25 Years of Evolution and Hurdles in Electronic Health Records and Interoperability in Medical Research: A Comprehensive Review

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Abstract

Electronic Health Records (EHRs) facilitate the accessibility and sharing of patient data among various healthcare providers, contributing to more coordinated and efficient care. EHRs are designed not only to collect and store health information but also to support other care-related activities like evidence-based decision support, quality management, and outcomes reporting. The adoption of EHRs has been encouraged globally as a critical component of modern healthcare systems, aiming to improve the accuracy and efficiency of patient care and to support better health outcomes. Over the past 25 years, EHRs have successfully been translated from digital records to scientific achievements. In this review, we examined the evolution of EHRs and their interoperability over the past 25 years. We explored the advancements in EHR technology, emphasizing how they have facilitated better management and understanding of diseases through comprehensive data collection and analysis. Challenges such as common data models, system compatibility, connection, linkage and privacy issues were discussed in detail. This review also highlighted the significance of these records in epidemiological studies, pragmatic clinical trials and health economic studies particularly in creating a more accurate representation of clinical practices and patient populations. Moreover, it considered the limitations of EHRs, including data cleaning complexities and potential biases arising from inconsistent records. Improved resource sharing and collaborations among healthcare providers were advocated, underscoring the need for consistent data formats and policy development in healthcare networks to maximize the potential of EHRs in clinical research and healthcare improvement.

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25 years of evolution and hurdles in electronic health records and interoperability in medical research: a comprehensive review

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Abstract:

Electronic Health Records (EHRs) facilitate the accessibility and sharing of patient data among various healthcare providers, contributing to more coordinated and efficient care. EHRs are designed not only to collect and store health information but also to support other care-related activities like evidence-based decision support, quality management, and outcomes reporting. The adoption of EHRs has been encouraged globally as a critical component of modern healthcare systems, aiming to improve the accuracy and efficiency of patient care and to support better health outcomes. Over the past 25 years, EHRs have successfully been translated from digital records to scientific achievements. In this review, we examined the evolution of EHRs and their interoperability over the past 25 years. We explored the advancements in EHR technology, emphasizing how they have facilitated better management and understanding of diseases through comprehensive data collection and analysis. Challenges such as common data models, system compatibility, connection, linkage and privacy issues were discussed in detail. This review also highlighted the significance of these records in epidemiological studies, pragmatic clinical trials and health economic studies particularly in creating a more accurate representation of clinical practices and patient populations. Moreover, it considered the limitations of EHRs, including data cleaning complexities and potential biases arising from inconsistent records. Improved resource sharing and collaborations among healthcare providers were advocated, underscoring the need for consistent data formats and policy development in healthcare networks to maximize the potential of EHRs in clinical research and healthcare improvement.

Introduction

Medicine is deeply rooted in the annals of human history. Spanning from the first use of stone tools around 3.3 million years ago, prehistoric medicine occurred with traits of early human use of medicinal plants, healing practices, and concepts of health and illness even before the appearance of written records. The concept of documenting patient information dates back to about 3,000 years ago, when the Egyptians, Greeks, Sumerians, Chinese, Indians and Romans made some of the earliest known medical records, inscribing case histories on papyrus, clay tablets, animal bones and other materials.[1-3] These records often included symptoms, diagnoses, and treatments. The healthcare delivery system developed with a long history and became more and more complex. During the time of classical medicine, healthcare providers frequently gathered and systematized medical knowledge, creating standardized textbooks, which were often recorded by case series rather than individual patients.[4] In the 19th century, with the progressive development of modern medicine, healthcare providers began keeping detailed paper records. These were used to track patients' medical histories, nursing information, treatments, and outcomes. Hospitals and clinics maintained handwritten notes, which were stored in file systems.[5-8] With the explosion of electronic technologies boosted in the 20th century, hospitals began using such technologies to store records, reducing physical storage space and improving record retrieval efficiency. Computerization is one of the revolutionary technologies. The concept of Electronic Health Records (EHRs) originated in the 1960s.[9] Several early systems were developed in the middle of 20th century such as the Computer Stored Ambulatory Record,[10,11] the Problem Oriented Medical Record System,[12,13] the Medical Record[14] and the Regenstrief Medical Record System.[15,16] It aimed to improve the storage, retrieval, and management of patient information. Healthcare professionals aimed to address clinical challenges and steer treatment decisions by utilizing data from these systems. This approach served as the foundational prototype for EHRs in medical research. Later, the 1990s brought about efforts to standardize EHR systems and the introduction of the internet, which significantly influenced EHR development. Health Level Seven International (HL7) played a crucial role in developing standards for the exchange, integration, sharing, and retrieval of electronic health information.[17] The 2000s saw increased government involvement in the adoption of EHRs. The Health Information Technology for Economic and Clinical Health (HITECH) Act of 2009 and the American Recovery and Reinvestment

Act of 2009 provided significant incentives for healthcare providers to adopt and use EHRs meaningfully in medical research.[18,19] The 2010s witnessed widespread adoption of EHRs, driven by government incentives and the recognition of their potential to improve healthcare quality, safety, and efficiency. Interoperability, or the ability of different EHR systems to exchange and interpret shared data, has been a major focus area.[20-23] Now in the 2020s, the use of EHRs in medical research has been boosted with the development of advanced technologies in health care. Digital health and artificial intelligence have led the future direction of diseases in research.

In the past 25 years, the use of EHRs has developed rapidly from initial scheduling and billing purposes to medical research and healthcare quality improvement. For the 25th anniversary of the *Journal of Medical Internet Research* Publications, this paper focuses on the evolution of EHRs and their interoperability in medical research over the past 25 years, especially in terms of chronic disease management, such as metabolic diseases, respiratory diseases, cardiovascular diseases and cancer. We explore the advancements in EHR technology, emphasizing how they have facilitated better management and understanding of diseases through comprehensive data collection and analysis. Challenges such as common data models, system compatibility, connection, linkage and privacy issues are discussed. This review also highlights the significance of these records in epidemiological studies, pragmatic clinical trials and health economic studies particularly in creating a more accurate representation of clinical practices and patient populations. Moreover, it considers the limitations of EHRs, including data cleaning complexities and potential biases arising from inconsistent records. Improved resource sharing and collaborations among healthcare providers will be advocated, underscoring the need for consistent data formats and policy development in healthcare networks to maximize the potential of EHRs in clinical research and healthcare improvement.

Methods

Literature Review

We focus on the advancements in EHR technology and the application and significance of these records in medical research in three eras. Therefore, we conducted an extensive literature search in the PubMed biomedical database, which provides ideal coverage of the publications of interest.

Our search strategy was divided into three parts: (1) all studies that contained the terms “Electronic health record” OR “Electronic medical record” in the title or abstract and “medical research” in all fields were identified. (2) According to the time of publication, the studies were divided into 2000s, 2010s, 2020-2023 and 2024, (3) and then were narrowed down to particular fields by specific terms (Figure 1). For example, the search term for the 2010s was: ((electronic health record[Title/Abstract]) OR (electronic medical record[Title/Abstract])) AND (medical research) AND ((real world study) OR (real world evidence) OR (pragmatic clinical trial) OR (pragmatic trial)).

The review yielded 1,421 studies, all of which were then screened and processed in a structured manner. In the framework shown in Figure 2, 11 of the 1421 studies were excluded because they did not have an English abstract, 28 were excluded because they were not directly related to EHRs, and 5 were excluded because of duplicate submissions and conference abstracts. Ultimately, 1377 studies were included in the review analysis with 902 studies from 2000-2009, 300 studies from 2010-2019, 131 studies from 2020-2023 and 44 studies in 2024.

Qualitative Structured Analysis

Qualitative analysis and structuring of the available sources were performed using Nvivo 14 software. All studies were coded using Nvivo to generate keywords. For visualization, we performed a word frequency analysis (Figure 3).

Results and discussions

Initial adoption and early research utilization before and in 2000s

The Problem-Oriented Medical Record (POMR)

One of the earliest known efforts to use electronic systems for medical research that could be considered a precursor to modern EHRs was by Dr. Lawrence L. Weed in the 1968.[24] Dr. Weed introduced the concept of the Problem-Oriented Medical Record (POMR), which organized patient data according to specific problems, making it more systematic and usable for both care and research. Researchers began to use POMR for cost analysis,[25] staff communications,[26] and decision making[27-29] in a wide range of diseases after the within the 10 years after the initial development of POMR. The POMR was also strongly advocated among medical students for training purpose.[30] As the patient-centered medical care always necessitates a patient-centered medical record, the POMR remained prevalent in the early 2000s, particularly in the daily practice of general practitioners.[31-33]

The Regenstrief Institute, established in 1969 in Indianapolis, Indiana, by Dr. Clement McDonald, is another pioneer in this field. The Institute developed the Regenstrief Medical Record System (RMRS), one of the first electronic medical record systems, which was used to support medical research, as well as improve patient care.[15,16] The RMRS allowed for the electronic capture, storage, and retrieval of patient data, serving as a model for later EHR systems. Researchers began to design randomized trials by using the system to test the effectiveness of medications.[34,35] The RMRS attempted to create a community wide linkage across healthcare systems, urgent care hospitals, clinics and health departments.[36] Now it still stands at a historical mission to develop, conduct and disseminate impactful scientific research in health systems and across communities.

Both Dr. Weed's work on POMR and the Regenstrief Institute's development of the RMRS played significant roles in the early use of electronic systems to support medical research, laying the groundwork for the EHR systems we see today. These systems not only improved healthcare delivery but also facilitated health research by providing easier access to comprehensive patient data including both digital and medical image data.

Technological and methodological developments

With the development of POMR and RMRS, some new technologies and methodologies were applied to support the use of EHRs in research. This included the creation of data warehouses and the development of tools for data mining and analysis, which would later become crucial for extracting meaningful insights from large EHR datasets. The recognition of the value of EHR data for research led to the formation of consortia and collaborative networks aimed at sharing data and best practices. These early collaborations laid the foundation for later, more extensive networks that would leverage EHR data for multicenter studies and nationwide research initiatives.[37]

In 2009, the HITECH Act was issued.[22] The HITECH Act represents a critical step in the digital transformation of the U.S. healthcare system. The primary aim of the HITECH Act was to improve American healthcare delivery and patient care through an unprecedented investment in Health IT. The Act supported the establishment and expansion of health information exchanges, e-prescribing and other novel technologies that can help to improve healthcare quality. The HITECH Act led to a substantial increase in the collection and digitization of patient health information. This vast repository of data became a valuable resource for researchers, offering a wealth of information on patient outcomes, disease patterns, and treatment effectiveness.[38-42] Most researches in 2000s leveraging EHRs have some features in common including single healthcare system or single hospital, observational study design, and limited data on clinical characteristics.[43] Additionally, Some researchers also tried to use EHRs for pharmacovigilance and comparative effectiveness of drugs.[44-47]

The limited duration of interventional and observational periods in clinical trials necessitated real-time monitoring of therapeutic effectiveness and safety, crucial for both physicians and patients. The utilization of EHRs effectively addressed these concerns.[48] Some early explorations on biomedical image data began with the incorporation of the digital imaging and communications in medicine (DICOM) within EHRs.[49-52] The de-identification of radiology clinical data allowed researchers to do case series studies and to follow-up the changing patterns of the biomedical images in a certain disease area.

Challenges and concerns

It also highlighted several challenges in using EHRs for medical research before and in 2000s, including issues with data quality, consistency, and interoperability between different EHR systems. Privacy and security concerns regarding the use of patient data for research purposes were significant, leading to regulatory efforts to protect patient information while enabling research. The Health Insurance Portability and Accountability Act (HIPAA), originally enacted in 1996, continued to influence EHR development throughout the 2000s with its privacy and security rules, which were critical in shaping how EHR systems handled sensitive patient data.[53,54]

The rise of big data in healthcare in 2010s

Data-driven research and big data analytics

In the 2010s, big data analytics in healthcare were popular, with EHRs serving as a primary data source. Researchers began leveraging EHR data to conduct large-scale studies on patient outcomes, disease patterns, and treatment efficacy. A lot of cohort studies have been designed and conducted using EHR data to provide evidence of the association between risk factors and occurrence as well as the prognosis of diseases. Additionally, a lot of quality improvement studies used EHRs to investigate the patients’ communication and clinical support. The disease areas covered almost every systems in body including primary care,[55] cardiology,[56] sepsis,[57] cancer,[58] diabetes,[59] rheumatology,[60] nephrology,[61] neurology,[62] hepatology,[63] gastroenterology,[64] etc. Our previous review has highlighted the practical use of electronic health records among patients with diabetes in medical research.[65] Several European national registries of diabetes[66-68] and the patient-centered outcomes research networks[69-71] were well introduced. Moreover, insurance claim data, like that from the Kaiser Permanente,[72-74] offers valuable insights for enhancing our understanding of health risks, improving patient outcomes, and informing policy and practice decisions.

On the other hand, researchers also started to analyze data from large patient populations to identify health trends, assess risk factors, and develop strategies for disease prevention and health promotion. They started to use these data for potential patient selections and recruitment for clinical trials.[75] Meanwhile, pragmatic clinical trials (PCTs) began to rise gradually.[76] The term “Real world study (RWS)” or “Real world evidence (RWE)” gathered a lot of attention during that time. Researchers had made great efforts to fill out the gap between clinical trial results and real-world outcomes.[77-80] This kind of trials was designed to evaluate the effectiveness of interventions or medications in real-world clinical settings, aiming to inform healthcare decision-makers about the trade-offs between benefits, harms, and costs of those interventions.[81-83] They mainly rely on the EHR data. Initially, it starts with the formulation of a relevant and practical research question, aimed at addressing key uncertainties in real-world clinical settings, focusing on comparing interventions or medications in ways that reflect usual care. This is followed by the inclusive design of the study, where broad eligibility criteria are set to capture a diverse patient population representative of those who will receive the intervention in practice. The choice of comparators and outcomes is crucial, prioritizing those that hold significant value to patients and healthcare providers, such as health outcomes that matter to patients' quality of life, adherence to treatment, and overall health economics. There were also some tools that were developed to help researchers design and implement PCTs including the

Pragmatic–Explanatory Continuum Indicator Summary (PRECIS-2).[84] Moreover, the stakeholder engagement is a pivotal step.[85,86] The implementation phase requires selecting appropriate sites that mirror the settings where the intervention will be applied, employing strategies for diverse participant recruitment, and integrating interventions and comparators seamlessly into routine clinical practice. Data collection leverages EHR to minimize disruption and enhance the efficiency of the trial process. PCTs seem more reliable to provide RWE than traditional randomized trials. Some claim data linked to EHRs can also provide detailed records of healthcare services received by patients, allowing researchers to accurately measure resource utilization and associated costs.[87-89] This information is crucial for cost-effectiveness analyses that compare the costs and outcomes of different healthcare interventions. EHR data enables the estimation of direct medical costs by documenting clinical procedures, medication prescriptions, hospital stays, and other healthcare services. In addition, EHR data have contributed to the evaluations of healthcare quality and system performance, which supported its use in health policy studies, as the data compromises vast information on healthcare procedures.[90-92] For example, the Louisiana Experiment Assessing Diabetes outcomes (LEAD) study since 2017 used EHR data to evaluate the impact of reimbursement for non-face-to-face chronic care management (NFFCCM) on healthcare utilization among patients with T2D.[93-97] The researchers also investigated the patient- specific factors associated with use of diabetes self-management education and support programs.[98]

The regulatory agencies including the U.S. Food and Drug Administration (FDA)[99] and the European Medicines Agency (EMA)[100] began to explore the potential of RWE from RWS by big cohorts or PCTs in supporting drug approvals and post-marketing surveillance. The 21st Century Cures Act, passed in the United States in 2016,[101] specifically highlighted the role of RWE in the regulatory process, marking a significant milestone in the formal acceptance of RWS. The Patient-Centered Outcomes Research Institute (PCORI) in the United States, which was established in 2010, also reflected a growing recognition of the value of real-world evidence in regulatory decisions and healthcare policy. PCORI has funded thousands of research projects, contributing significantly to the understanding of effective healthcare from a patient-centered perspective. It has supported studies across a wide range of health conditions and interventions, emphasizing the involvement of patients and other stakeholders in all its research processes from the real world.[102,103]

Challenges and regulatory and ethical considerations

Despite the progress, researchers still faced challenges related to the interoperability of EHR systems. The ability to share and integrate data across different platforms and healthcare institutions was still limited, posing hurdles to multi-site studies and collaborative research efforts. Addressing these challenges became a priority for advancing the use of EHRs in research.

As the use of EHR data in research expanded, so did concerns over patient privacy and data security. Increased attention to regulatory and ethical issues surrounding the use of health information came up. Policies and guidelines, such as the HIPAA in the United States and the General Data Protection Regulation (GDPR) in the European Union,[104-106] were updated to ensure the protection of patient information while facilitating research. Despite these concerns, all the efforts during this time underscore a shift towards a more holistic approach to evidence generation, aiming to improve patient outcomes and healthcare decision-making by bridging the gap between research such as clinical trials and real-world practice.

Meanwhile, researchers also encountered challenges during the use of EHRs on the common data models and data cleaning complexities. Although PCORI has made great efforts to this issue by establishing the PCORnet common data model[69,107,108] and the Observational Health Data Sciences and Informatics (OHDSI) consortium has developed the Observational Medical Outcomes

Partnership (OMOP) Common Data Model,[109-111] significant challenges remain in achieving interoperability between different EHR systems and healthcare databases. This inconsistency can hinder the seamless exchange and integration of health data for comprehensive analyses. Common data models rely on the assumption that data across systems can be standardized into a uniform format. However, variations in how data are recorded, missing information, and inconsistent use of terminologies across different EHR systems can lead to gaps and inconsistencies that affect data quality and utility. For the concerns of data cleaning and linkage, although several standardized coding systems (i.e. ICD, CPT, HCPCS, LOINC, SNOMED, etc.) were introduced in the EHRs, they still contain a vast amount of unstructured or semi-structured data, including free-text clinical notes. Cleaning such data to extract meaningful information may require other tools and algorithms (like SQL environment, Python), which can be resource-intensive and complex to develop and apply for researchers without computer science backgrounds. Patients’ data is often shared among different EHR systems including primary care and specialty registries. Linking these fragmented data sources to achieve a holistic view of a patient's health history is challenging but essential for effective research and care management.

Global health, precision medicine and artificial intelligence in 2020s

COVID-19 pandemic and real-time surveillance

The global nature of healthcare challenges, highlighted by the COVID-19 pandemic, increased the importance of international collaboration in medical research. While the healthcare providers were busy taking actions against the pandemic, they used retrospective EHR to learn lessons and analyze the trends and responses they had made.[112-118] The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first found in Wuhan, China in 2019. The World Health Organization (WHO) declared the outbreak a public health emergency of international concern (PHEIC) in early 2020[119] and ended the PHEIC declaration in 2023.[120] During the early stages of the COVID-19 pandemic in

2020, Chinese physician-scientists played a crucial role in understanding the disease by conducting retrospective reviews of medical records.[113,115-118] This process was instrumental in identifying the clinical characteristics and transmission patterns of COVID-19, at a time when the world was scrambling for information on how to deal with the novel coronavirus. Their work provided an early warning system and valuable experiences that guided global responses to the pandemic. The insights gathered from these early studies were foundational in recognizing COVID-19's symptoms, which range from mild flu-like symptoms to severe respiratory distress and multi-organ failure in critical cases. Importantly, the research highlighted the disease's high transmissibility, both from symptomatic and asymptomatic carriers, underlining the importance of widespread testing, contact tracing, and quarantine measures to control its spread.[121-126] This group of physician-scientists from Wuhan, China also contributed to the understanding of risk factors associated with severe outcomes, including age, pre-existing health conditions, and certain demographic factors. Their findings on the efficacy of various public health interventions, such as the use of face masks, social distancing, and the implementation of lockdowns, informed policies not just in China but around the world.[127,128] Furthermore, the early identification of the SARS-CoV-2 virus's genome sequence by researchers facilitated the rapid development of diagnostic tests and the initiation of vaccine development efforts.[129-131] This early sharing of data was pivotal in the global race to develop vaccines and therapeutics against COVID-19.

During the mid-pandemic period, EHR data became instrumental for comparative effectiveness research, aimed at evaluating and improving health outcomes across various populations and healthcare systems. This research spanned a broad spectrum of topics crucial to pandemic management, including the effectiveness of personal protective equipment,[132-134] the impact of social distancing,[135,136] the accuracy and efficiency of different testing strategies,[137,138] and the efficacy safety of anti-viral medications and vaccines[139-143] and health supplements.[144] Additionally, it explored the role of telemedicine in sustaining patient care and the importance of primary care services during the pandemic.[135,145-148] The use of EHR data allowed researchers to conduct comprehensive analyses, comparing the outcomes of different health interventions and policies in real-time. This approach provided valuable insights into which practices were most effective in controlling the spread of the virus, treating infected patients, and maintaining overall public health. For example, comparative effectiveness research helped identify which types of personal protective equipment were most effective in preventing virus transmission among healthcare workers and the public. Similarly, studies on social distancing and lockdown measures offered evidence-based guidance on how to balance public health concerns with economic and social implications. The investigation into testing strategies elucidated the strengths and weaknesses of various diagnostic approaches, leading to improvements in testing strategies and the quicker identification of COVID-19 cases. Research on anti-viral drugs, anti-inflammatory drugs and some health supplements informed treatment protocols, contributing to the development of therapeutic strategies that reduced the severity and duration of the disease. Telemedicine emerged as a vital tool for providing continuous care while minimizing the risk of virus transmission, demonstrating its potential to revolutionize healthcare delivery beyond the pandemic. Comparative effectiveness research during the COVID-19 pandemic underscored the importance of agile and evidence-based decision-making in public health emergencies. It highlighted the critical role of EHR data in enabling rapid, informed responses to an evolving crisis, guiding interventions that saved lives and mitigated the pandemic's impact.

The pandemic has accentuated the critical role of social determinants of health (SDOH) as well, revealing stark disparities in disease outcomes across different populations. EHRs have provided a rich dataset for analyzing these disparities, uncovering the disproportionate burden of COVID-19 on specific groups such as the elderly, individuals with chronic diseases, and those with autoimmune diseases. Studies leveraging EHR data have identified various social determinants that contribute to the increased vulnerability of these populations. Factors such as socioeconomic status, access to healthcare, living conditions, and occupational hazards have been linked to higher rates of infection, severe disease outcomes, and mortality.[149-155] For instance, individuals in lower socioeconomic brackets often face barriers to accessing healthcare services, leading to delayed or inadequate treatment for COVID-19. Similarly, patients with pre-existing chronic conditions such as diabetes, cardiovascular diseases, and respiratory diseases have been shown to experience more severe outcomes when infected with the virus. Furthermore, the research has highlighted the importance of addressing these social determinants in pandemic response strategies. Interventions targeting SDOH can help mitigate the adverse outcomes of COVID-19 among vulnerable populations. This includes improving access to healthcare, enhancing support for individuals with chronic diseases, ensuring the availability of protective measures for immunocompromised individuals, and addressing the broader socioeconomic and environmental factors that contribute to health disparities. The findings underscore the necessity of integrating an understanding of SDOH into public health policies and healthcare practices. By focusing on the root causes of health disparities, policymakers and healthcare providers can develop more effective strategies for preventing and managing COVID-19 and other diseases.

Even after the end of the PHEIC declaration, the use of EHR in studying long COVID continues to be of paramount importance. Research into the long-term impacts of COVID-19, particularly on mental health[156-159] and cognitive functions,[160-162] remains a critical area of public health inquiry. EHRs are expected to provide invaluable, real-time data that can link early exposure to COVID-19 with outcomes that may manifest decades later or even across a lifetime. As humanity progresses, EHRs stand as a vital resource, equipping us to face global crises and unpredictable challenges with resilience and informed action. This will underscore the disease's extensive reach, promising to shape future healthcare strategies and interventions aimed at mitigating the long-term consequences of any pandemic.

Precision medicine and genomics

Precision medicine represents a transformative approach to healthcare in the past 10 years, focusing on the customization of treatment based on an individual's genetic makeup, environment, and lifestyle.[163] EHRs played a pivotal role in the advancement of precision medicine, where treatments are tailored to the individual characteristics of each patient. The integration of genomics data with EHRs allows researchers to study the genetic bases of diseases and to personalize healthcare at an unprecedented level. However, integration is still facing several challenges and opportunities. While the routine clinical application of genomic data is still emerging, some EHR-connected biobanks and initiatives are actively addressing the challenges involved.

The UK Biobank (UKB) stands as a prominent figure in the realm of biomedical research, featuring an expansive database and research resource. It encompasses de-identified genetic, lifestyle, and health information, along with biological samples from half a million UK participants.[164] This rich data set is further augmented by linkage to the UK's EHRs, such as the Hospital Episode Statistics and the Patient Episode Databases.[165,166] The UKB's comprehensive dataset has been instrumental in propelling forward the fields of medicine and research, offering profound insights into the prevention, diagnosis, and treatment of numerous serious and life-threatening diseases, including cancer and cardiovascular diseases. The UK biobank has released a set of whole genome sequencing data. Since 2018, numerous studies were conducted using these data and mendelian randomization to find out the causality between genetic background the diseases. While the UKB serves as a notable instance of linking a study cohort with EHRs, it does not exemplify direct integration. Despite encompassing data from half a million individuals, the UKB faces potential selection bias.[167] This is attributed to the fact that the initiative dispatched over 9 million invitations across the nation, suggesting that the participants may not fully represent the broader population.

Like the approach of the UKB, the National Institutes of Health (NIH) in the United States initiated the All of Us (AoU) Research Program in 2018, aiming to enroll over a million individuals.[168] By January 1, 2024, the program had successfully registered over 760,000 participants, securing access to more than 539,000 samples for genomic sequencing and 420,000 EHRs. This extensive collection of data underscores the program's commitment to advancing personalized medicine by exploring the diversity of human biology, lifestyle, and environmental exposure, ultimately aiming to tailor healthcare to individual needs. Through its comprehensive data collection, AoU seeks to address critical gaps in medical research, particularly in areas underserved by existing studies, thereby fostering a deeper understanding of various health conditions and improving strategies for prevention, diagnosis, and treatment across the spectrum of both common diseases and rare diseases. However, it is still a good example connecting cohort with EHRs.

Other local-based or nationwide biobanks with linkage to EHRs or national registries include the Danish Biobank Register,[169] BioBank Japan,[170] China Kadoorie Biobank,[171] Kaiser Permanente Research Bank,[172] deCODE Genetics,[173] FinnGen biobank,[174] Vanderbilt University’s bioVU,[175] Michigan Genomics Initiative,[176] BioMe biobank,[177] the Estonian biobank[178] and the Norwegian Mother, Father and Child Cohort Study.[179] These initiatives vary in scope and scale but collectively contribute to the growing field of genomic research linked to EHRs, facilitating advances in personalized medicine and the understanding of genetic influences on various diseases.

The true sense of integrating genomic data into EHRs presents challenges such as diverse data structures, storage limitations, interpretation complexities, and financial constraints. The National Human Genome Research Institute (NHGRI) supports the Electronic Medical Records and

Genomics (eMERGE) network to address these issues by harmonizing data and developing guidelines for genomic data integration and usage.[180] Solutions are on the way, and it now has more than 10 clinical site partners and its network affiliates with major areas across the US. The eMERGE network is not only developing best practices for electronic phenotyping and biobanking consultation but also exploring EHRs for additional Genome-Wide Association Studies (GWAS) outcomes among genotyped individuals, leveraging the rich phenotypic data available.

Data analytics and artificial intelligence

The use of data analytics and artificial intelligence (AI) in analyzing EHR data has grown exponentially. Researchers were employing machine learning algorithms to identify patterns, predict outcomes, and generate insights into disease progression, treatment efficacy, and patient care optimization.[181,182] These technologies enabled the analysis of vast amounts of data in ways that were not previously possible.

Predictive analytics for high-risk patients' identification and their outcomes

One of the most significant applications of AI in healthcare is in identifying patients at high risk of developing specific conditions and predicting outcomes among patients who were already diagnosed with a health condition. By analyzing historical EHR data, including patient demographics, previous health conditions, treatment histories, and lifestyle factors, AI models can predict which patients are more likely to develop diseases such as diabetes, cardiovascular diseases, or chronic respiratory conditions, as well as the potential outcomes of various treatment options.[183-187] Early identification of these patients allows healthcare providers to implement preventative measures, tailor treatments to individual needs, and in doing so, significantly reduce the risk of severe outcomes or the need for hospitalization. This predictive capability enables doctors to choose the most effective treatment plans, thereby improving the quality of care and patient satisfaction. Moreover, it facilitates a more efficient allocation of healthcare resources by focusing efforts on interventions that are most likely to succeed.

In the context of infectious diseases, AI models are invaluable for tracking and forecasting the spread of diseases. By integrating EHR data with information from other sources, such as public health records and social media, AI algorithms can predict outbreaks, model the spread of infections, and inform public health interventions.[188,189] This was particularly evident during the COVID-19 pandemic, where AI played a pivotal role in predicting hospitalization rates, identifying potential hotspots, and guiding the allocation of medical resources.[190,191]

Personalized medications and clinical decision support systems

Leveraging EHR data, AI is facilitating personalized medicine by tailoring treatment plans to individual patient characteristics, genetic information, and historical health data. This approach helps in predicting how different patients will respond to various treatments, thereby improving treatment effectiveness and reducing side effects. While medications only serve one part of the disease management, AI integrated with EHR systems can provide clinicians with decision support by offering diagnostic suggestions, recommending treatment options, and alerting healthcare providers to potential adverse drug interactions or necessary screenings, thereby enhancing patient care quality.[192-196] AI tools also analyze EHR data to optimize hospital operations and predict perioperative complications. This can lead to improved patient satisfaction, and lower surgery related adverse events and lower healthcare costs.[197-201]

Among the AI strategies, natural language processing (NLP) technologies represent a pivotal advancement in the utilization of EHR data, transforming the landscape of healthcare data analytics and decision-making.[182] NLP enables the extraction of valuable information from unstructured text within EHRs, such as clinical observations, patient histories, and diagnostic notes, which traditionally have been difficult to analyze systematically due to their unstructured nature. This capability not only enhances the richness of data available for clinical decision-making but also significantly expands the potential for personalized patient care and advanced healthcare analytics.[202-205] One notable example of NLP's application in healthcare is the development of GatorTron, a large clinical language model trained on over 90 billion words from clinical notes, PubMed articles, and Wikipedia.[206-208] GatorTron significantly outperforms previous models in clinical NLP tasks like clinical concept extraction, medical relation extraction, semantic textual similarity, natural language inference, and medical question answering. This model showcases how scaling up the number of parameters and data size can lead to substantial improvements in performance across various NLP tasks, ultimately enhancing the extraction and interpretation of critical information from EMR data for better healthcare delivery and research.

Challenges in data quality, standardization, patient engagement, cost, data cleaning and global health disparities

Ensuring high-quality, standardized data entry into EHRs is challenging yet essential for effective healthcare delivery and research. Inconsistent data, incomplete records, and variation in data capture practices can compromise the reliability and usefulness of EHR data for clinical decision-making and research purposes. While patient portals and digital access to health records aim to empower patients, engaging patients effectively remains a challenge. Issues such as digital literacy, accessibility, and varying levels of interest in active health management can affect the extent to which patients utilize EHRs to participate in their care.

For many healthcare providers, especially smaller practices and those in low-resource settings, the cost of EHR implementation and ongoing maintenance is a significant barrier. Additionally, the process of transitioning from paper-based systems to EHRs, or switching between EHR systems, can be disruptive and resource-intensive. Global disparities in EHR adoption and utilization highlight the challenge of ensuring equitable access to the benefits of digital health records. Differences in infrastructure, funding, and healthcare policies contribute to varying levels of EHR integration and use worldwide. Integrating AI and advanced analytics into EHR systems presents both opportunities and challenges. While these technologies have the potential to transform healthcare delivery and research, they also raise questions about data accuracy, algorithmic bias, and the interpretability of AI-generated insights.

EHRs in medical research in the next decades

The next decades will likely see significant advancements in EHR capabilities, focusing on interoperability, precision medicine, AI and digital health technologies, the integration of social determinants of health, public health monitoring, and the enhancement of data analytic tools (Figure 4).

Enhanced interoperability and data sharing

Future EHR systems are likely to achieve higher levels of interoperability, enabling seamless data sharing across different healthcare systems, providers, and even countries. This will facilitate comprehensive patient care, collaborative research, and public health monitoring on a national or even a global scale. Regulations governing the use of EHRs and related technologies will evolve to keep pace with advancements, addressing ethical considerations, data ownership, and the use of digital health data in research and healthcare delivery. As the use of EHRs grows, the focus on protecting patient data will also be important. Advanced security technologies and privacy-preserving methods, such as blockchain and federated learning, may be employed to safeguard information while enabling its use for care and research.

As a good example, the CODE-EHR framework represents a crucial advancement, focusing on improving the design of studies that utilize structured electronic healthcare records.[209] This framework emphasizes the importance of verification, validation, and data privacy, along with addressing social mandates to undertake research. It proposes minimum standards to enhance study transparency and provides a roadmap toward more effective utilization of healthcare data for research. By enabling the embedding of controlled trials within real-world settings, such as registries or routine clinical practice, CODE-EHR aims to produce more generalizable results that can inform patient care, healthcare cost containment, and quality of life improvements.

Integration of genomic and other omics related precision medicine data

As genomic sequencing becomes more affordable and commonplace, EHRs are expected to integrate multi-omics information, supporting the advancement of precision medicine. This will allow healthcare providers to tailor treatments to individual patients based on their individualized profiles, improving outcomes and minimizing adverse reactions.[210]

The PennChart Genomics Initiative has demonstrated significant progress and potential in integrating genomic data into EHRs for optimizing patient care and facilitating medical research.[211,212] By creating a centralized document display for genetic results in the EHR, researchers and clinicians can improve patient care while addressing privacy concerns. This initiative has already led to the integration of thousands of genetic documents into the EHR, highlighting the potential for EHRs to support precision medicine and accelerate the discovery of novel genomic medicine applications. Future efforts aim to expand this integration and address challenges such as educational needs, infrastructure compatibility, and maintaining privacy and security protections.

The GUARDIAN study in the United States is a pioneering initiative planning to enroll 100,000 newborns for whole genome sequencing.[213] This program aims to explore the potential of genomic data in newborn screening, with the goal of enhancing early diagnosis and treatment in neonatal intensive care units (NICUs) and pediatric intensive care units. By identifying genomic markers early on, the program seeks to save lives and reduce hospital stays for undiagnosed disease patients, showcasing the transformative power of genomics in precision healthcare.

The Genomics England's program is another potential effort to integrate genetic data with EHR data, aiming to sequence 100,000 genomes from NHS patients with rare diseases and their families, as well as patients with cancer.[214] Launched to enhance our understanding of genetics in disease and to pioneer a UK genomic medicine service, the project's success has paved the way for further genomic research and integration into healthcare. This initiative highlights the potential of genomic data in advancing personalized medicine and improving treatment strategies.

Expansion of artificial intelligence and other digital health technologies

EHRs in the future will increasingly incorporate AI and machine learning algorithms to analyze health data in real-time, predicting patient risks (such as for chronic diseases or hospital readmissions) and suggesting personalized prevention and treatment plans. AI-driven models, utilizing big data from EHRs, outperform traditional methods in sensitivity, specificity, and other metrics. The implementation of these models into web and mobile applications could significantly aid clinical decision-making, emphasizing the need for effective strategies to integrate AI algorithms in clinical tools.

The future use of NLP in EHR is also expected to significantly enhance healthcare delivery and research. By harnessing NLP, healthcare professionals can continuously unlock valuable insights from growing amounts of unstructured data embedded in EHRs. This advancement will allow for more accurate patient stratification, personalized treatment plans, and improved predictive models for disease outcomes in the future. NLP technologies are set to automate the extraction and interpretation of clinical information, reducing manual data entry and analysis burdens. Additionally, real-time processing of patient data through NLP will facilitate more rapid clinical decision support, optimizing treatment approaches and patient care pathways. The integration of NLP with EHR systems promises a shift towards more data-driven, efficient, and patient-centered healthcare, highlighting its critical role in advancing medical research, enhancing disease surveillance, and ultimately improving patient outcomes.

In addition, EHRs will also become more integrated with other digital health technologies, such as wearable devices, telehealth platforms, and digital therapeutics.[215,216] Wearable devices, ranging from fitness trackers to advanced biosensors, have become increasingly sophisticated, capable of monitoring a wide array of health metrics such as heart rate, activity levels, sleep patterns, and blood glucose levels. Integrating these devices with EHRs can provide clinicians with a more comprehensive view of a patient's health status, extending beyond the snapshots captured during clinical visits. This continuous stream of real-time data can enhance preventive care strategies, enable early detection of potential health issues, and support personalized treatment plans. For patients with chronic conditions, this integration can facilitate closer monitoring and adjustments to treatment regimens based on near-real-time data, potentially improving outcomes and patient engagement in their care. Telehealth platforms have experienced exponential growth, a trend significantly accelerated by the COVID-19 pandemic. The integration of telehealth with EHRs ensures that virtual consultations are informed by the patient's medical history, current medications, and recent test results, allowing for more informed clinical decision-making.[217] This seamless flow of information can improve the efficiency and effectiveness of virtual care, making healthcare more accessible, especially for individuals in remote or underserved regions. Furthermore, integrating telehealth encounters into EHRs ensures that all aspects of a patient's care are documented in a single, comprehensive record, supporting continuity of care across different healthcare settings.

Digital therapeutics, which include software-driven evidence-based interventions, are an emerging field within healthcare.[218] These interventions, which can range from cognitive behavioral therapy apps for mental health to digital programs for chronic disease management, offer new avenues for treatment that are accessible and scalable. Integrating digital therapeutics with EHRs can enhance the personalization of care, enabling healthcare providers to track patients' engagement and progress with these interventions in parallel with traditional treatments. This integration can also facilitate the collection of outcomes data, supporting the evaluation of the effectiveness of digital therapeutics in real-world settings and informing future care decisions.

Incorporation of social determinants of health

Addressing SDOH is crucial for improving health outcomes and reducing health disparities. Future EHR systems may include more comprehensive data on patients' social, economic, and environmental conditions, which is currently lacking in most systems and platforms. This data integration will empower healthcare providers to address not just the clinical but also the contextual aspects of health, leading to more targeted interventions, improved health outcomes, and reduced healthcare disparities. The evolution of EHR systems to include comprehensive SDOH data will necessitate advancements in data collection, privacy protocols, and analytics. Collecting SDOH data in EHR in the future could involve leveraging technology to automate data capture from various sources, including patient self-reporting through digital platforms, integrating community health data, and utilizing NLP to extract SDOH information from clinical narratives as well.

Future use in public health and epidemiology

EHRs will continuously play a vital role in monitoring public health trends due to its performance during COVID-19 pandemic, managing outbreaks of infectious diseases, and conducting large-scale epidemiological studies in the future in case of other unpredictable pandemics. Real-time data analysis will enable quicker responses to public health emergencies and more effective preventive strategies. However, these potential opportunities will depend mainly on the enhanced interoperability and data sharing, as was mentioned previously.

Integration of data analytic tools with EHRs

Integrating data analytics tools with EHRs involves connecting the capabilities of data analysis software with the wealth of patient information stored in EHR systems. This integration can enhance healthcare delivery, improve patient outcomes, and facilitate healthcare research by leveraging advanced analytics on EHR data. A recent effort for an integrated online phenomics knowledgebase within the EHR data was the development of the Centralized Interactive Phenomics Resource (CIPHER) knowledgebase.[219,220] The CIPHER is a comprehensive, public-facing knowledgebase designed to streamline the development of clinical phenotypes, aiming at facilitating clinical and health services research. It also featured scalable metadata management, integrated tools and user workflows, and enabled complex searches through stored phenotype metadata adhering to the CIPHER standard. Phenotypes can be contributed via a webform that validates metadata, and the platform includes data visualization tools to improve user engagement and speed up phenotype development. Hopefully the CIPHER knowledgebase can expand the phenotype algorithm repository and the collaborations among users in the future.

Conclusions

The evolution of EHRs marks a significant milestone in healthcare's journey towards integrating technology and medicine. From early documentation practices to the sophisticated use of AI and big data analytics today, EHRs have become central to improving patient care, enhancing public health surveillance, and advancing medical research. As we look forward, the integration of social determinants of health, genomic data, and real-time analytics into EHRs promises to further personalize medicine, improve disease prevention strategies, and address health disparities. Collaborative efforts across borders, disciplines, and sectors will be crucial in realizing the full potential of EHRs in shaping a healthier future for all.

Conflict of interest

The authors declared no conflict of interests.

Author contributions

Y.S. and J.Y. did the search and wrote the manuscript. J.Z. and G.H. did the literature review and edited the manuscript. Y.S. and J.Z. are the guarantors of this work and, as such, have full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analyses. All authors read and approved the final manuscript.

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Figure legends

Figure 1. Search strategy and results by timeline.

Figure 2. PRISMA framework.

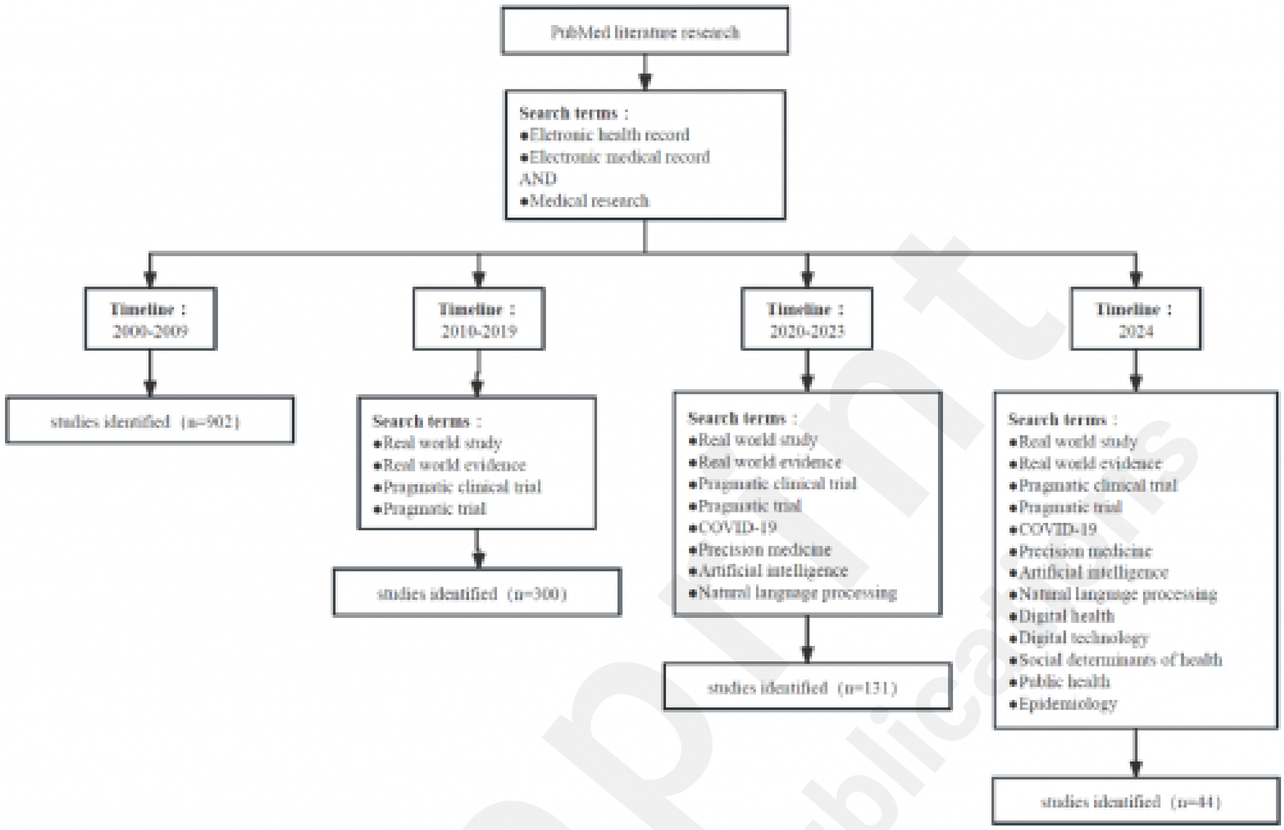
Figure 3. Key words frequency analysis. A. word cloud. B. Frequency of the key words.

Figure 4. Future landscape of electronic health records.

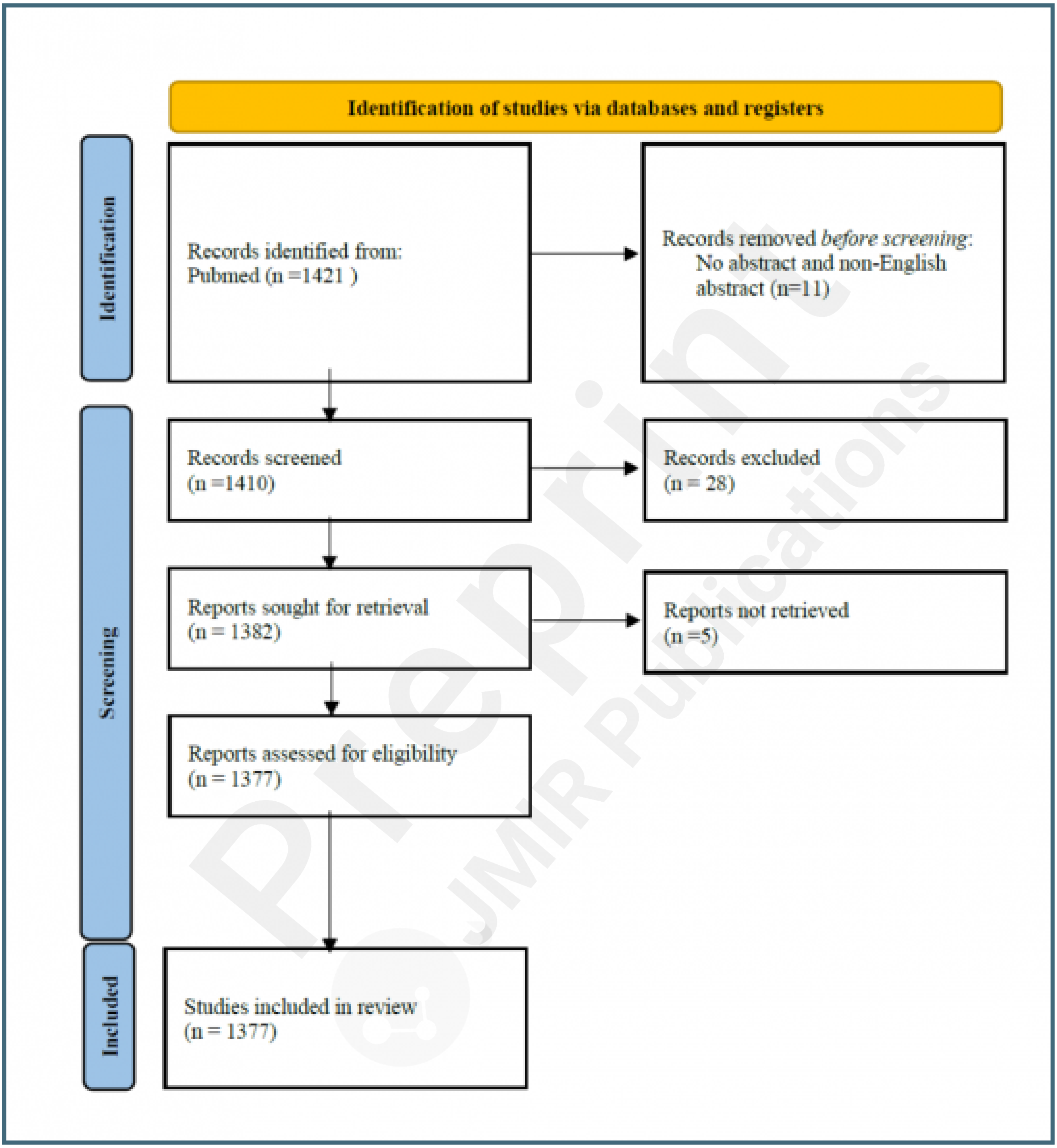
Supplementary Files

Figures

Search strategy and results by timeline.



PRISMA framework.



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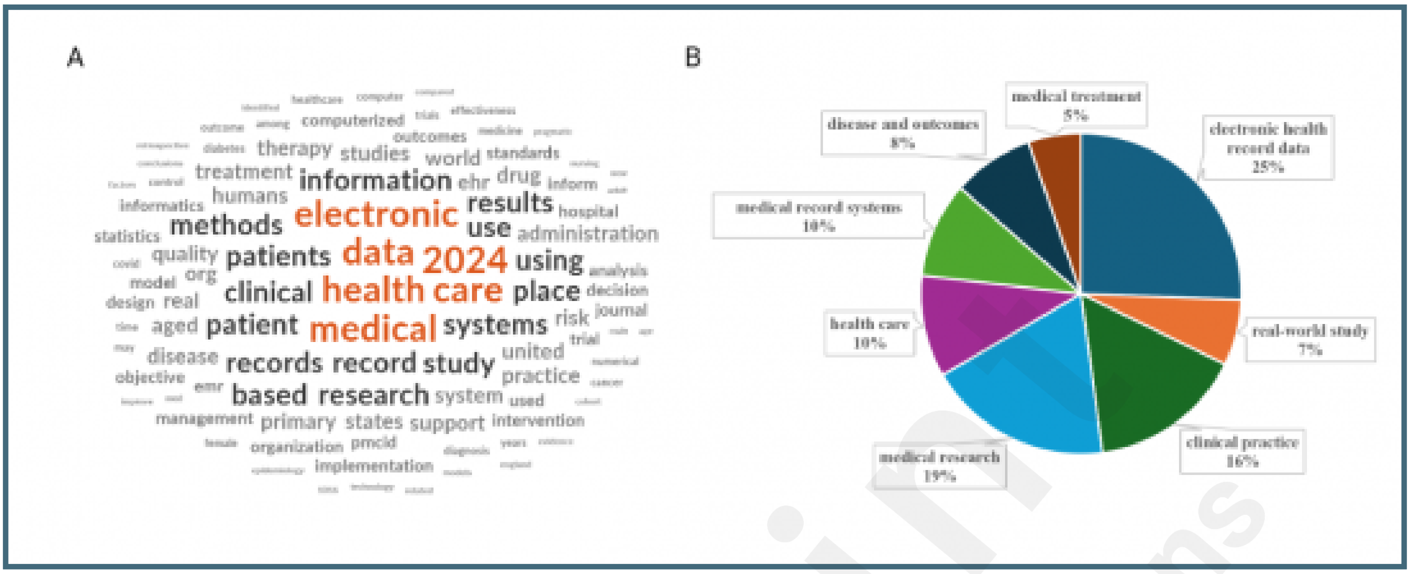

Future landscape of electronic health records.