# Advancing the potential of AI in rare disease


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## 1. Introduction

In recent years, the field of artificial intelligence (AI) has surged forward, catalysing transformative changes across various sectors, with healthcare being a focal point of innovation. Among the myriad areas where AI demonstrates promise, its potential in revolutionizing the diagnosis and treatment of rare diseases stands out prominently. Rare diseases, often referred to as orphan diseases, affect a small fraction of the population, yet collectively, they impact a significant number of individuals worldwide. Despite their low prevalence, these conditions present unique challenges in diagnosis and treatment due to limited awareness, scarce research, and diverse clinical presentations.

## 2. AI: A beacon of hope

AI technologies, particularly machine learning and deep learning algorithms, offer a beacon of hope in addressing the intricate challenges associated with rare diseases. By harnessing the power of AI to analyse vast datasets encompassing patient information, genetic data, and clinical records, healthcare providers can uncover patterns and correlations that might elude human observation. This analytical prowess enables more accurate and timely diagnoses, facilitating the initiation of appropriate treatment strategies at an earlier stage

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## 3. The diagnostic revolution

### 3.1 AI in clinical triage and diagnosis

Razzaki et al. (1) compared an AI system with human doctors in triaging and diagnosing patients using clinical vignettes. They found the AI system, trained on comprehensive EHRs and clinical notes, outperformed humans in triage and diagnosis tasks due to its proficiency in pattern recognition. However, the AI showed less accuracy in predicting hospital stay length. This underscores AI's potential to enhance clinical decision-making, especially in pattern recognition tasks, while emphasizing the need for further research to optimize its performance across healthcare settings. Similarly, AI algorithms like Aidoc (2), are employed to aid radiologists in detecting abnormalities in medical scans, including rare conditions such as Moyamoya disease or Wilson's disease, potentially enabling early intervention for improved treatment outcomes.

### 3.2 AI in medical image classification

In a seminal study by Esteva et al., (3) a deep convolutional neural network (CNN) demonstrated expert-level diagnostic capabilities by accurately classifying 1,29,450 clinical images across over 2,000 different diseases, comparable to 21 board-certified dermatologists. This underscores AI's potential to excel in complex medical image classification tasks, offering the promise of automated screening and triage, thereby enhancing diagnostic accessibility.

### 3.3 AI in pathology

Furthermore, AI extends its reach into pathology with investigations such as that by Ehteshami Bejnordi et al., (4) where multiple deep learning algorithms exhibited proficiency in detecting lymph node metastases in breast cancer using whole-slide pathology images, akin to pathologists. This convergence of AI and human expertise elevates cancer staging precision and augments patient care quality, paving the way for broader clinical validation of deep learning models in critical diagnostic domains.

## 4. Pioneering applications in acute care

In acute care settings like intensive care units (ICUs) and emergency departments, where timely interventions are critical, machine learning (ML) emerges as a vitality. Studies like that by Komorowski et al., (5) showcase successful ML applications in early warning systems for conditions like sepsis and acute kidney injury, highlighting the importance of integration with electronic health records (EHRs) and clinical workflows. Interdisciplinary teamwork between clinicians, data scientists, and ML experts is paramount for the effective development and deployment of ML systems in acute care environments.

### 4.1 Data scarcity and class imbalance

Despite these advancements, challenges persist. The study by Li et al., (6) delves into the nuances of utilizing deep learning methods for predicting rare diseases, emphasizing the hurdles posed by data scarcity due to their low prevalence, class imbalance, atypical presentations and the imperative for effective data augmentation techniques. Additionally, the necessity of interpretability and explainability in deep learning models is underscored to establish clinician trust, reducing healthcare cost and foster adoption.

## 5. Tackling data challenges in healthcare

Navigating the intricacies of electronic health record (EHR) data poses a significant challenge in healthcare AI. Studies by Eraslan et al., (7) and Shickel et al., (8) surveys recent advances in applying deep learning techniques such as recurrent neural networks, convolutional neural networks and autoencoders to analyse EHR data, emphasizing the importance of interpretability and trustworthiness in ensuring effective integration and acceptance of AI models. Methodological obstacles, including high dimensionality, noise, irregularity, and missingness, necessitate rigorous evaluation and collaboration between domain experts and data scientists, as highlighted by Xiao et al. (9)

## 6. Harnessing electronic health record data for improved patient care

Pivovarov et al., (10) delve into the analysis of temporal patterns of haemoglobin A1c (HbA1c) testing using electronic health record (EHR) data. Their study focuses on a large urban medical centre and examines the frequency and regularity of HbA1c testing over time.Findings reveal significant gaps in adherence to recommended testing intervals among patients, potentially impacting diabetes management. Factors influencing testing regularity, including patient age, gender, and comorbidities, are identified. The study underscores the value of EHR data mining and analytics in identifying care gaps and enhancing adherence to clinical guidelines, thus improving patient care outcomes.

## 7. Pioneering genomic discoveries

Genomics emerges as a frontier in disease diagnosis and treatment, with AI playing a pivotal role in unravelling genetic mysteries. Rostami et al., (11) review various AI techniques employed for detecting genetic diseases, showcasing their potential in gene expression analysis, variant pathogenicity prediction, and disease risk assessment and more. The integration of multi-omics data holds promises in enhancing genetic disease diagnosis and advancing personalized medicine, as emphasized by Eraslan et al.(7)

### 7.1 Genetic data analysis and personalized treatment

AI holds great potential for precision medicine by tailoring treatments to individual genetic profiles. By analysing genetic data, AI can uncover disease causes and guide personalized therapies. Research by Ghorbani et al., (12) emphasizes the need for collaboration among AI researchers, clinicians, and healthcare stakeholders to maximize AI's impact in clinical decision support, medical imaging, and drug discovery. Interdisciplinary efforts are crucial for developing AI solutions that benefit patients with rare diseases. For example, IBM Watson for Genomics (13) analyses genetic data to find targeted treatments for conditions like cystic fibrosis and Duchenne muscular dystrophy

### 7.2 Epigenetic therapies in personalized medicine

In the similar vein, Feinberg (14) highlights the pivotal role of epigenetics in disease prevention and management, shedding light on how epigenetic mechanisms influence disease susceptibility, progression, and treatment response. This underscores the potential of epigenetic therapies in personalized medicine, offering tailored interventions based on individual epigenetic profiles. Additionally, Guinney et al., (15) contribute to precision oncology by identifying distinct molecular subtypes of colorectal cancer, paving the way for subtype-specific targeted therapies and emphasizing the integration of multi-omics data for comprehensive patient stratification.

## 8. Navigating challenges with precision

Miotto et al., (16) provide a comprehensive overview of the evolving landscape of deep learning applications within healthcare. They highlight the potential of deep learning to extract valuable insights from complex healthcare data, including medical imaging, electronic health records (EHRs), and genomics. The paper emphasizes the importance of collaboration between clinicians, data scientists, and domain experts to address challenges such as data quality, privacy concerns, and the critical need for interpretability and transparency in healthcare applications of deep learning. Additionally, future opportunities and research directions, such as transfer learning, federated learning, and integration of multi-modal data sources, are discussed to advance deep learning's impact on healthcare.

## 9. Addressing behavioural health challenges

Beyond genetics, AI extends its reach into understanding behavioural health challenges. Yip et al., (17) explores the relationship between childhood and adult trauma experiences and behavioural health problems among incarcerated individuals, shedding light on the profound impact of trauma on mental health outcomes. Their findings underscore the importance of trauma-informed care in both correctional and community-based treatment settings.

## 10. Unravelling metabolomics and cancer complexity

### 10.1 Metabolic alterations and obesity

Cirulli et al., (18) elucidates the metabolic alterations associated with obesity, providing valuable insights into personalized risk assessment and intervention strategies for obesity-related conditions such as diabetes, cardiovascular diseases, and cancer. Their findings highlight the reversibility of metabolic perturbations with weight loss, offering hope for targeted interventions.

## 10.2 Cancer biology and precision medicine

Furthermore, Hanahan and Weinberg (19) expanded cancer biology knowledge by identifying new hallmarks, emphasizing their importance in targeted cancer therapies. Personalized approaches, informed by metabolomics and the tumour microenvironment, hold promise in combating cancer. Hyman et al., (20) showcased successful targeted therapy in non-melanoma cancers with BRAF V600 mutations, illustrating precision medicine's potential across tumour types. AI reveals cancer's complexity and offers precision medicine avenues. Mayr and Bartel (21) uncovered novel cancer progression mechanisms, suggesting new therapeutic targets. The Cancer Genome Atlas Network (22) revealed genomic heterogeneity in head and neck squamous cell carcinomas, informing tailored precision oncology strategies.

# 11. Ethical Guidelines and Regulatory Compliance for AI in Healthcare

In the rapidly evolving landscape of healthcare technology, ethical considerations emerge as a pivotal concern. Topol (23) advocates for "high-performance medicine," stressing the harmonious collaboration between AI and human intelligence, highlighting the imperative for responsible AI development and implementation. Anagnostou et al., (24) underscore the paramount importance of human-AI collaboration, particularly in leveraging genomic sequencing and personalized medicine to advance disease prevention and wellness.

Ethical integration of AI into healthcare is emphasized by the World Health Organization (25), offering comprehensive guidelines that prioritize transparency, fairness, accountability, and privacy protection. These principles, accessible on the WHO website, aim to instil trust among patients, healthcare providers, and regulatory bodies. Additionally, the American Medical Association (AMA) contributes tailored ethical guidelines for healthcare practitioners and patients.

Regulatory bodies such as the FDA and EMA play a crucial role in ensuring the ethical use of AI in healthcare. The FDA's guidance on "Artificial Intelligence and Machine Learning in Software as a Medical Device" (2021) and similar efforts by the EMA focus on ethical standards and patient safety, aiming to establish clear regulatory frameworks that uphold ethical practices in AI technology deployment within medical settings (26).

# 12. Other real-world examples of AI applications

Real-world examples of AI applications in healthcare extend beyond rare diseases:

- **12.1 Drug discovery and development:** BenevolentAI (27) harnesses AI for swift drug discovery, analysing biomedical data to pinpoint potential drug candidates and forecast their effectiveness and safety across diseases. Atomwise (28) and Insilico Medicine (29) also leverage AI algorithms to predict molecule activity and screen vast compound databases, focusing on rare diseases like ALS or Huntington's.
- **12.2 Remote patient monitoring:** Ling and Xu (30) discuss AI-powered wearable devices and remote monitoring systems, enabling continuous tracking of patient health parameters. These devices equipped with AI algorithms detect early signs of deterioration in chronic conditions like heart disease or diabetes, facilitating timely intervention.
- **12.3 Natural language processing (NLP) in healthcare:** Linguamatics (31) develops NLP solutions to extract insights from unstructured healthcare data, including clinical notes and patient transcripts. These solutions aid healthcare providers in extracting relevant information to support clinical decision-making and research.
- **12.4 Collaborative research networks:** AI fosters collaborative research and data-sharing among healthcare institutions, researchers, and pharmaceutical companies to advance rare disease research. Projects like RDCA-DAP (32) use AI to integrate and analyse diverse data, speeding up the discovery of rare disease treatments.

# 13. Emerging trends in AI technology

Emerging trends in AI technology include Explainable AI (XAI), which emphasizes transparency and interpretability of AI algorithms. Lundberg and Lee's research (33) highlights methods like LIME and SHAP to aid clinicians in understanding AI-driven clinical decisions. AI-driven Clinical Trials, exemplified by Deep 6 AI (34), optimize patient recruitment and predict outcomes, enhancing trial success rates. Personalized Health Assistants, like those offered by Ada Health (35) and Babylon Health, provide tailored health recommendations and support through AI-powered chatbots, improving access to healthcare services remotely. These advancements showcase AI's potential to revolutionize healthcare delivery and patient outcomes.

## 14. Conclusion

As AI continues to evolve, the potential for enhancing rare disease diagnosis and treatment grows exponentially. By combining AI's analytical prowess with the expertise of healthcare professionals, we can unlock new insights, develop innovative therapies, and improve outcomes for patients with rare diseases. Through collaborative efforts and a commitment to ethical AI practices, we can propel the field of rare disease medicine forward, offering hope to individuals facing these challenging conditions.

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