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A Survey on Using Large Language Models in Healthcare

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Abstract: Large language models (LLMs) have emerged as transformative tools in healthcare, leveraging advanced natural language processing to enhance clinical workflows, patient communication, and medical education. This survey paper provides a comprehensive analysis of LLMs' applications, including named entity recognition, clinical decision support, and patient-friendly report generation, highlighting their ability to process unstructured medical data such as electronic health records and biomedical literature. Domain-specific models like BioBERT and ClinicalBERT, alongside generative models like GPT-3 and Med-PaLM, demonstrate superior performance in tasks requiring medical context, achieving high accuracy in predictive analytics and question answering. However, significant challenges impede their widespread adoption, including computational intensity, data biases, privacy concerns, and regulatory uncertainties. Ethical issues, such as perpetuating healthcare disparities, and technical limitations, like sensitivity to noisy data, necessitate innovative solutions like federated learning, differential privacy, and explainable AI. The paper also explores multimodal LLMs integrating text with imaging or genomic data, which promise holistic diagnostic capabilities. Future directions focus on developing lightweight, interpretable models and standardized frameworks to ensure equitable and safe deployment. By synthesizing current advancements, methodologies, and obstacles, this survey underscores the transformative potential of LLMs in healthcare while advocating for collaborative efforts among researchers, clinicians, and policymakers to address challenges and realize their full impact on improving patient outcomes and healthcare efficiency.

Keywords: Large language models, healthcare informatics, clinical decision support, ethical challenges, multimodal AI.

1. INTRODUCTION

The rapid advancement of large language models (LLMs) has ushered in a new era of artificial intelligence applications in healthcare, transforming the way medical data is processed, analyzed, and utilized. LLMs, built on transformer architectures, leverage vast computational power and extensive training data to understand and generate human-like text, making them uniquely suited for handling the unstructured and complex nature of medical data, such as electronic health records (EHRs) and biomedical literature [17]. These models, ranging from general-purpose architectures like GPT-3 to domain-specific variants like BioBERT, have demonstrated remarkable capabilities in tasks such as named entity recognition (NER), clinical decision support, and patient communication [38], [42]. As healthcare systems grapple with increasing data volumes and the need for efficient, accurate, and patient-centered solutions, LLMs offer unprecedented opportunities to enhance clinical workflows and improve patient outcomes.

The evolution of LLMs in healthcare has been driven by their ability to adapt to domain-specific contexts through pre-training and fine-tuning on medical corpora. Early models like BERT were adapted into BioBERT and ClinicalBERT by pre-training on PubMed and MIMIC datasets, enabling them to capture specialized medical terminology and context [38], [39]. These advancements have led to significant improvements in tasks such as relation extraction and automated ICD coding, reducing manual effort and improving diagnostic accuracy [40], [65]. More recently, generative models like GPT-3 and Med-PaLM have expanded the scope of LLMs to include patient-friendly report generation and medical question answering, achieving near-human performance in complex clinical tasks [42], [43]. This evolution underscores the potential of LLMs to bridge the gap between data-driven insights and practical healthcare applications.

Despite their promise, the integration of LLMs into healthcare is fraught with challenges, including technical, ethical, and regulatory hurdles. The computational intensity of training and deploying LLMs, coupled with their sensitivity to noisy clinical data, limits their scalability in resource-constrained settings [63], [65]. Ethical concerns, such as biases in training data and lack of interpretability, raise risks of perpetuating healthcare disparities and undermining clinician trust [66], [67]. Privacy issues and the need for compliance with regulations like HIPAA and GDPR further complicate deployment, necessitating innovative approaches like federated learning and differential privacy [68], [69]. These challenges highlight the need for robust methodologies and frameworks to ensure the safe, equitable, and effective use of LLMs in clinical practice.

This survey paper aims to provide a comprehensive overview of LLMs in healthcare, synthesizing their development, applications, challenges, and future directions. By examining the taxonomy, methodologies, key findings, and obstacles, the paper seeks to offer insights for researchers, clinicians, and policymakers navigating the integration of LLMs into healthcare systems. Through a detailed literature review, we explore the state-of-the-art models and their impact on clinical workflows, patient engagement, and medical education [38], [42], [43]. The paper also addresses critical challenges, such as bias, privacy, and regulatory compliance, proposing strategies to overcome them [66], [68], [70]. Ultimately, this survey underscores the transformative potential of LLMs while advocating for responsible development to ensure their safe and equitable deployment in healthcare.

2. LITERATURE REVIEW

The advent of large language models (LLMs) has significantly transformed the landscape of healthcare informatics, enabling advanced natural language processing (NLP) capabilities for tasks such as clinical decision support, medical record analysis, and patient interaction. LLMs, such as BERT (Bidirectional Encoder Representations from Transformers) and its derivatives, have been

adapted for healthcare applications due to their ability to understand and generate human-like text. For instance, BioBERT, a domain-specific adaptation of BERT, was pre-trained on large-scale biomedical corpora, including PubMed abstracts and PMC full-text articles, achieving superior performance in tasks like named entity recognition (NER) and relation extraction in biomedical texts [1]. Similarly, ClinicalBERT, fine-tuned on clinical notes from the MIMIC-III database, has demonstrated efficacy in extracting meaningful insights from unstructured electronic health records (EHRs) [2]. These models leverage transfer learning, allowing them to adapt pre-trained knowledge to specific healthcare tasks with minimal additional training. The ability of LLMs to process vast amounts of unstructured medical data has opened new avenues for improving diagnostic accuracy and operational efficiency in healthcare settings.

Recent advancements in LLMs, such as GPT-3 and its successors, have further expanded their utility in healthcare by enabling generative capabilities for tasks like medical dialogue systems and automated report generation. GPT-3, with its 175 billion parameters, has been employed in generating patient-friendly explanations of medical conditions, enhancing patient-provider communication [3]. Studies have shown that fine-tuning GPT-3 on medical question-answering datasets, such as MedQA, improves its ability to provide accurate responses to clinical queries, though limitations in factual accuracy remain [4]. Moreover, models like Med-PaLM, developed specifically for medical applications, have achieved near-human performance in answering USMLE-style questions, demonstrating the potential of LLMs to assist in medical education and decision-making [5]. These generative models excel in synthesizing coherent narratives from complex medical data, which is particularly valuable for summarizing patient histories or generating discharge summaries. However, their reliance on large datasets and computational resources poses challenges for widespread adoption in resource-constrained healthcare environments.

The integration of LLMs into clinical workflows has been explored extensively, particularly in the automation of EHR analysis and clinical decision support systems (CDSS). For example, transformer-based models like T5 have been used to extract structured information from unstructured clinical notes, enabling automated coding of diagnoses and procedures [6]. This capability reduces administrative burdens and improves billing accuracy. Additionally, LLMs have been applied in predictive analytics, such as identifying patients at risk of adverse events. A study by Jiang et al. [7] demonstrated that a fine-tuned BERT model could predict hospital readmissions with an AUC of 0.85 by analyzing discharge summaries. However, the black-box nature of these models raises concerns about interpretability, which is critical in clinical settings where transparency is necessary for trust and regulatory compliance [8]. Techniques like attention visualization and explainable AI (XAI) are being explored to address these concerns, but their integration into LLMs for healthcare remains an active area of research.

Ethical and regulatory challenges associated with LLMs in healthcare have garnered significant attention in recent literature. Issues such as data privacy, bias, and accountability are critical, given the sensitive nature of medical data. LLMs trained on biased datasets may perpetuate disparities in healthcare delivery, particularly for underrepresented populations [9]. For instance, Obermeyer et al. [10] highlighted how biases in EHR data can lead to skewed predictions in risk assessment models. Furthermore, the use of LLMs in patient-facing applications, such as chatbots for mental health support, raises concerns about the potential for harm due to incorrect or misleading advice [11]. Regulatory frameworks, such as the FDA's guidelines on AI in medical devices, are evolving to address these challenges, but gaps remain in standardizing the evaluation of LLMs for clinical use [12]. Researchers advocate for robust validation protocols and continuous monitoring to ensure the safety and efficacy of LLM-based healthcare applications. Table 1 shows the key LLMs used in healthcare.

Table 1. Summarizes key LLMs used in healthcare, their training data, and primary applications

Model	Training Data	Primary Applications	Reference
BioBERT	PubMed, PMC	NER, relation extraction	[1]
ClinicalBERT	MIMIC-III clinical notes	EHR analysis, clinical prediction	[2]
GPT-3	General web, fine-tuned on MedQA	Medical dialogue, patient education	[3], [4]
Med-PaLM	Medical corpora, USMLE datasets	Medical question answering, education	[5]
T5	General and clinical text	Automated coding, information extraction	[6]

Emerging trends in LLM research for healthcare focus on multimodal models and federated learning to address limitations in data availability and model generalization. Multimodal LLMs, which integrate text with other data types like medical images or genomic data, are gaining traction. For instance, models combining NLP with computer vision have shown promise in radiology report generation by analyzing both imaging data and clinical notes [13]. Federated learning, which allows models to be trained across decentralized datasets without sharing sensitive patient data, addresses privacy concerns and enables collaborative model development across institutions [14]. These approaches are particularly relevant for scaling LLMs in low-resource settings, where access to large, centralized datasets is limited. However, challenges such as computational complexity and the need for standardized data formats remain barriers to their widespread implementation.

Looking ahead, the future of LLMs in healthcare lies in enhancing their robustness, interpretability, and accessibility. Research is increasingly focused on developing lightweight models that retain high performance while being deployable on edge devices, such as mobile health applications [15]. Additionally, efforts to create open-source medical LLMs aim to democratize access to advanced NLP tools for healthcare providers worldwide. The integration of LLMs with knowledge graphs and real-time data streams could further enhance their utility in dynamic clinical environments [16]. Nevertheless, addressing ethical concerns, such as ensuring fairness and mitigating bias, will be critical to realizing the full potential of LLMs in healthcare. Collaborative efforts between researchers, clinicians, and policymakers are essential to establish guidelines that balance innovation with patient safety and equity.

3. TAXONOMY AND METHODS

The application of large language models (LLMs) in healthcare necessitates a systematic taxonomy to classify these models based on their architectures, training paradigms, and specific use cases. Broadly, LLMs in healthcare can be categorized into three main types: general-purpose models fine-tuned for healthcare, domain-specific models pre-trained on medical corpora, and multimodal models integrating text with other data modalities. General-purpose models, such as GPT-3 and LLaMA, are initially trained on diverse internet corpora and subsequently fine-tuned on healthcare datasets like MIMIC-IV or PubMed to address tasks such as clinical note summarization and medical question answering [17]. Domain-specific models, such as BioBERT and ClinicalBERT, are pre-trained on biomedical or clinical texts, enabling them to capture specialized vocabulary and context inherent to healthcare [18]. Multimodal models, which combine text with imaging or genomic data, are emerging as powerful tools for tasks like radiology report generation [19]. This taxonomy facilitates a structured understanding of LLMs' capabilities and limitations in healthcare applications.

Training methodologies for LLMs in healthcare typically involve a combination of pre-training, fine-tuning, and transfer learning to adapt models to specific clinical tasks. Pre-training is conducted on large-scale datasets, such as PubMed or EHR databases, to imbue models with domain knowledge. For instance, BioMedLM, a model pre-trained on biomedical literature, leverages self-supervised learning to predict masked tokens in medical texts, enhancing its performance in named entity recognition (NER) and relation extraction [20]. Fine-tuning further refines these models on task-specific datasets, such as MedNLI for natural language inference in clinical texts [21]. Transfer learning enables the adaptation of pre-trained models to new tasks with limited labeled data, a critical advantage in healthcare where annotated datasets are often scarce [22]. These methods ensure that LLMs can generalize across diverse clinical scenarios while maintaining high accuracy in specialized tasks.

Supervised and unsupervised learning approaches are central to the development of LLMs for healthcare. Supervised fine-tuning is commonly used for tasks requiring labeled data, such as predicting patient outcomes from EHRs. For example, a fine-tuned BERT model achieved an F1 score of 0.92 in identifying adverse drug events from clinical notes [23]. Unsupervised methods, such as masked language modeling, are employed during pre-training to learn contextual representations from unannotated medical texts. Recent advancements include contrastive learning, where models like SimCSE are trained to maximize similarity between semantically related medical texts, improving performance in tasks like clinical text classification [24]. Hybrid approaches combining supervised and unsupervised learning are also gaining traction, particularly for tasks like automated ICD coding, where models leverage both labeled and unlabeled EHR data to improve accuracy [25]. These methods address the challenge of data scarcity while enhancing model robustness.

The integration of LLMs into clinical workflows relies heavily on methods for model optimization and deployment. Techniques such as knowledge distillation and quantization are used to create lightweight models suitable for resource-constrained environments, such as mobile health applications or rural clinics [26]. Knowledge distillation involves training a smaller "student" model to replicate the behavior of a larger "teacher" model, reducing computational requirements without significant performance loss. For instance, a distilled version of ClinicalBERT was deployed on edge devices for real-time EHR analysis, achieving comparable accuracy to its larger counterpart [27]. Quantization reduces model size by lowering the precision of weights, enabling faster inference on low-power devices [28]. These optimization techniques are critical for scaling LLMs to diverse healthcare settings, particularly in low-resource regions where computational infrastructure is limited. Table 2 illustrates the key methods used in developing and deploying LLMs for healthcare.

Table 2: Summarizes key methods used in developing and deploying LLMs for healthcare

Method	Description	Applications	Reference
Pre-training	Self-supervised learning on medical corpora	NER, relation extraction	[20]
Fine-tuning	Task-specific training with labeled data	Outcome prediction, ICD coding	[23]
Contrastive Learning	Maximizing similarity between related texts	Text classification, semantic search	[24]
Knowledge Distillation	Training smaller models from larger ones	Edge deployment, mobile health apps	[27]
Quantization	Reducing model size via low-precision weights	Real-time inference, resource-constrained settings	[28]

Ethical considerations in the development of LLMs for healthcare have led to the adoption of methods like federated learning and differential privacy to address data security and fairness. Federated learning enables collaborative training across multiple institutions without sharing sensitive patient data, preserving privacy while leveraging diverse datasets. A study by Rieke et al. [29] demonstrated that federated learning improved the performance of an LLM-based mortality prediction model across hospitals by 15% compared to single-institution training. Differential privacy adds noise to training data to prevent the reconstruction of individual patient records, a critical safeguard for EHR-based models [30]. These methods mitigate risks associated with data breaches and ensure compliance with regulations like HIPAA and GDPR. However, they introduce computational overhead and may reduce model accuracy, necessitating careful trade-offs in their implementation.

Evaluation and validation methods are critical for ensuring the reliability of LLMs in healthcare. Standard metrics like F1 score, AUC-ROC, and BLEU are used to assess model performance in tasks such as NER, classification, and text generation [31]. However, clinical applications demand additional validation to ensure generalizability and robustness. Cross-institutional validation, where models are tested on data from different hospitals, is increasingly employed to assess performance across diverse patient populations [32]. Adversarial testing, which evaluates model robustness against perturbed inputs, is also gaining attention to address vulnerabilities in clinical LLMs [33]. Furthermore, human-in-the-loop evaluation, where clinicians validate model outputs, is essential for ensuring clinical relevance and safety, particularly in high-stakes applications like CDSS [34]. These rigorous evaluation methods are vital for building trust in LLM-based healthcare tools.

Emerging methods in LLM development focus on enhancing interpretability and integrating real-time data for dynamic healthcare applications. Explainable AI (XAI) techniques, such as SHAP (SHapley Additive exPlanations) and attention-based visualization, are employed to elucidate model decision-making processes, addressing the black-box nature of LLMs [35]. For example, SHAP was used to interpret predictions of a BERT-based model for sepsis detection, improving clinician trust [36]. Real-time integration with clinical data streams, such as vital signs or lab results, is another frontier, with models like Med-PaLM 2 leveraging APIs to provide up-to-date recommendations [37]. These methods enhance the practical utility of LLMs in fast-paced clinical environments but require robust infrastructure for seamless data integration and real-time processing. Future research is likely to focus on standardizing these methods to ensure scalability and interoperability across healthcare systems.

4. KEY FINDINGS

The application of large language models (LLMs) in healthcare has yielded significant advancements in processing and analyzing unstructured medical data, particularly in electronic health records (EHRs) and biomedical literature. Studies have demonstrated that domain-specific models like BioBERT and ClinicalBERT outperform general-purpose LLMs in tasks such as named entity recognition (NER) and relation extraction, achieving F1 scores above 0.90 in extracting clinical entities from unstructured texts [38]. These models leverage pre-training on large biomedical corpora, such as PubMed and MIMIC-IV, to capture domain-specific semantics, enabling precise identification of medical terms and relationships [39]. For instance, BioBERT's ability to identify drug-disease associations has improved drug repurposing efforts, reducing manual review time by up to 40% in some studies [40]. These findings underscore the importance of domain adaptation in enhancing the accuracy and utility of LLMs for healthcare applications.

LLMs have shown remarkable promise in clinical decision support systems (CDSS), particularly in predictive analytics and diagnostic assistance. Fine-tuned models, such as those based on BERT and GPT architectures, have achieved high accuracy in predicting patient outcomes, such as hospital readmissions and mortality risk. A study by Zhang et al. [41] reported that a BERT-based model predicted 30-day readmissions with an AUC of 0.87, surpassing traditional statistical models. Similarly, Med-PaLM demonstrated near-human performance on USMLE-style questions, correctly answering 85% of medical queries, highlighting its potential as an educational and diagnostic tool [42]. These findings suggest that LLMs can augment clinical decision-making, though their integration into real-world workflows requires careful validation to ensure reliability and generalizability across diverse patient populations.

The generative capabilities of LLMs, particularly models like GPT-3 and its successors, have transformed patient-provider communication and medical education. These models excel in generating patient-friendly explanations of complex medical conditions, improving health literacy among patients. A study by Liu et al. [43] found that GPT-3-generated summaries of radiology reports were rated as 90% comprehensible by patients, compared to 60% for original reports. Additionally, LLMs have been used to develop virtual tutors for medical students, providing interactive learning experiences that adapt to individual learner needs [44]. However, limitations in factual accuracy and the risk of generating misleading information remain significant challenges, necessitating human oversight to ensure clinical safety [45]. These findings highlight the dual role of LLMs in enhancing communication and education while emphasizing the need for robust validation mechanisms.

Ethical challenges, including bias and privacy concerns, have emerged as critical issues in the deployment of LLMs in healthcare. Research has shown that LLMs trained on biased datasets can perpetuate disparities in healthcare delivery, particularly for underrepresented groups. For example, a study by Chen et al. [46] revealed that a BERT-based risk prediction model underestimated mortality risk for minority patients due to biased training data. Federated learning has been proposed as a solution to enhance privacy by training models across decentralized datasets without sharing sensitive patient information, with studies reporting a 10-15% improvement in model performance across institutions [47]. Differential privacy techniques have also been effective in protecting patient data, though they may reduce model accuracy by up to 5% [48]. These findings emphasize the need for ethical frameworks to guide the development and deployment of LLMs in healthcare.

The integration of multimodal LLMs, which combine text with other data types like medical imaging or genomic data, has opened new avenues for comprehensive healthcare applications. Models integrating NLP and computer vision have shown promise in radiology, where they generate detailed reports by analyzing both images and clinical notes. A study by Wang et al. [49] reported that a multimodal LLM achieved a BLEU score of 0.75 in radiology report generation, significantly outperforming text-only models. Similarly, LLMs combined with genomic data have improved the prediction of disease susceptibility, with one model achieving an AUC of 0.90 for breast cancer risk assessment [50]. These findings indicate that multimodal approaches can enhance diagnostic accuracy and enable holistic patient assessments, though they require significant computational resources and standardized data formats. Table 3 shows the key findings regarding LLMs in healthcare.

Table3: Summarizes key findings on LLMs in healthcare

Application	Key Finding	Performance Metric	Reference
NER and Relation Extraction	BioBERT achieves F1 > 0.90 in clinical entity extraction	F1: 0.90–0.95	[38], [40]
Predictive Analytics	BERT predicts readmissions with high accuracy	AUC: 0.87	[41]
Medical Question Answering	Med-PaLM answers 85% of USMLE questions correctly	Accuracy: 85%	[42]
Patient Communication	GPT-3 summaries improve patient comprehension by 30%	Comprehension: 90%	[43]
Multimodal Applications	Multimodal LLMs enhance radiology report generation	BLEU: 0.75	[49]

The scalability of LLMs in resource-constrained healthcare settings has been a focus of recent research, with knowledge distillation and quantization emerging as effective methods. Knowledge distillation has enabled the deployment of lightweight models on edge devices,

maintaining 95% of the performance of larger models while reducing computational requirements by 70% [51]. Quantization has further reduced model size, enabling real-time inference in mobile health applications with minimal latency [52]. These advancements are particularly significant for low-resource regions, where access to high-performance computing is limited. However, the trade-off between model size and accuracy remains a challenge, with some studies reporting a 3-5% performance drop in distilled models [53]. These findings highlight the potential for scalable LLM deployment while underscoring the need for optimization strategies tailored to specific healthcare contexts.

Interpretability remains a critical barrier to the widespread adoption of LLMs in clinical settings, where transparency is essential for trust and regulatory compliance. Explainable AI (XAI) techniques, such as SHAP and attention visualization, have been employed to elucidate model predictions, with studies showing that SHAP improved clinician understanding of sepsis prediction models by 25% [54]. However, current XAI methods are often computationally intensive and may not fully capture the complexity of LLM decision-making [55]. Human-in-the-loop validation, where clinicians review model outputs, has proven effective in ensuring clinical relevance, with one study reporting a 20% reduction in diagnostic errors when LLMs were paired with human oversight [56]. These findings suggest that combining XAI with human validation is essential for bridging the interpretability gap in clinical LLMs.

The robustness of LLMs in handling diverse and noisy clinical data has been a significant finding, though challenges persist. Cross-institutional validation studies have shown that LLMs trained on diverse datasets maintain performance across different healthcare systems, with one BERT-based model achieving consistent F1 scores of 0.88 across five hospitals [57]. However, adversarial testing has revealed vulnerabilities, with models showing a 10-15% performance drop when exposed to perturbed inputs, such as misspellings in clinical notes [58]. Techniques like data augmentation and adversarial training have been proposed to improve robustness, with studies reporting a 7% improvement in model stability [59]. These findings indicate that while LLMs are robust in controlled settings, their performance in real-world, noisy environments requires further enhancement.

Looking forward, the future of LLMs in healthcare lies in their integration with real-time data streams and the development of open-source models to democratize access. Real-time integration with clinical data, such as vital signs or lab results, has enabled dynamic decision support, with Med-PaLM 2 achieving a 90% accuracy rate in real-time sepsis detection [60]. Open-source initiatives, such as the release of BioMedLM, have lowered barriers to entry for smaller institutions, with adoption rates increasing by 30% in low-resource settings [61]. However, standardization of data formats and regulatory frameworks remains a hurdle, with ongoing efforts to establish global guidelines for LLM deployment in healthcare [62]. These findings highlight the transformative potential of LLMs while emphasizing the need for collaborative efforts to address technical and ethical challenges.

5. CHALLENGES

The deployment of large language models (LLMs) in healthcare is hindered by significant technical challenges, particularly related to computational resources and model robustness. LLMs, such as GPT-3 and Med-PaLM, require substantial computational power for training and inference, often necessitating high-performance GPUs or TPUs that are inaccessible to many healthcare institutions, especially in low-resource settings [63]. This resource intensity limits scalability, with studies estimating that training a single large model can cost upwards of $1 million and emit significant carbon emissions [64]. Furthermore, LLMs struggle with robustness when processing noisy or incomplete clinical data, such as misspellings or inconsistent terminology in EHRs. A study by Patel et al. [65] found that BERT-based models experienced a 12% drop in performance when tested on datasets with simulated noise, highlighting vulnerabilities in real-world clinical environments. Addressing these technical barriers requires the development of lightweight models and robust training strategies, such as adversarial training, to enhance resilience to data variability.

Ethical challenges, particularly around bias and fairness, pose significant obstacles to the equitable use of LLMs in healthcare. Models trained on biased datasets, such as EHRs that underrepresent minority populations, can perpetuate disparities in clinical predictions. For instance, Obermeyer et al. [66] demonstrated that a widely used risk prediction algorithm underestimated risk for Black patients due to biased training data, a concern equally applicable to LLMs. Additionally, the lack of transparency in LLM decision-making processes exacerbates trust issues among clinicians and patients. Explainable AI (XAI) techniques, such as SHAP, have been proposed to improve interpretability, but their computational complexity and incomplete explanations limit their practical utility [67]. These ethical challenges necessitate rigorous dataset curation and the integration of fairness-aware algorithms to ensure equitable healthcare delivery.

Data privacy and security remain critical challenges in deploying LLMs, given the sensitive nature of medical data. The use of large-scale EHR datasets for training raises concerns about patient confidentiality, particularly under regulations like HIPAA and GDPR. Federated learning has been proposed to address this by enabling collaborative training without sharing raw data, but its implementation introduces complexities, such as increased communication costs and potential model performance degradation [68]. Differential privacy offers another solution by adding noise to training data, but a study by Lee et al. [69] reported a 5-8% reduction in model accuracy when applying stringent privacy measures. Balancing privacy with model utility remains a significant hurdle, requiring innovative approaches to secure data handling and compliance with evolving regulatory standards. Table 4 illustrates the key challenges in deploying LLMs in healthcare.

Table 4: Summarizes key challenges in deploying LLMs in healthcare

Challenge	Description	Implications	Reference
Computational Resources	High GPU/TPU requirements for training/inference	Limits scalability in low-resource settings	[63], [64]
Model Robustness	Sensitivity to noisy or incomplete clinical data	Reduced performance in real-world scenarios	[65]
Bias and Fairness	Biased datasets perpetuate healthcare disparities	Inequitable clinical predictions	[66]

Data Privacy	Risk of breaching patient confidentiality	Regulatory non-compliance, reduced trust	[68], [69]
Regulatory Compliance	Lack of standardized AI evaluation frameworks	Delays in clinical deployment	[70]

Regulatory compliance presents a formidable challenge, as the integration of LLMs into clinical practice must align with stringent healthcare regulations. The U.S. Food and Drug Administration (FDA) and other regulatory bodies have yet to establish comprehensive guidelines for evaluating AI-based tools like LLMs, leading to uncertainty in deployment [70]. For example, the black-box nature of LLMs complicates validation processes, as regulatory agencies require evidence of safety and efficacy. A study by Topol et al. [71] highlighted that only 10% of AI-based healthcare tools, including LLMs, have received regulatory approval due to insufficient validation protocols. Additionally, the dynamic nature of LLMs, which may require continuous updates with new data, poses challenges for maintaining compliance over time. Developing standardized evaluation frameworks and post-market surveillance systems is critical to ensuring the safe integration of LLMs into clinical workflows.

The generalizability of LLMs across diverse healthcare settings remains a persistent challenge, particularly when models are applied to populations or institutions different from those in their training data. Cross-institutional studies have shown that LLMs trained on data from a single hospital may underperform when applied to others due to variations in clinical practices and patient demographics [72]. For instance, a BERT-based model trained on U.S.-based EHRs exhibited a 10% performance drop when tested on European datasets, underscoring the need for diverse training corpora [73]. Addressing this challenge requires large-scale, multi-institutional datasets and transfer learning techniques to enhance model adaptability. Collaborative efforts to create global data-sharing frameworks, while addressing privacy concerns, will be essential to improving the generalizability and real-world impact of LLMs in healthcare.

6. CONCLUSION

The exploration of large language models (LLMs) in healthcare reveals their transformative potential in enhancing clinical workflows, patient communication, and medical education. Models like BioBERT, ClinicalBERT, and Med-PaLM have demonstrated remarkable capabilities in tasks such as named entity recognition, clinical decision support, and patient-friendly report generation, significantly improving the efficiency and accuracy of healthcare delivery. Their ability to process vast amounts of unstructured medical data, such as electronic health records and biomedical literature, has streamlined administrative tasks and supported clinicians in making informed decisions. Moreover, the generative capabilities of LLMs have empowered patient-centered applications, fostering better health literacy and engagement. These advancements underscore the pivotal role of LLMs in addressing longstanding challenges in healthcare informatics, paving the way for more personalized and data-driven medical practice.

Despite their promise, the deployment of LLMs in healthcare is fraught with challenges that must be addressed to ensure their safe and equitable integration. Technical limitations, such as high computational demands and sensitivity to noisy data, restrict scalability, particularly in resource-constrained settings. Ethical concerns, including bias in training data and lack of interpretability, pose risks of perpetuating healthcare disparities and undermining clinician trust. Privacy issues and the absence of standardized regulatory frameworks further complicate adoption, as healthcare systems must comply with stringent data protection laws. These challenges highlight the need for a balanced approach that prioritizes robustness, fairness, and transparency to fully realize the benefits of LLMs in clinical environments.

Looking ahead, the future of LLMs in healthcare lies in overcoming these challenges through innovative methodologies and collaborative efforts. Advances in knowledge distillation and quantization can enable the development of lightweight models suitable for low-resource settings, while federated learning and differential privacy can address privacy concerns. Integrating multimodal LLMs with imaging and genomic data holds promise for holistic patient assessments, enhancing diagnostic precision. Furthermore, improving interpretability through explainable AI techniques and human-in-the-loop validation will be critical for building trust and ensuring regulatory compliance. Open-source initiatives can democratize access to these technologies, enabling smaller institutions to leverage LLMs effectively.

LLMs represent a paradigm shift in healthcare, offering unprecedented opportunities to enhance clinical practice and patient outcomes. However, their successful integration requires addressing technical, ethical, and regulatory hurdles through interdisciplinary collaboration among researchers, clinicians, and policymakers. By fostering standardized evaluation frameworks, diverse training datasets, and ethical guidelines, the healthcare community can harness the full potential of LLMs while ensuring safety and equity. As these models continue to evolve, they hold the promise of transforming healthcare into a more efficient, accessible, and patient-centered system, ultimately improving the quality of care worldwide.

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