REVIEW

Artificial intelligence for medicine: Progress, challenges, and perspectives

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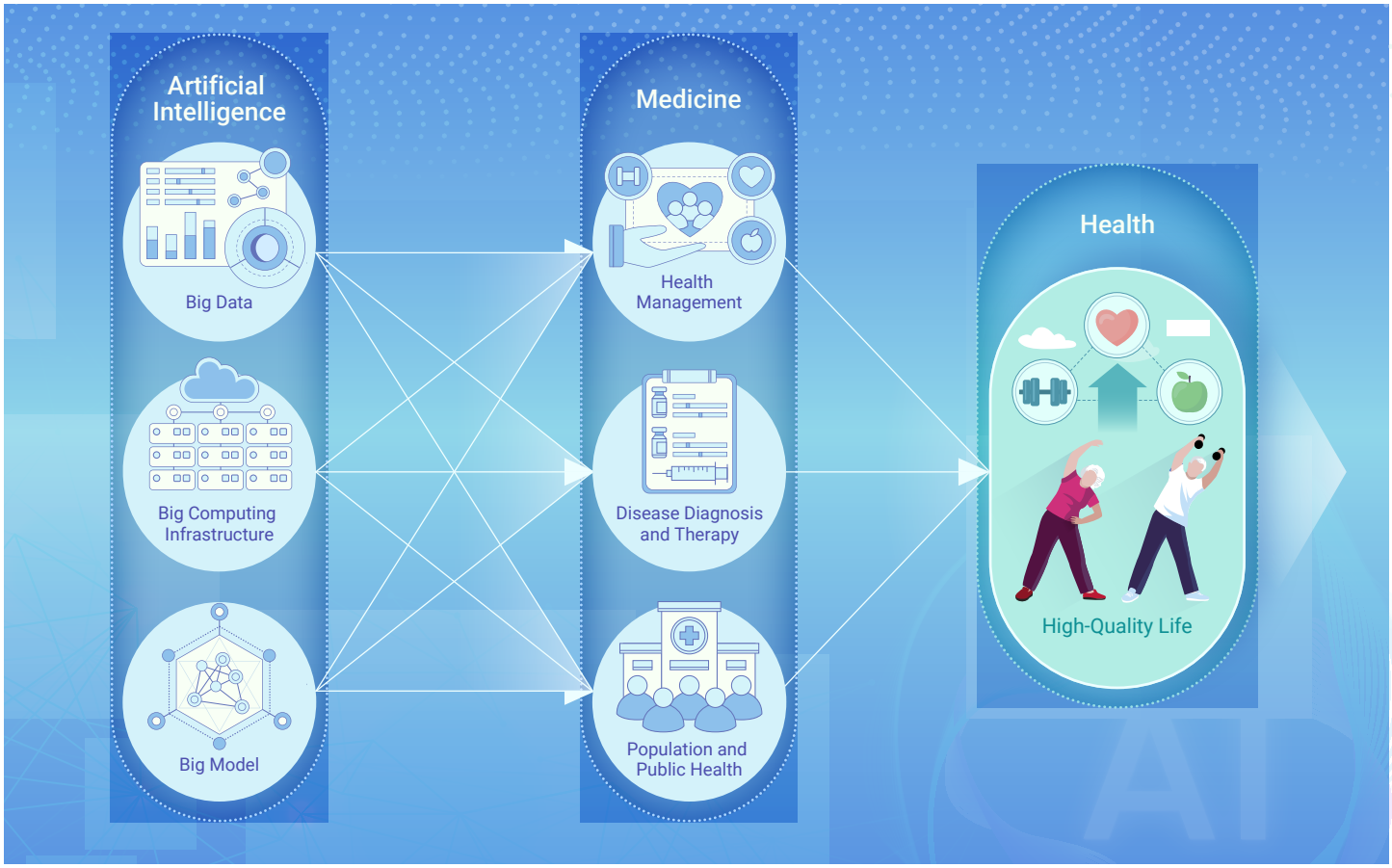
GRAPHICAL ABSTRACT



PUBLIC SUMMARY

- Data, computing power, and algorithm drive artificial intelligence.
- Artificial intelligence has changed the practice of medicine.
- Artificial intelligence is improving the quality of life.

REVIEW

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Artificial Intelligence (AI) has transformed how we live and how we think, and it will change how we practice medicine. With multimodal big data, we can develop large medical models that enables what used to unimaginable, such as early cancer detection several years in advance and effective control of virus outbreaks without imposing social burdens. The future is promising, and we are witnessing the advancement. That said, there are challenges that cannot be overlooked. For example, data generated is often isolated and difficult to integrate from both perspectives of data ownership and fusion algorithms. Additionally, existing AI models are often treated as black boxes, resulting in vague interpretation of the results. Patients also exhibit a lack of trust to AI applications, and there are insufficient regulations to protect patients' privacy and rights. However, with the advancement of AI technologies, such as more sophisticated multimodal algorithms and federated learning, we may overcome the barriers posed by data silos. Deeper understanding of human brain and network structures can also help to unravel the mysteries of neural networks and construct more transparent yet more powerful AI models. It has become something of a trend that an increasing number of clinicians and patients will implement AI in their life and medical practice, which in turn can generate more data and improve the performance of models and networks. Last but not the least, it is crucial to monitor the practice of AI in medicine and ensure its equity, security, and responsibility.

INTRODUCTION

Artificial intelligence (AI) is a rapidly advancing field which employs a variety of technologies to address diverse tasks and problems.[1] It is characterized by the ability of computers to learn, reason, perceive, infer, communicate, and make decisions in a manner comparable to or surpassing humans.[2] AI has been applied in medicine as a tool for information synthesis, clinical decision support, disease management, patient engagement, and performance enhancement.[3] The economic benefits of AI have also been noted with forecasted savings of 150 billion USD in healthcare expenses by 2025.[4]

Clinical decision support has been utilized in medical practice since 1985.[5] Over the past four decades, machine learning, deep learning, expert systems, fuzzy logic, and natural language processing have emerged as the most frequently employed types of AI, with applications in monitoring, prediction, diagnosis, information management, data collection, and clinical practice.[6] Despite of these wide applications, the validation of its clinical utility remains insufficient.[7] On the other hand, ethical and legal concerns, such as potential biases in AI models, safeguarding patient privacy, and establishing trust among clinicians and patients, have recently elicited public attention with regards to the integration of AI in healthcare.[8,9] Whilst promising, there it still a long way ahead before AI becomes a norm or regular practice in medicine. Figure 1 summarizes the progress, challenges, as well as perspectives for the application of AI in medicine. Basically, AI has the capability to assist in monitoring and managing health information, enhance disease diagnosis and treatment strategies, and aid in the formulation of public health policies. Meanwhile, there exist critical challenges to be addressed, including but are not limited to, isolated systems, low-quality data, ineffective learning algorithms, neglection of patient rights, and the absence of regulatory policies. If these obstacles or concerns can be cleared, the field may undergo a transformation from being problem-driven to data-driven, and the implementation of large-scale real-world AI models may induce revolutionary impacts to medical practice and our society.

PROGRESS OF AI IN MEDICINE

AI in health monitoring and management

AI aids in health monitoring and personalized health management by analyzing individual biomarkers, behavioral patterns, and environmental data to identify potential health issues and prevent risk events.[10,11] Through the analysis of big data, AI can also provide tailored recommendations for diet,[12] exercise,[13] sleep,[14] and other aspects, thereby assisting personalized health management. In recent years, the emergence of AI-driven technologies has presented promising opportunities to enhance the quality of life for the elderly population. These technological advances, including intelligent hearing aids,[15] prosthetics,[16] and wearable devices,[17] lead to improved healthcare and support, enabling greater competence in managing the aging process. An example of this is the development of OvaRePred (Figure 2), an ovarian reserve evaluation system that utilizes real-world data to assess ovarian reserve function in different scenarios.[18-21] The system can predict the onset age of fertility decline related to diminished ovarian reserve (DOR) with ovarian reserve score of 50 and the onset age of perimenopause, by considering the current ovarian reserve function and the ovarian aging curve. This tool has seen trials for clinical use in several hospitals and third-party laboratories in China. The information it provides is crucial not only in empowering women to effectively manage their perimenopausal period but also in helping them create a personalized childbearing plan based on their individual ovarian reserve status. Another example is Robot Handy 1. It can help patients

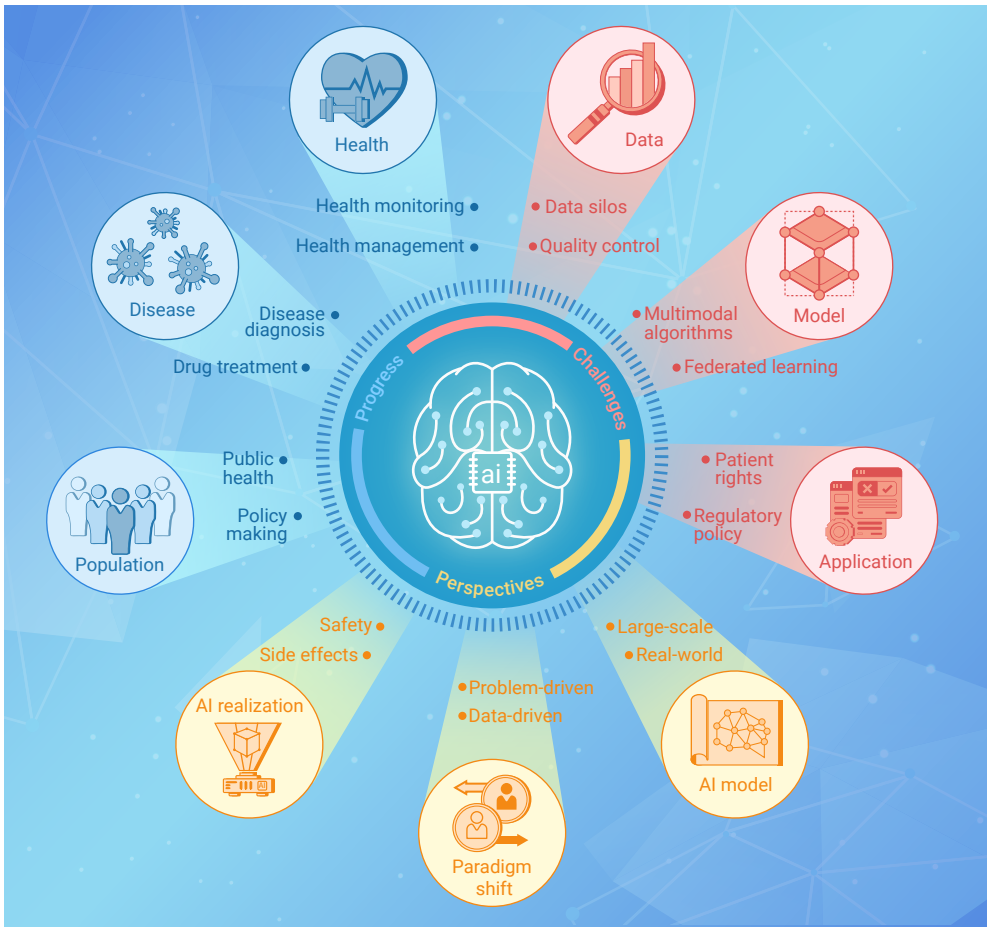

Figure 1. Applications, challenges, and perspectives of AI in medicine

with severe disabilities to complete essential care functions from daily activities like eating, drinking, bathing, and teeth brushing to fine activities such as shaving and putting on makeup.[22] These intelligent robots also have potentials to assist patients in more complicated tasks like furniture moving and object transportation, which helps to considerably expand their radius of daily activities while taking full consideration of the safety of the patients.[23]

AI is also often utilized for monitoring the vital signs of patients in emergency departments, operating rooms, and intensive care units.[24-26] The implementation of an intelligent monitoring system that allows clinicians to anticipate changes in a patient's vital signs and prevent the deterioration of his or her condition.[26] This system is particularly vital for patients with acute mental epilepsy or behavioral disorders.[27-29] Studies have demonstrated that AI-assisted nursing observation systems can facilitate real-time monitoring of psychiatric patients and improve their treatment experience.[28] In addition, epilepsy electroencephalograph (EEG) classification, visualization, and ultrasound recognition algorithms can be utilized to monitor seizures in epilepsy patients and provide nurses with timely information on changes in a patient's condition.[29] A few more examples include an application for early warning of falls and lowering the incidence of falls [30-33] and a risk assessment system that can effectively predict the risk of stress injury, enabling nurses to focus their attention on high-risk patients without increasing their workload.[34-36] Further, with the use of classification algorithm, a prediction model of pressure injury for inpatients has been established, allowing nurses to identify high-risk patients with an accuracy rate of 87.2%.[37]

AI in disease diagnosis and drug treatment

Compared with human experts,[38] AI has already exhibited better performance in a variety of diagnostic tasks such as cancer early detection,[39,40] disease classification,[41,42] clinical outcome prediction,[43,44] and precision medication.[45,46] One of the most promising applications of AI in cancer diagnosis is the use of deep learning algorithms to analyze medical images like CT,[41] MRI,[47] and histological images.[48] These algorithms are able to learn from large medical image datasets to identify patterns or features that are indicative of cancer, and have the potential to revolutionize cancer diagnosis by improving the diagnostic accuracy and speed.[49] It has been reported that deep learning framework utilizing transfer learning can achieve performance comparable to that of human experts in classifying age-related macular degeneration and diabetic macular edema,[50] as well as predicting the treatment response of lung cancer.[51] AI software has also been applied to classify breast density and arrange additional MRI screenings for patients with high breast density, which has been found to reduce the incidence of interval cancer.[52] Similarly, AI fluorescence image interpretation software has gradually been applied in the field of indirect immunofluorescence detection of autoantibodies, [53] and been developed to improve the precision of bone age assessment beyond what is possible with conventional G-P bone age mapping.[54] Additionally, deep learning methods have been employed to analyze patients' speech data, which could successfully identify early linguistic features of Alzheimer's disease via narrative speech.[55]

An example worthy of being noted is Controlled Ovulation Stimulation (COS) in combination with in-vitro fertilization and embryo transfer (IVF-ET), which stands as the most prevalent and efficacious method within the realm of assisted reproductive technology. The crux of decision-making in COS revolves around determining the appropriate dosage of exogenous follicle stimulating hormone (FSH) for ovulation induction. Presently, most clinicians adhere to a fixed standard dosage of exogenous FSH, typically falling within a range from 150 to 225 IU. The span is usually adopted based on a combination of the clinician's professional experience and the patient's past responses to ovarian stimulation, with certain dosage adjustment whenever deemed necessary. That said, it is paramount to acknowledge that the selection of the exogenous FSH dose primarily hinges on the patient's ovarian reserve and response, both of which exhibit significant individual variations. Consequently, precise dose selection necessitates a high level of clinical expertise; achieving standardization and personalization in FSH dose selection poses a formidable challenge. Recently, a team has developed an online tool referred as POvaStim,[46] accessible at http://121.43.113.123:8004. With an r-squared value exceeding 0.9, indicating that POvaStim can account for >90% of outcome variables, the tool currently stands as the foremost model for guiding exogenous FSH dosage on an international scale, and it has been successfully implemented in local hospitals where it was developed. The assistance of POvaStim can significantly accelerate the learning curve of junior clinicians, so that they can achieve comparable levels of effectiveness in COS treatment as their more experienced senior counterparts.

Another exampled application of AI in disease early diagnosis is related to Polycystic Ovary Syndrome (PCOS), one of the most prevalent endocrine and metabolic disorders among women worldwide that has affected approximately 6-20% of women in their childbearing years.[56-61] PCOS is associated with a range of adverse health outcomes such as infertility, metabolic disorders, sleep apnea, emotional disorders, cardiovascular disease, and endometrial cancer. Therefore, early identification and long-term management of PCOS are critical to mitigate the potential risks associated with the condition. Xu *et al.* from Peking University Third Hospital have developed a standardized, non-invasive, and user-friendly screening model referred as PCOSt (Figure 3) based on real-world data from their reproductive center.[62] This model is straightforward and easy to implement, offering a simpler yet more accessible alternative to the widely accepted Rotterdam standard, [62,63] which

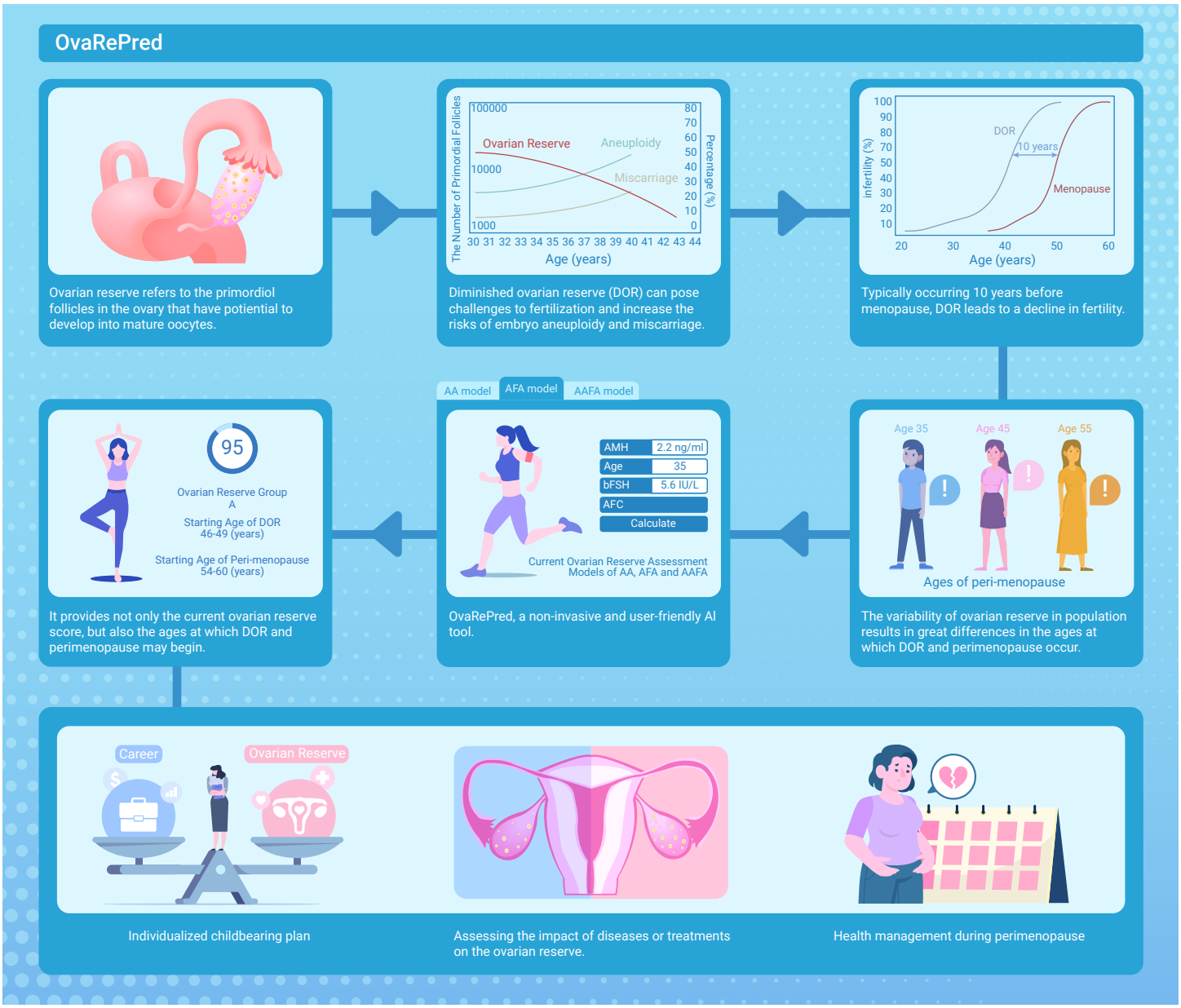

Figure 2. OvaRePred, an AI tool for ovarian reserve assessment OvaRePred is an online tool designed to evaluate not only user's current ovarian reserve but also to predict the future age of DOR and perimenopause, which allows for a better balance between fertility and career aspirations based on one's ovarian reserves. Additionally, it aids in the management of women's perimenopausal health.

empowers PCOSt an valuable asset in expanding the reach of early PCOS screening to minimize missed diagnoses. Simultaneously, it provides a robust tool for managing PCOS-related patient care. Currently, the tool has been explored for clinical applications, for example as a screening tool to assess the risk levels of patients visiting the hospital. Those identified with medium or high risk will receive additional consultations and treatment for PCOS complications using the hospital's available resources. This initiative holds the promise of significant improvement in the long-term health management for the captioned group of women.

AI in public health and policy making

During the COVID-19 pandemic, AI has made significant contributions to epidemiological modeling and forecasting, risk assessment and mitigation, contact tracing and exposure notification, vaccine distribution and prioritization, public health communication and education, and more.[64-66] A good example is the Health QR code that has played vital roles in not only making travelling easier and faster, but also improving the efficiency of epidemic prevention and control in a more scientific manner. By analyzing multimodal data like infection rates, mobility patterns, and social interactions, AI algorithms can provide valuable insights for policymakers in modeling the spread of COVID-19 and predicting its trajectory.[67]

Beyond the pandemic, AI has become an essential tool in the field of public health policymaking and has made noteworthy contributions to the advancement of the field (Figure 4).[68-70] One of the significant benefits of AI is its capability to analyze health big data such as electronic health records, disease surveillance systems, social media posts, and environmental data. AI can analyze individual and population-level data to uncover insights into health behaviors, lifestyle choices, and risk factors. These data can also be utilized to develop evidence-based interventions and health promotion campaigns that effectively target specific populations, and to address key public health challenges like smoking cessation, healthy eating, and physical activity. Lastly, AI can support the analysis of extensive amounts of scientific literature, clinical trials, and research studies, which further advances the field of public health.

CHALLENGES OF AI IN MEDICINE

As discussed above, the transformative potential of AI in healthcare is profound. By leveraging vast amounts of data, AI can offer insights that promise to redefine patient care, diagnosis, and treatment methodologies. However, this landscape is not without challenges and addressing them is

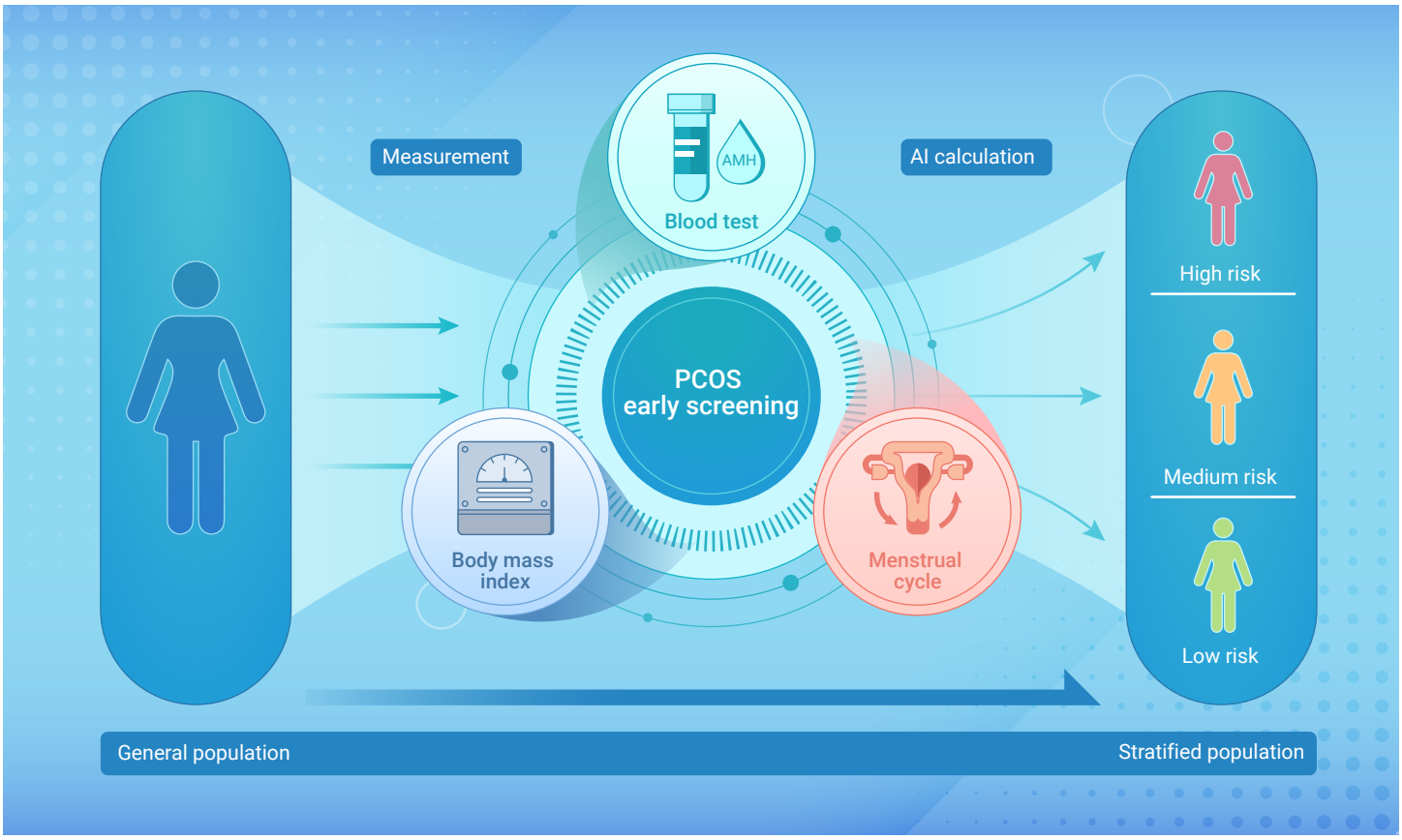

Figure 3. PCOSt, an AI tool for early screening of polycystic ovary syndrome (PCOS) PCOSt is a screening tool for PCOS that is diagnosed based on the observation results of anti-mullerian hormone (AMH), the upper limit of menstrual cycle length, and body mass index (BMI). Women identified with medium or high risk of PCOS via this screening will receive recommendations for follow-up health management. This may include addressing PCOS-related complications, assisting with online or offline clinician appointments or consultations, and providing guidance on weight management, *etc.*

crucial for the seamless integration of AI into healthcare. The biggest one is the data challenge (Figure 5). There are too many data types (Figure 5A), and the data quality is often low (Figure 5B), with many missing values (Figure 5C). Moreover, it is difficult to integrate data from diverse sources (Figure 5D) and interpret the "black box" model in a transparent and comprehensible manner (Figure 5E).

Data silos: the fragmentation challenge

In healthcare sectors worldwide, the challenge of data silos is becoming increasingly pronounced. These silos, characterized by isolated storage systems with their unique formats and/or structures, act as barriers to efficient sharing and integration of crucial patient data. Such fragmentation not only hampers researchers in their quest for comprehensive datasets but also curtails the potential of AI applications, which inherently rely on diverse and integrated data sources for optimal performance. Recognizing the gravity of this issue, there's a concerted push within the community towards adoption of standardized data formats. Leading this transformation are protocols like Fast Healthcare Interoperability Resources (FHIR) and open Electrical Health Record (openEHR).[71] These standards, by promoting interoperability, aim to bridge the existing data gaps and facilitate seamless data exchange across platforms. However, as the industry gravitates towards greater data integration, the spotlight is firmly on patient privacy and data security. It's imperative to ensure that as data becomes more accessible, it doesn't compromise patient confidentiality. To this end, robust data governance frameworks are being developed, with clear guidelines on data access, consent management, and anonymization, striking a balance between promoting data sharing and safeguarding patient privacy.[72,73]

Data standardization and interoperability in healthcare

In the evolving landscape of healthcare, data standardization and interoperability are undeniably crucial. However, they are fraught with challenges. The sheer diversity of data sources, each with its distinct format and structure, complicates standardization.[74] Instruments from different eras produce data with varying quality, granularity, and formats, making integration a daunting task. Even when data is harmonized, achieving true interoperability—where different healthcare systems can seamlessly communicate and interpret this data —is persistently demanding. Legacy systems, deeply entrenched in many healthcare sectors, often resist integration with newer, interoperable platforms. The absence of universally embraced standards can lead to fragmented efforts, with organizations adopting divergent approaches, further muddying the waters. While standards like Integrating the Healthcare Enterprise (IHE), Health Level Seven (HL7), Fast Healthcare Interoperability Resources (FHIR), and Digital Imaging and Communications in Medicine (DICOM) have made commendable progress, their global adoption and consistent implementation remain aspirational.[75]Multi-institutional initiatives like Quantitative Imaging Biomarkers Alliance (QIBA),[76] Image Biomarker Standardization Initiative (IBSI),[77] UK Biobank,[78] The Cancer Imaging Archive (TCIA),[79] and The Cancer Genome Atlas (TCGA),[80] underscore the importance of standardized, curated data.

Data quality control

The efficacy and dependability of AI systems in medicine are contingent upon the quality of the utilized data in their development and online deployment.[74] Medical data often contains missing values, outliers, and inconsistencies which necessitate attention. The insufficiency of data completeness may result from a variety of factors such as incomplete records or errors during data entry. Noise and outliers may occur due to measurement errors or anomalous values. To prevent biased predictions, misleading outcomes, and potential harm to patients, it is crucial to establish robust quality control processes and adhere to standardized guidelines.[81] The process of data quality control includes assessing the completeness, accuracy, consistency, representativeness, and timeliness of the collected data (Figure 5B). In medical AI research, the initial step in enhancing the quality and integrity of

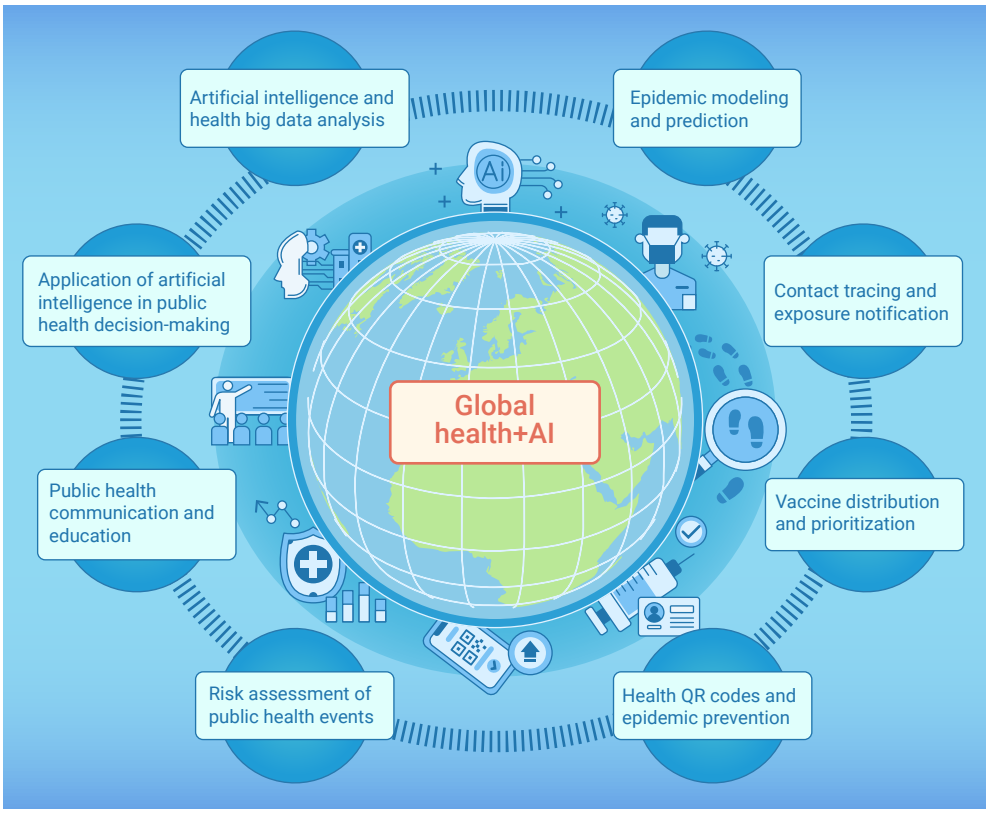

Figure 4. Eight exampled application directions of AI in global health

datasets is data cleaning or preprocessing. To streamline the data cleaning process and improve the accuracy and completeness of medical datasets, automated algorithms, statistical techniques, and machine learning approaches such as data profiling, outlier detection, and anomaly detection are being developed. The second step is to ensure accurate and consistent annotation and labeling to train and validate the supervised learning models. Well-defined annotation guidelines and appropriate training for annotators are crucial to ensure the inter-annotator agreement.

Multimodal data fusion algorithms

Current biomarkers used in diagnosis are in majority limited to one modality,[82] which may not fully capture the different facets of the disease. Multimodality in biomedical research integrates diverse data types, from electronic health records and wearable biosensors to genomics and metabolomics, offering a comprehensive view of an individual's health (Figure 5A). Discovering associations between various modalities such as cellular morphology, genetic profiling, and radiology findings, can lead to the identification of new biomarkers and improve large-scale population screening.[83] Despite of the substantial potential of multimodal fusion techniques in medical AI, several challenges need attention. Firstly, multimodal medical data often have different formats, resolutions, dimensions, and feature representations that make data fusion intricate. Researchers must establish standards and interoperability for medical data to guarantee seamless integration and communication across various data sources.[71] This includes, but is not limited to, defining uniform data formats, terminology standards, and protocols for effective data sharing and integration between different healthcare systems and institutions. Secondly, selecting an appropriate fusion strategy and model architecture for multimodal data is crucial but challenging owing to the intricate relationships between different modalities and levels of data interaction. Researchers can explore different fusion strategies, such as early fusion (combining raw data), late fusion (combining model outputs), or hybrid fusion (combining intermediate representations), based on the nature of data and task at hand (Figure 5C).[84] Thirdly, in some cases, certain modalities may have incomplete or missing data, i.e., modality missingness, posing difficulties for data fusion and online use of models.[85]

Solutions to address modality missingness include data interpolation/imputation, information transfer, leveraging knowledge and priors, and integrating multimodal features. By aggregating, integrating, and analyzing these complementary digital assets across large patient populations, deep learning models can identify patterns from images as well as histological, genomic, and clinical data that may be difficult for humans to detect.[86,87] Built upon that, it is potential to developed non-invasive alternatives for existing biomarkers to support large-scale population screenings,[88] which is essential to further boost the discovery of multimodal prognostic features and learning capability from collective history of large cohorts of patients to inform better clinical management (Figure 6).[89]

Bridging the gap between accuracy and interpretability

The opaque "black box" nature of complex AI models like deep neural networks poses a challenge for their acceptance in healthcare. In medical contexts, where elucidating biological mechanisms is paramount, model interpretability becomes imperative. Although black-box models may excel at initial screenings, their recommendations - especially for treatment or research - must be explainable. To enable this, a concerted effort is required to demystify AI and render its logic transparency (Figure 5D). For example, decision trees or linear regression models, albeit being less accurate than neural networks, provide more visibility into reasoning.[90] Techniques like Local Interpretable Model-Agnostic Explanations (LIME) approximate complex models with simpler, interpretable ones to explain individual predictions.[91] Modular architectures allow dissecting reasoning across different stages.[92] Methods like activating hidden neurons shed light on neural networks' inner workings.[93] Model introspection tools let users query feature importance and confidence levels.[93] Extensive testing characterizes failure modes and ensures safety, like validating an AI-assisted treatment recommendation by requiring justifications against established clinical guidelines.[94] Throughout these procedures, humans must remain empowered to scrutinize AI-assisted decisions. Close collaboration between clinicians and AI researchers, infusing medical knowledge, will open the black box - engendering trust in AI where it matters most (Figure 5E).

Ethical and regulatory issues

The application of AI in medicine raises ethical concerns and poses a challenge to protect patient privacy and rights. AI applications collect patients' personal data, which necessitates privacy protection regulations to minimize the risk of unauthorized access by malicious entities. The collection and utilization of private data should respect patients' wishes, and the training and learning mechanisms of AI must be transparent to ensure the diagnosis and decision-making processes are comprehensible to involved personnel. Failure to do so may infringe the informed rights of patients during diagnosis and treatment.[95-97] Effective regulation and policy frameworks that address ethical concerns, privacy issues, algorithm transparency, and patient safety are hence necessary. The regulatory environment varies across countries and organizations, depending on the technology development stages and legal coverage of AI innovation. The World Health Organization (WHO) advocates for medical AI and has outlined ethical principles specific to AI, including transparency, privacy protection, fairness, and accountability. In 2020, the United States signed Executive Order 13960, which prioritizes the principles of public trust, fairness, transparency, and accountability in the use of AI within the federal government. The National Institutes of Health (NIH) then released a strategic plan that underscores AI's integration into biomedical research and healthcare. In the regulation of medical AI products as medical devices, the Food and Drug Administration (FDA) has issued guidance docu-

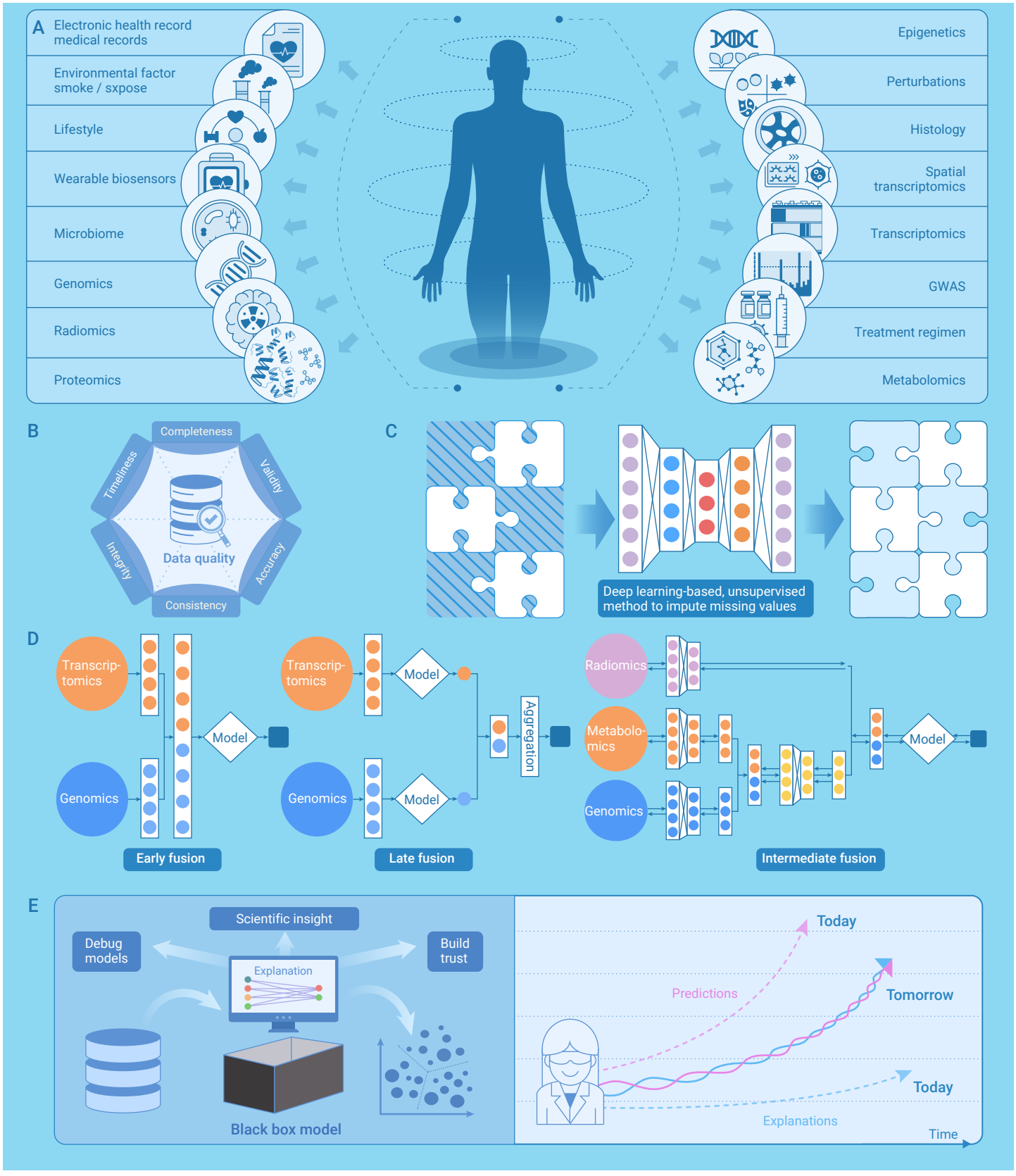

Figure 5. Navigating the data challenge in AI for medicine (A) An overview of diverse data types in AI for medicine, encompassing electronic medical records, environmental factors, lifestyle, wearable biosensors, microbiome, genomics, radiomics, proteomics, epigenetics, perturbations, histology, spatial transcriptomics, transcriptomics, metabolomics, GWAS (genome-wide association studies), and treatment regimens. (B) Key components to ensure the quality of data. (C) A depiction of the missing value imputation process, with a focus on deep learning-based unsupervised method for data completion. (D) An exploration of multimodal data fusion algorithms, showcasing techniques for integrating diverse data sources. (E) Opening the "black box" for enhanced model interpretability, spotlighting methods that harmonize model accuracy with lucid explanations for transparent and comprehensible predictions.

ments such as "Clinical Decision Support Software" and "Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device". The FDA's Digital Health Software Precertification (Pre-Cert) Program enables rapid market approval for software as a medical device (SaMD) product. In

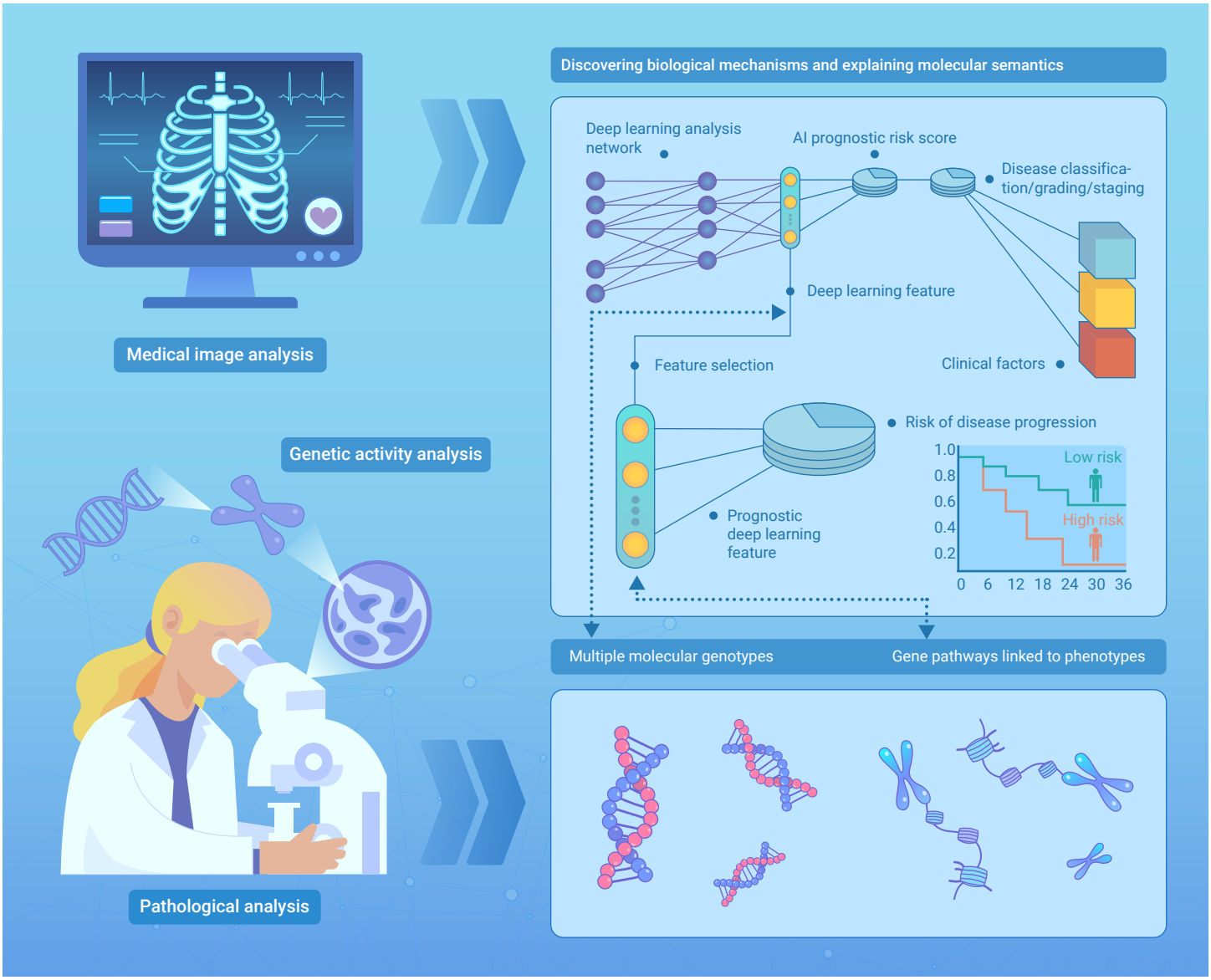

Figure 6. AI for uncovering correlations between different modalities data across different scales In longitudinal exploration, deep learning combined with various omics techniques can identify gene pathways related to phenotypes, revealing the underlying molecular mechanisms of individual disease progression.

2018, the European Union implemented the General Data Protection Regulation (GDPR), which aims to protect personal data and establish guidelines for AI use in areas including healthcare. The Declaration of Cooperation on Artificial Intelligence, signed by the EU and 42 countries, stresses ethical and legal implications and endeavors to steer AI development and implementation toward human well-being and international collaboration. The EU has also implemented the Medical Device Regulation (MDR) and In Vitro Diagnostic Regulation (IVDR) to regulate medical devices, including AI-based products. Ongoing initiatives, such as the European Health Data Space (EHDS), enable secure and authorized cross-border sharing of health data, ensuring interoperability and promoting research and innovation, which has effectively supported the growth of the European medical AI industry.

In 2017, China released the "Next Generation Artificial Intelligence Development Plan" and followed it up with "The Beijing AI Principles" in 2019. These releases were aimed at providing guidelines for responsible development and use of AI, including its utilization in medicine. Since then, regulations related to medical AI in China have undergone significant development, for example with the introduction of the "Special Review and Approval Procedure" for innovative medical devices by the National Medical Products Administration (NMPA) in 2018. More recently, in 2021, the NMPA published "Guiding Principles for the Classification of Artificial Intelligence Medical Software Products" to provide guidance for AI product registration. Despite regulatory challenges, some innovative medical AI products have received regulatory approval. Nevertheless, data availability and quality regulations in China are still under construction, leading to challenges such as data privacy, fragmentation, and limited interoperability between healthcare systems.

These challenges are not unique to China but are common to the global medical AI industry. The accessibility and quality of data are significant obstacles to the wide application of AI in healthcare. Obtaining high-quality, diverse, and accessible data is crucial for AI success, but obtaining such data that is properly structured remains to be further explored. Developing countries like China, even with vast amounts of data and relatively open privacy rules, encounters obstacles in utilizing their data due to interoperability and privacy concerns. Additionally, setting up interpretation ability with trust is a non-trivial task. The operation of AI algorithms often occurs as an opaque process, lacking the ability to provide explanations for decision-making. Ethical guidelines underscore the criticality of human control and oversight in maintaining authority over AI systems. To establish trust amongst healthcare professionals, patients, and regulatory bodies, it is vital to ensure transparency and interpretability within AI models.

It is also worthy of being noted that with the rapid development of large language models like ChatGPT and Claude in 2023, related policies and regulations have been updated frequently in major entities. For example, the US White House announced New Actions to Promote Responsible AI Innovation

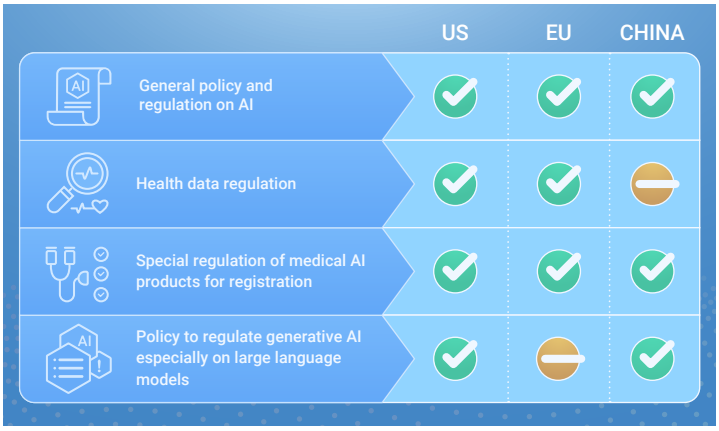

Figure 7. AI related regulation and policy coverage in major entities This table illustrates the coverage of AI related regulations and policies released by the government of United States, European Union, and China. Mark indicates the existence of respective regulation and/or policy, while Question Mark indicates the non-existence of specific regulation and/or policy.

that Protects Americans' Rights and Safety in May 2023, top US AI companies like OpenAI, Google, and others started to watermark AI contents for safety in July 2023. China's Cyberspace Administration has released the Interim Measures for the Management of Generative AI Services, focusing on the management of politically and legally sensitive content and content risk assessment and traceability. The UK government has also released its AI regulation that has specifically encouraged the development of large language models, and The EU has released its first regulation on AI, the AI ACT, highlighting different rules for different risk levels. As seen, regulations are being updated at an accelerated pace, which is aimed to support and encourage rapid and stable development of medical AI industry and to regulate and manage the risks (Figure 7). At last, it should be noted that the imbalance coverage of AI related regulations and policies among entities may raise potential issues.

PERSPECTIVES OF AI IN MEDICINE

Paradigm shift from "problem-driven" to "data-driven"

Advancements in AI technology and its integration with medicine promise to yield remarkable outcomes in three key areas: data, algorithms, and applications. With the widespread application of Internet Healthcare and Smart Healthcare Information Systems, a vast collection of health big data has been amassed, which has potentials to enhance model accuracy without interfering with the algorithm itself.[98]The popularity of "data-driven" research based on real-world data is on the rise, which may lead to a shift from the current "problem-driven" pattern.[99,100] It is important to consider the comprehensiveness of databases when dealing with real-world data, as the skewness of such data can pose challenges. A unified standard for multidimensional and multimodal medical big data, including clinical basic information, medical imaging, physiological signals, laboratory examination, and genes, must be established for distinct diseases and patient groups.[101]

Large-scale real-world AI models

The GPT model has revolutionized the field of algorithms, spurring a transition from a "small workshop" to a "giant factory" in AI research.[102] As a result, research teams are now actively involved in organized scientific research guided by the technical roadmap of foundation models, leading to the development of a variety of models [103] ranging from large models, such as GPT,[104]which serve as the backbone to support AI tasks, to more complex models, such as Segment Anything,[105]deep learning for predicting disease progression, and reinforcement learning for optimizing the treatment plans.

In the development of algorithms, it is critical to consider the quality challenges posed by real-world data (Figure 8). For example, due to the complexity and time-consuming nature of medical data acquisition and annotation, traditional supervised learning approaches are insufficient for AI medicine, necessitating specialized research on algorithms for limited-sample and label-deficient data. Additionally, given the ethical considerations in medical practices, it is essential to ensure that the algorithm's fairness is not compro-

Figure 8. Challenges for large-scale real-word AI models

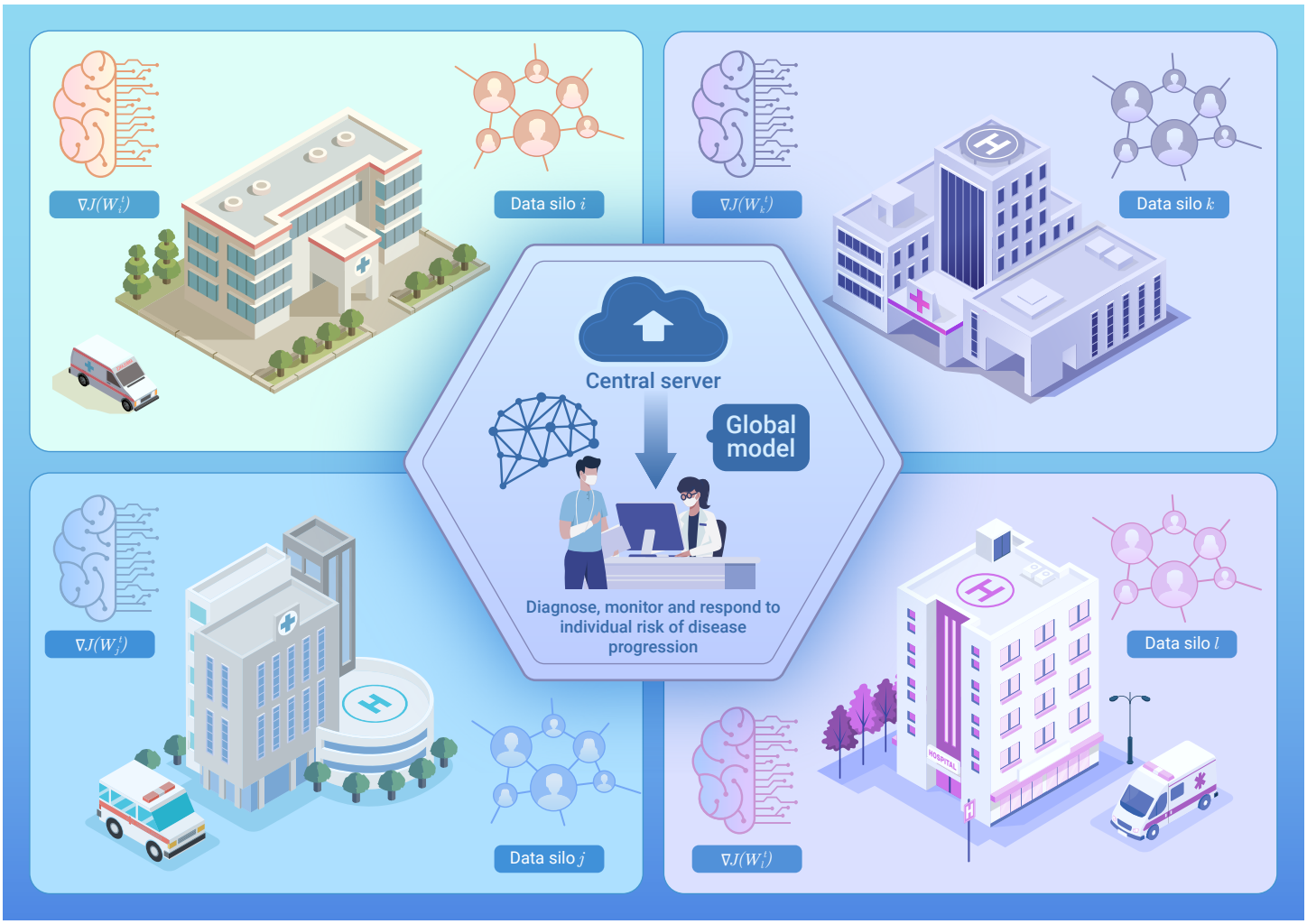

Figure 9. Schematic of federated learning. In a multi-party collaboration, to preserve the privacy of data, federated learning only allows remote devices to exchange model gradients with a central server During this process, each distributed model is trained only using local data, and then the computed gradients are uploaded to the central server. Subsequently, the central server updates the global model based on the collected gradients and sends back the updated parameters of the global model. Finally, the well-trained global model applies for different locations and data sources.

mised by any potential gender, racial, family, or other biases. Despite the remarkable outcomes achieved by end-to-end AI models, more research is required to explore how to integrate them with existing methods, such as clinical decision support systems, medical knowledge graphs, and medical gold standards.[106] Finally, medical research not only investigates "what" but also closely scrutinizes "why". The current state of AI methods can produce highly accurate predictions of "association" by fitting real-world data but is still limited in its ability to analyze "causality". Although there have been attempts by several researchers to provide interpretable justifications from a clinical perspective to aid in diagnosis, these efforts have yet to achieve the goal of determining causality.

Federated learning for data collaboration and privacy protection

In the field of AI, data plays a pivotal role and serves as the fundamental component of model training.[107] However, data often exists in the form of data silos. Due to the challenges posed by privacy protection regulations, traditional methods have been limited with data silos.[108] In recent years, with the significant advancement in privacy AI techniques, federated learning has provided a novel training approach to build personalized models without compromising user privacy which opens up new research directions to address privacy concerns associated with data collection.[109,110] Compared with centralized training methods, federated learning is a distributed training approach that enables individual users from different locations or sources to collaboratively learn models while keeping all potentially sensitive personal data stored on their respective devices (Figure 9).[111-113] Through the utilization of federated learning, individual users can benefit from obtaining a well-trained machine learning model without the need to transmit their privacy-sensitive personal data to a central server. This offers significant promise for establishing connections among dispersed medical data sources while ensuring robust privacy protection. As a novel approach for cross-platform data collaboration and privacy protection, federated learning holds the promise of providing more secure services and strategies for the practical deployment of models, further driving the advancement of AI in medicine.

Realization of AI in vertical areas

It is essential to consider specific requirements of different scenarios, such as pre-hospital screening, in-hospital diagnostic assistance, and post-hospital health management, and to adjust and deploy AI models accordingly. Maintaining a balance between sensitivity and specificity for AI algorithms is crucial in achieving desired outcomes. For instance, screening requires higher sensitivity to avoid missing potential positive cases and delay in treatment, while diagnosis requires higher specificity to avoid unnecessary treatment that could cause harm.[114] Additionally, it is imperative to systematically develop strategies and workflows to facilitate collaboration between humans (clinicians) and machines (AI-assisted diagnostic systems). As a tool, AI models can only be effective when being utilized properly by humans. To advance the field of AI medicine, it is imperative to provide a clear and detailed account of the potential "side effects" of AI models, akin to the instructions present in drug manuals. This includes information about the recommended "dose" and "date" of AI model usage, as well as guidelines for

their integration into current clinical pathways. Additionally, fostering collaboration between algorithm researchers and clinicians is vital to the development of medical AI. To this end, algorithm researchers should prioritize the creation of user-friendly tools, starting with basic logistic regression.[115] Furthermore, clinicians should be encouraged to explore unconventional questions and propose inquiries that have never been interrogated.

In brief, AI has attracted considerable attention in the areas of medical diagnosis, health management, and public health. Meanwhile, there are critical data and regulatory challenges associated with these applications, which have been partially resolved by the continuous development of AI algorithms and models. Multimodal data fusion techniques can also lead to wider picture of diseases progression by integrating various types of data. Furtherly, federated learning makes it feasible to collaborate on data without worrying about data sharing and information leakage. Last but the not least, to make AI applications in medicine fairer and more accountable, governments and organizations are updating pertinent laws and regulations. Albeit not perfect yet, it has become something of a trend that an increasing number of clinicians and patients will implement AI in their life and medical practice, which in turn can generate more data and improve the performance of medical AI and quality of our healthcare practices.

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AUTHOR CONTRIBUTIONS

T.H., P.L. and J.Q. supervised and revised the manuscript. H.X., H.W., H.H., Y.X., B.L., S.H., G.F., S.K., G.L., D.J., Z.L., Y.L., C.M., C.S., W.W. and R.L. wrote and edited the manuscript. All authors contributed to the article and approved the submitted version.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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