generation is expected to peak. Additionally, moving away from rigid daily collection routes toward "predictive routing" allows MCC to sync vehicle deployment with actual waste loads. This approach reduces fuel costs and more importantly brings down carbon footprint, making the Chandigarh city greener. Investments in automated sorting systems, such as optical sensors, magnetic and eddy current separators, and advanced conveyors, significantly reduce manual burden and improve recovery rates. Predictive planning by aligning resource deployment with anticipated peak waste periods, use of forecasting data to pre-plan manpower, vehicle routing, and processing capacity coupled with real-time digital dashboards and the ARIMA-based automated municipal planning systems can be adopted. Finally, Chandigarh must foster a local circular economy for long-term sustainability by supporting micro, small, and medium enterprises (MSMEs) and start-ups that reuse or recycle waste materials into marketable products to create a future-ready SWM system that is adaptive, data-driven, and socially inclusive.

CONCLUSIONS

This research has showcased the practical application of the ARIMA model-based forecasting technique to predict weekly MSW generation in Chandigarh, India. By analyzing historical waste data of MRF facility, Sector 25, Chandigarh, the study provided useful insights into growth patterns and short-term fluctuations in waste generation. These findings are significant for optimizing logistics, enhancing planning, and preparing contingency measures along with the predictive routing of waste collection vehicles in Chandigarh's SWM system. The findings revealed that while the urban expansion is steadily contributing to waste volumes, certain periods still experience unexpected deviations because of holidays, seasonal events, or operational inconsistencies, which can help the MCC frame policies toward network optimization. It underlines the importance of integration of municipal decision-making processes with data-driven forecasting. By incorporating predictive planning, waste processing operators can anticipate peak load periods, and allocate resources more efficiently. The recommendations put forth—ranging from digital dashboards and real-time monitoring to strengthening source segregation—highlight a shift toward a more resilient and sustainable wastemanagement model. Overall, the study contributes to filling a critical gap in the existing localized forecasting research and provides a scalable framework for other Indian cities aiming for transition to predictive, smart waste management systems.

AUTHOR CONTRIBUTIONS

Conceptualization, A.S. and M.T.; Methodology, A.S. and M.T.; Formal Analysis, P.J. and A.S.; Investigation, P.J. and A.S.; Writing–Original Draft Preparation, P.J. and A.S.; Writing–Review & Editing, R.S.W and S.A.; Visualization, R.S.W and S.A.

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DATA AVAILABILITY STATEMENT

Not applicable.

CONFLICTS OF INTEREST

The authors declare they have no competing interests.

ETHICS APROVAL AND CONSENT TO PARTICIPATE

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

FURTHER DISCLOSURE

Not applicable.

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